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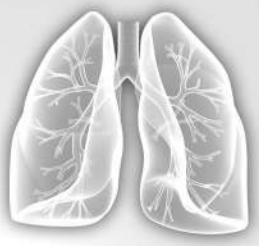

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RESPIRATORY CASE REPORTS

EVALI Case Report: A New Form of Self-Destruction

EVALI Olgu Sunumu: Kendini Yok Etmenin Yeni Yolu

Fidan Layijova[1], Alper GÜNDÜZ[2], Nilsu Buket Ercan[2], Bilge Kaan Er[2], Elif Kupeli[1]

Abstract

E-cigarette or vaping product use-associated lung injury (EVALI) is an acute or subacute pulmonary condition that was recognized in 2019. Its incidence has risen in parallel with the rise in e-cigarette use among adolescents and young adults. EVALI remains a diagnosis of exclusion in patients with a history of vaping. No standardized treatment protocol exists, and most cases are managed with empirical antibiotics and systemic corticosteroids. Smoking cessation counseling is a crucial component of both treatment and long-term follow-up. Here, we present the case of a 63-year-old woman with a 4-year history of e-cigarette use who was admitted with symptoms of dyspnea, cough, and sputum production and was subsequently diagnosed with EVALI.

Keywords: *Acute lung injury, e-cigarette, EVALI.*

Öz

Elektronik sigara veya vaping ilişkili akciğer hasarı (EVALI), ilk olarak 2019 yılında tanımlanan, akut veya subakut seyirli bir akciğer hastalığıdır. Görülme sıklığı, özellikle ergenler ve genç erişkinler arasında e-sigara kullanımının artması ile birlikte paralel olarak yükselmiştir. Vaping öyküsü olan bireylerde, EVALI halen bir dışlama tanısıdır. Standart bir tedavi protokolü bulunmamakla birlikte, olguların çoğu ampirik antibiyotikler ve sistemik kortikosteroidler ile tedavi edilmektedir. Sigara bırakma danışmanlığı, hem tedavi sürecinin hem de uzun dönem izlemin temel bir bileşenidir. Bu yazıda, dört yıllık e-sigara kullanım öyküsü bulunan, nefes darlığı, öksürük ve balgam yakınmaları ile başvuran ve EVALI tanısı alan 63 yaşındaki bir kadın hastayı sunmaktayız.

Anahtar Kelimeler: *Akut akciğer hasarı, e-sigara, EVALI.*

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Electronic cigarettes (vaping devices) were first patented by a pharmacist in China in 2003, and have since gained widespread global popularity. The trend has been particularly prominent among adolescents, and various devices, brands, and flavored products have been introduced to the market to promote usage. The aerosols generated by e-cigarette devices are known to contain numerous toxic substances, including volatile organic compounds, heavy metals, and ultrafine particles (1).

Although e-cigarettes contain no tar or some of the other carcinogens found in combustible tobacco smoke, several mechanisms of potential lung injury have been proposed. These include thermal injury from heated vapor; lipid accumulation in the lungs due to oil-based additives; allergic reactions such as eosinophilic pneumonia and hypersensitivity pneumonitis; and direct toxic effects associated with the chemical components in the vapor (2).

These pathophysiological mechanisms have been implicated in the development of a clinical syndrome known as e-cigarette or vaping-associated lung injury (EVALI). Formally recognized in 2019, EVALI is defined as an acute or subacute respiratory illness occurring in individuals with a history of e-cigarette or vaping product use within the previous 90 days (3). Diagnosis is based on a recent vaping history, and the presence of pulmonary infiltrates on chest radiography or ground-glass opacities on computed tomography (CT), while other potential causes such as infectious, cardiac, or connective tissue diseases must be excluded (3-7).

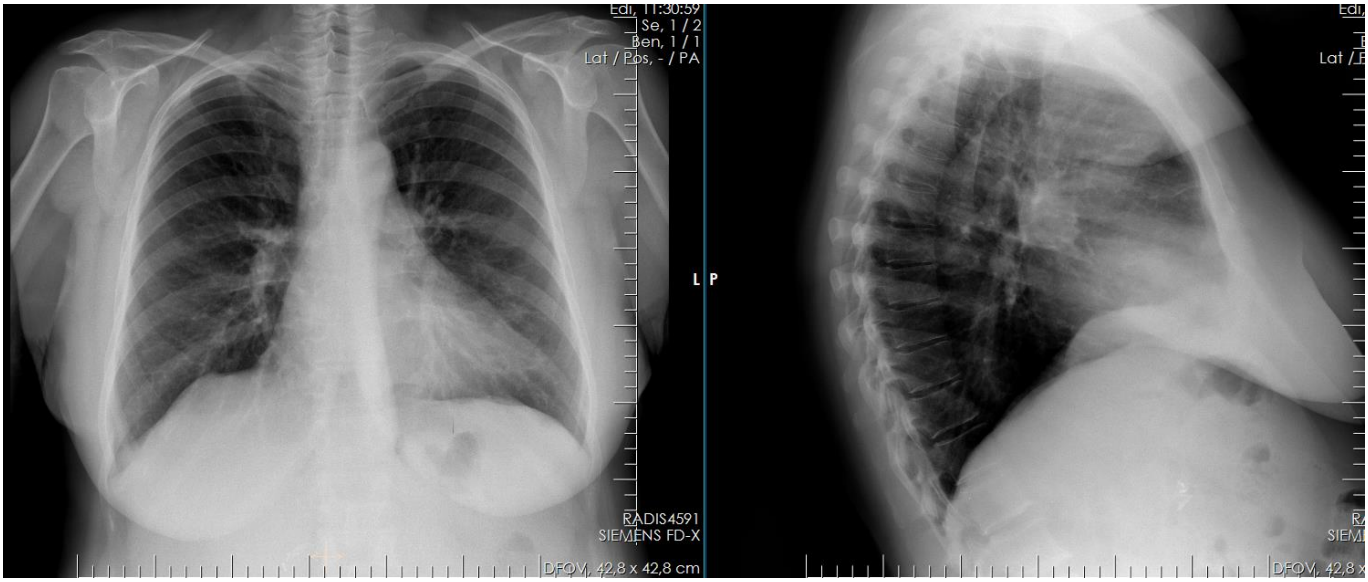
In light of this information, we present the case of a patient with a 4-year history of e-cigarette use who was diagnosed with EVALI.

Written informed consent was obtained for publication of this report.

CASE

A 63-year-old female retired bank employee with a 4-year history of e-cigarette use presented to our clinic with complaints of intermittent dyspnea, wheezing, productive cough, and sputum. Her past medical history included gastroesophageal reflux disease (GERD), rheumatoid arthritis (RA), and type-2 diabetes mellitus (T2DM). The patient had prior history of conventional cigarette smoking and had been using e-cigarettes 4–5 times per day for the past 4 years. On physical examination, bilateral rhonchi and prolonged expiratory phase were noted on auscultation, while other findings were unremarkable.

A chest X-ray and blood work were performed, and a pulmonary function test (PFT) was conducted to investigate the history of breathlessness and wheezing, monthly attacks over the past year, and current presentation with dyspnea, cough, and sputum production. An evaluation of the triggers of the asthma attacks revealed no association with environmental factors, exposures, or seasonal variability, and no asthma-related family history was reported. Chest radiograph appeared normal (Figure 1).



Pre-bronchodilator PFT results were as follows: FEV_1/FVC, 59%; FEV_1, 46% (0.97 L); and FVC, 66% (1.65 L), while post-bronchodilator results were FEV_1/FVC, 52%; FEV_1, 53% (1.12 L); and FVC, 86% (2.17 L). The patient was diagnosed with asthma based on her PFT results, and started on a combination of long-acting beta-agonist and inhaled corticosteroid therapy, along with a leukotriene receptor antagonist (Figure 2).

Standart PFT

		Pred	Best	%...	Post	%...	%Chg...	Z-Score	Z-Score
FVC	L	2.52	1.65	66	2.17	86	31	-0.81	
FEV 1	L	2.11	0.97	46	1.12	53	15	-2.60	
FEV 1 % FVC	%	83.69	58.94	70	51.51	62	-13	-1.55	
MMEF 75/25	L/s	2.77	0.20	7	0.27	10	34	-2.94	
MEF 50	L/s	3.48	0.32	9	0.38	11	19	-2.82	
PEF	L/s	5.75	4.03	70	3.46	60	-14	-2.54	
VBEex	L		0.05		0.05		17		
VBEin	L		0.08		0.09		17		
FET	sec		7.93		13.63		72		
MVV	L/min	85.84							
MIP	kPa	5.35							
MEP	kPa	6.69							
Level date			25.04.24		25.04.24				
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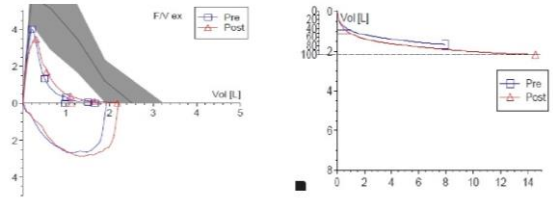

Figure 2: Pulmonary function test revealing an obstructive pattern compatible with asthma

The patient returned the following day with worsening dyspnea and was admitted to the hospital with a presumptive diagnosis of asthma exacerbation. Bilateral rhonchi persisted on auscultation. Oxygen saturation on room air was 89%, requiring 2 L/min of supplemental oxygen via nasal cannula. Her body temperature was 36.7°C. Laboratory results revealed mild eosinophilia (1,190/μL; normal: 0–500/μL) and a slightly elevated C-reactive protein (12.6 mg/L; normal: 0–5 mg/L). Serum lactate dehydrogenase (LDH) was mildly increased. The respiratory pathogen PCR panel, including Mycoplasma, Legionella, and CMV-PCR, was negative.

Thoracic CT demonstrated patchy ground-glass opacities with a crazy paving pattern in the apical segment of the right upper lobe (Figure 3). To aid in the differential diagnosis, bronchoscopy was performed, and analysis of the bronchoalveolar lavage (BAL) fluid revealed no microbial growth. Cytological examination of BAL fluid revealed a predominance of macrophages, and neutrophils and lymphocytes present to a lesser extent. The eosinophil count in BAL fluid was 2.94%. The patient was diagnosed with EVALI based on her clinical, radiological, and laboratory findings, and was treated with methylprednisolone 60 mg, inhaled bronchodilators, and supplemental oxygen. After 3 days of hospitalization, her symptoms improved, and she was discharged with inhaler and oral prednisolone 40 mg daily, which was gradually tapered. At a 10-day follow-up, clinical improvement was sustained, and so the corticosteroid regimen was extended with maintenance therapy continued at 4 mg daily. High-resolution CT (HRCT) 6 weeks later revealed complete resolution of the previously noted ground-glass opacities (Figure 4).

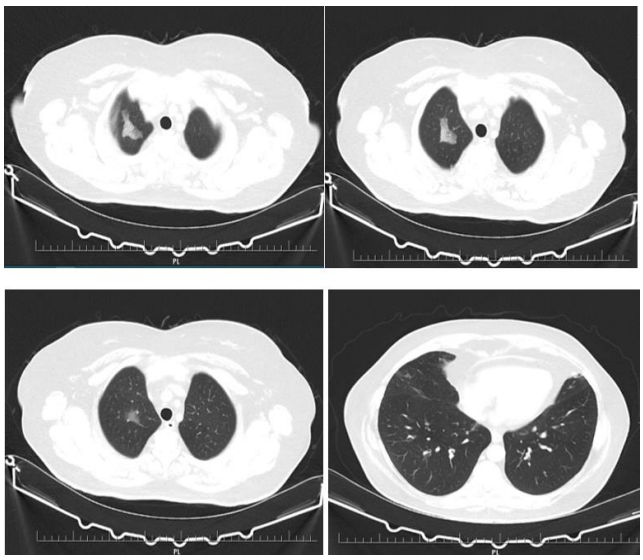

Figure 3: Thoracic CT on admission: Patchy ground-glass opacities in a crazy-paving pattern localized to the apical segment of the right upper lobe. Findings were suggestive of organizing pneumonia, consistent with EVALI. No significant lymphadenopathy or pleural effusion were noted

DISCUSSION

EVALI was first formally recognized in 2019. Some 80% of cases are under 35 years of age and 66% are male (4). Asthma is a known comorbidity in approximately 22% of cases (5). Mortality risk is elevated in those over 35 years of age and in patients with underlying asthma, cardiovascular disease, or psychiatric conditions (6). Our patient, an elderly woman with previous history of tobacco smoking, had been using e-cigarettes for 4 years and was newly diagnosed with asthma. She presented with respiratory symptoms typical of EVALI, including dyspnea and cough, without gastrointestinal involvement – commonly reported symptoms include nausea (66%), vomiting (61%), diarrhea (44%), and abdominal pain (34%) (5).

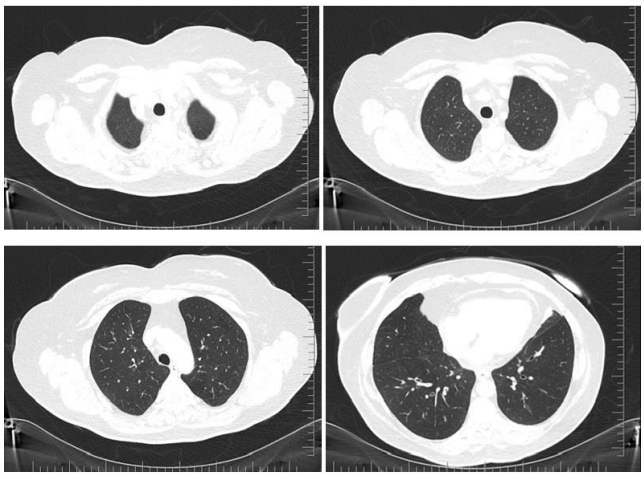

Figure 4: Follow-up HRCT: Complete resolution of prior ground-glass opacities. No signs of pneumonic infiltration or mass lesions. Minimal pericardial effusion persisted, and previously noted nonspecific nodules remained stable.

Initial workup should include a complete blood count, basic metabolic panel, and liver function tests, particularly in patients with gastrointestinal symptoms. Community-

Acquired Pneumonia (CAP) is a more prevalent condition and should be excluded, along with acute eosinophilic pneumonia. Thoracic CT often reveals diffuse, bilateral ground-glass opacities with subpleural sparing. Bronchoscopy is recommended to exclude alternative diagnoses (7). In our patient, potential pathogens including Mycoplasma and Legionella were investigated using a respiratory PCR panel and blood CMV-PCR, all of which were negative. Furthermore, cultures of BAL fluid obtained via bronchoscopy showed no microbial growth, and the eosinophil count was not at a level considered significant for eosinophilic pneumonia. Unilateral ground-glass opacities with a crazy-paving pattern were observed on chest CT, which is an atypical finding with the predominantly bilateral involvement described in EVALI. A previously published case report described a young adult with a 2-year history of e-cigarette use who also exhibited unilateral pulmonary involvement on thoracic CT (8). These observations suggest that, although uncommon, EVALI should be included in the differential diagnosis of patients with a history of vaping who present with unilateral lung disease.

There is no established standard of care for EVALI. Empirical antibiotics and systemic corticosteroids are commonly used, although there are variations in the reported doses and durations. Smoking cessation and behavioral counseling are essential to prevent recurrence (9). While most patients respond well to treatment, some may progress to respiratory failure, requiring advanced interventions such as extracorporeal membrane oxygenation (ECMO) or even lung transplantation (10).

Our patient was successfully managed with methylprednisolone, inhaled bronchodilators, and supplemental oxygen, and was referred to a smoking cessation program upon discharge.

CONCLUSION

The increasing prevalence of EVALI, driven by the increasing use of e-cigarette products, underscores the importance of clinical vigilance. Although EVALI is predominantly reported in younger people, older adults are also at risk, and diagnosis may be delayed in this cohort due to atypical presentations, comorbidities, and underreported vaping history. Clinicians should consider EVALI in the differential diagnosis of patients presenting with acute respiratory symptoms and imaging findings of bilateral ground-glass opacities, regardless of age. Early recognition and intervention are particularly important in older adults due to the slower recovery and higher complication rates. Smoking cessation support remains a cornerstone of both treatment and prevention.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - F.L., A.G., N.B.E., B.K.E., E.K.; Planning and Design - F.L., A.G., N.B.E., B.K.E., E.K.; Supervision - F.L., A.G., N.B.E., B.K.E., E.K.; Funding -; Materials -; Data Collection and/or Processing -; Analysis and/or Interpretation -; Literature Review - F.L., A.G., N.B.E., B.K.E.; Writing - F.L.; Critical Review - F.L., A.G., N.B.E., B.K.E., E.K.

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RESPIRATORY CASE REPORTS

Massive Hemoptysis in Bronchial Dieulafoy's Disease: Suspect Early

Bronşiyal Dieulafoy Hastalığına Bağlı Masif Hemoptizi: Erken Şüphelenin

Shengquan Wei, Huixia Wang, Tiantian Lv, Gen Li, Ruzhen Jia

Abstract

Bronchial Dieulafoy's disease (BDD) is a rare vascular anomaly in which an enlarged, dysplastic submucosal bronchial artery can rupture through focally attenuated or even intact epithelium, causing life-threatening hemoptysis. A 65-year-old lifelong non-smoking female presented with massive hemoptysis. Bronchoscopy revealed a 5-mm pulsatile polyp in the basal segment of the left lower lobe; a bronchoscopic biopsy precipitated torrential bleeding that was temporarily controlled with vasoconstrictors. Selective arteriography demonstrated a tortuous bronchial artery with a 5-mm saccular ectasia and rapid arteriovenous shunting. Super-selective embolization achieved immediate homeostasis; however, a durable cure required subsequent lobectomy. BDD should be considered in cases presenting with cryptogenic massive hemoptysis. Endobronchial biopsy is contraindicated, and treatment requires either embolization or surgery.

Keywords: *Bronchial Dieulafoy's disease, massive haemoptysis, bronchial artery embolization, endobronchial vascular anomaly.*

Öz

Bronşiyal Dieulafoy hastalığı (BDH), anormal genişlemiş ve displastik bir submukozal bronşiyal arterin, lokal olarak incelmiş veya sağlam epitelden yırtılarak yaşamı tehdit eden hemoptizi oluşturduğu nadir bir vasküler anomalidir. Sigara içmeyen 65 yaşındaki bir kadın, masif hemoptizi ile başvurdu. Bronkoskopide sol alt lob bazal segmentinde 5 mm'lik pulsatil bir polip görüldü; kazara yapılan biyopsi, vazokonstriktörler ile geçici olarak durdurulan şiddetli bir kanamaya yol açtı. Selektif arteriyografide, 5 mm'lik sakküler ektazi ve hızlı arteriyovenöz şant içeren tortuöz bir bronşiyal arter saptandı. Süper-selektif embolizasyon hemostazı sağladı; ancak kalıcı tedavi için sonrasında lobektomi gerekli oldu. Kriptojenik masif hemoptizide BDH akla getirilmelidir. Endobronşiyal biyopsi kontrendikedir ve tedavi embolizasyon veya cerrahidir.

Anahtar Kelimeler: *Bronşiyal Dieulafoy hastalığı, massif hemoptizi, bronşiyal arter embolizasyonu, endobronşiyal vasküler anomali.*

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Dieulafoy's disease was first described in the gastrointestinal tract as a submucosal arteriolar malformation prone to catastrophic bleeding (1). Its bronchial counterpart is rare and typically affects middle-aged or older adults, with a strong predilection for heavy smokers (2). Patients typically present with recurrent or massive hemoptysis, despite the absence of underlying parenchymal disease. Endobronchial visualization may reveal small, pulsatile polyps, although such findings are nonspecific, and biopsy is hazardous. On histopathology, an abnormally large, dysplastic bronchial artery is revealed coursing immediately beneath the mucosa, occasionally protruding through focal epithelial attenuation. Acute hemorrhage is controlled by embolization and surgical lobectomy prevents recurrence (3).

CASE

A 65-year-old, lifelong non-smoking female with hypertension and a remote lacunar stroke was referred for scant hemoptysis.

Bronchoscopy revealed a 5-mm, sessile, pulsatile polyp at the orifice of the basal segment of the left lower lobe with arborizing surface vessels but no surrounding inflammation (Figure 1A). A hypervascular surface was observed on narrow-band imaging (Figure 1B). Despite the necessary caution, a second biopsy pass triggered immediate arterial spurting that rapidly filled the bronchial lumen. Bleeding was controlled by left lateral positioning, suction, topical epinephrine (1:10 000, 10 mL), intravenous emocoagulase (6 U), carbazochrome sodium sulfonate (80 mg), and vasopressin (12 U). Histopathology revealed only chronic inflammatory changes. The patient was discharged on day 5 with a provisional diagnosis of "inflammatory polyp".

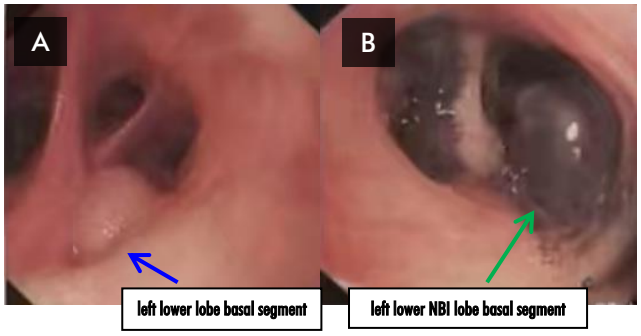

Figure 1: Bronchoscopy revealed a 5-mm, sessile, pulsatile polyp at the orifice of the left lower-lobe basal segment with arborizing surface vessels but no surrounding inflammation (A), Narrow-band imaging highlighted a hypervascular surface (B)

Pathology: The submitted mucosal tissue from a left lower-lobe pulmonary nodular elevation was lined with ciliated columnar epithelium, with chronic inflammatory cell infiltration in the stroma that was morphologically consistent with chronic inflammatory changes (Figure 2).

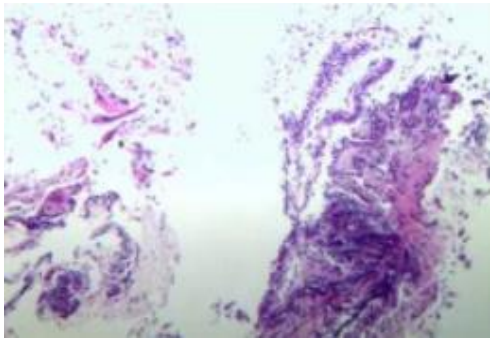

Figure 2: The submitted mucosal tissue is lined with ciliated columnar epithelium, with chronic inflammatory cell infiltration in the stroma, which is morphologically consistent with chronic inflammatory changes (H&E X40) .

The patient re-presented 8 days later with 600 mL of fresh hemoptysis and dyspnea (Figure 3A). Emergency contrast-enhanced CT demonstrated focal ground-glass opacities and a dilated (4 mm) left bronchial artery. Vital signs were stable and oxygen saturation was 87% on room air, improving to 97% on 3 L min^{-1} of oxygen.

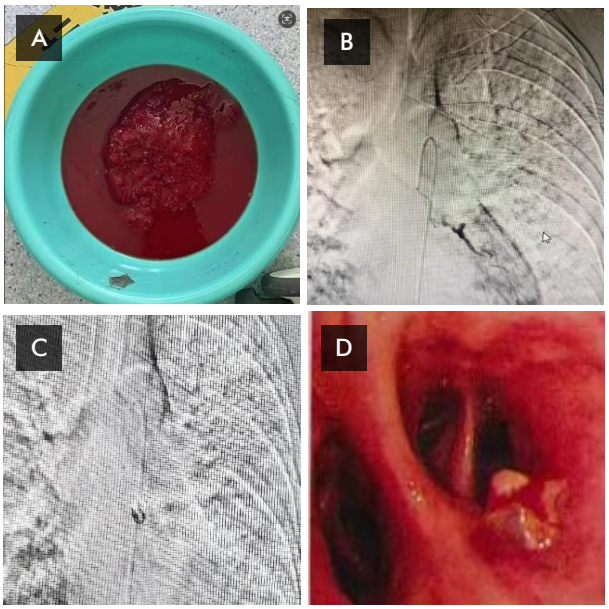

Figure 3: Fresh hemoptysis (A), Digital-subtraction angiography via right femoral access confirmed a single, markedly tortuous left bronchial artery with a 5-mm saccular aneurysm angiographic hallmark of BDD (B), Completion angiography demonstrated complete occlusion without non-target embolization (C), Follow-up bronchoscopy evacuated residual clots and revealed a ruptured, crater-like , non-bleeding polyp (D)

Digital subtraction angiography via right femoral access confirmed a single, markedly tortuous left bronchial artery with a 5-mm saccular aneurysm – an angiographic hallmark of BDD (Figure 3B). A microcatheter was advanced coaxially, and distal embolization was performed using 500–710 μm gelatin-sponge particles until the parenchymal blush ceased. The proximal artery was then se-

cured with three micro-coils (two 3/2 mm, one 5/2 mm). Completion angiography demonstrated complete occlusion without non-target embolization (Figure 3C). Hemoptysis resolved within 2 hours.

Follow-up bronchoscopy 2 days later evacuated residual clots and revealed a ruptured, crater-like, non-bleeding polyp (Figure 3D). The patient was discharged on day 10 and remains hemorrhage-free at 6 months.

DISCUSSION

Our pathology revealed only chronic mucosal inflammation overlying a pulsatile nodule, maybe fails to reach the submucosal Dieulafoy vessel. This finding reinforces the consensus in the literature that any endobronchial lesion exhibiting pulsation or focal hypervascularity should be regarded as a vascular anomaly until proven otherwise, and that biopsy is contraindicated. It should be immediate angiographic evaluation followed by super-selective embolization. This case highlights three key factors: First, endobronchial pulsatile lesions mandate avoidance of biopsy, as even minimal trauma can precipitate exsanguination (4-6). Second, embolization effectively arrests acute bleeding, although recurrence is common. In a retrospective surgical series only two out of seven patients remained hemostatic after embolization (7). Third, although heavy smoking is a recognized risk factor, sporadic cases have been recorded in non-smokers, as illustrated here, emphasizing the need for broad clinical suspicion (7-10). Surgical resection provides definitive therapy and allows precise pathological confirmation.

CONCLUSION

BDD should be suspected in any patient presenting with massive or recurrent cryptogenic hemoptysis. Endobronchial pulsatile lesions require urgent angiographic evaluation, as biopsy is contraindicated. Embolization serves as a valuable bridge to definitive surgical resection.

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CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.W., H.W., T.L., G.L., R.J.; Planning and Design - S.W., H.W., T.L., G.L., R.J.; Supervision - S.W., H.W., T.L., G.L., R.J.; Funding - T.L., G.L.; Materials - T.L.; Data Collection and/or Processing - G.L.; Analysis and/or Interpretation - S.W., G.L; Literature Review - G.L; Writing - S.W.; Critical Review - R.J.

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Chemotherapy-Induced Lung Disease: A Case Series

Kemoterapötikler ile İlişkili Akciğer Hasarı: Olgu Serisi

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Abstract

Chemotherapy-induced lung disease (CILD) is a serious complication that can negatively impact quality of life. It usually presents with inflammation and interstitial fibrosis, accompanied by symptoms ranging from mild dyspnea and cough to severe respiratory failure. Diagnosis is challenging, as it is often confused with infections or other interstitial lung diseases, as bronchoalveolar lavage results are usually nonspecific. We retrospectively evaluated eight CILD cases that were treated in our clinic between 2023 and 2024. Most patients had pulmonary symptoms, and thoracic CT scans often showed bilateral ground-glass opacities. Most patients improved clinically and radiologically after chemotherapy was halted and methylprednisolone treatment initiated, although some did not survive, especially those with additional comorbidities. Timely diagnosis and management are crucial in reducing morbidity and mortality in affected patients. This case series aims to raise awareness about CILD and to emphasize the importance of a multidisciplinary approach to avoid misdiagnosis and unnecessary treatment.

Keywords: *Chemotherapy-induced lung disease (CILD), Drug-induced lung injury, Interstitial lung disease, Chemotherapy complications.*

Öz

Kemoterapiye bağlı akciğer hastalığı (KBAH), yaşam kalitesini ciddi şekilde etkileyebilen önemli bir komplikasyondur. Genellikle inflamasyon ve interstisyel fibrozis ile ortaya çıkar; öksürük ve nefes darlığı gibi hafif semptomlardan ciddi solunum yetmezliğine kadar geniş bir yelpazede bulgular verir. Tanısı zordur ve sıklıkla enfeksiyonlar veya diğer interstisyel akciğer hastalıkları ile karıştırılır; bronkoalveoler lavaj sonuçları çoğunlukla özgül değildir. Kliniğimizde 2023-2024 yılları arasında tanı almış sekiz KBAH olgusunu retrospektif olarak değerlendirdik. Hastaların çoğu solunumsal şikayetler ile başvurdu ve toraks BT'de en sık iki taraflı buzlu cam opasiteleri izlendi. Kemoterapinin kesilmesi ve metilprednizolon tedavisine başlanması ile çoğu hasta klinik ve radyolojik olarak iyileşti. Ancak ek hastalıkları olan bazı hastalarda mortalite gelişti. Erken tanı ve uygun tedavi, bu hastalarda morbidite ve mortalitenin azaltılmasında kritik öneme sahiptir. Bu olgu serisi, KBAH farkındalığını artırmayı ve multidisipliner yaklaşımın önemini vurgulamayı amaçlamaktadır.

Anahtar Kelimeler: *Kemoterapiye bağlı akciğer hastalığı, İlaç ilişkili akciğer toksisitesi, Pulmoner fibrozis, CILD.*

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Chemotherapy-related lung involvement is a serious complication observed during treatment and can significantly impact the quality of life of patients undergoing therapy. The incidence rates reported in different studies are in the 0.1–15% range (1,2). The pulmonary effects of these medications vary depending on several factors, including dosage, duration of treatment, and the immune status of the patient. Chemotherapy-induced lung disease (CILD) typically presents with signs of inflammation and interstitial fibrosis within the lung tissue (3).

Clinically, patients may exhibit a broad spectrum of symptoms, ranging from nonspecific complaints such as cough and shortness of breath, to severe respiratory failure in advanced cases. Diagnosing CILD is often challenging due to the overlap of symptoms with other pulmonary conditions, making multidisciplinary differential diagnosis essential.

Between 2023 and 2024, eight cases with chemotherapeutic drug-induced lung disease were diagnosed, treated, and followed up following multidisciplinary council review in the pulmonary clinic of our tertiary care center. A retrospective evaluation of these cases is presented to contribute to the existing literature and to raise awareness about this important and potentially life-threatening complication. Early recognition and appropriate management of chemotherapy-related lung injury are crucial to improving patient outcomes and minimizing long-term pulmonary damage.

CASE

The diagnostic processes of these patients began either due to the presence of symptoms prompting further investigation, or based on an assessment of thoracic CT scans performed for the evaluation of treatment response after chemotherapy. After a CILD diagnosis was made, chemotherapy was discontinued in all patients.

Case 1: A 70-year-old female nonsmoker with a history of diabetes was diagnosed with metastatic invasive breast carcinoma. The patient underwent chemotherapy with letrozole and ribociclib for 5 months, and reported no symptoms. Chest CT revealed bilateral ground-glass opacities (Figure 1A). Bronchoscopy was performed, and *Stenotrophomonas maltophilia* was identified in the bronchoalveolar lavage culture. Antibiotic therapy was subsequently initiated. The patient was started on methylprednisolone at a dose of 0.5 mg/kg, which was gradually tapered, resulting in clinical and radiological improvement. Radiological improvement was observed after 3 months of treatment (Figure 1B).

Case 2: A 68-year-old female nonsmoker with no comorbidities presented with dyspnea. She was diagnosed with adenocarcinoma of the pancreatic head and underwent chemotherapy with gemcitabine for 13 months. Chest CT revealed bilateral ground-glass opacities (Figure 1C). Shortly after the discontinuation of chemotherapy, a radiological regression in the ground-glass opacities was observed (Figure 1D). The patient failed to respond to steroid therapy and subsequently died due to sepsis.

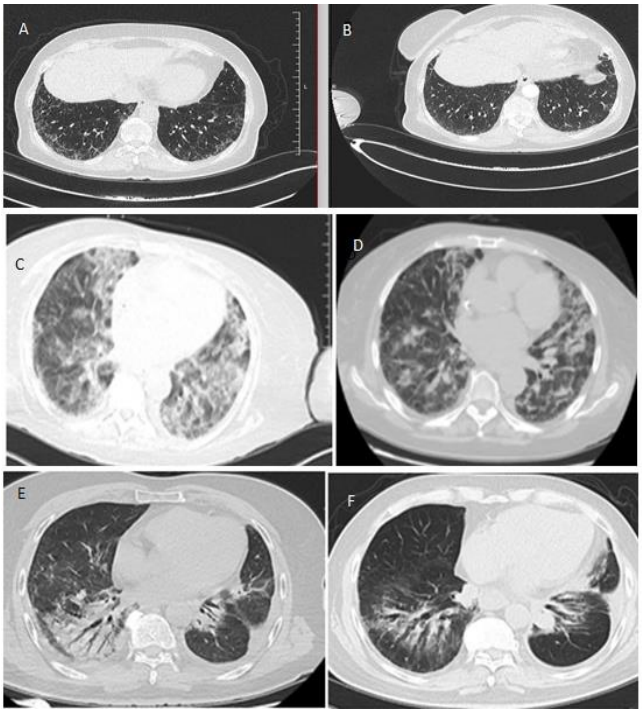

Figure 1: Diagnostic and follow-up thoracic CT slices of cases 1, 2, and 3. (A) Case 1 Thoracic CT at diagnosis, (B) Case 1 Thoracic CT one year after treatment, (C) Case 2 Thoracic CT at diagnosis, (D) Case 2 Thoracic CT one month after treatment, (E) Case 3 Thoracic CT at diagnosis. (F) Case 3 Thoracic CT three months after treatment.

Case 3: A 61-year-old male nonsmoker with diabetes presented with cough and sputum production. His primary malignancy was rectal adenocarcinoma for which he was treated with pembrolizumab for 4 months. Physical examination revealed fine crackles as the predominant auscultatory finding. Chest CT revealed bilateral ground-glass opacities with consolidation and air bronchogram (Figure 1E). The patient had a concurrent diagnosis of uncontrolled diabetes mellitus, necessitating inpatient steroid treatment with gradual tapering before discharge. While hospitalized, a thoracic CT performed 1 month after the discontinuation of chemotherapy showed marked regression in the air bronchograms (Figure 1F). The patient developed empyema during follow-up requiring tube thoracostomy, and later succumbed to sepsis.

Case 4: A 65-year-old male with a 50 pack-year smoking history and chronic obstructive pulmonary disease presented with dyspnea, and was subsequently diagnosed with metastatic non-small cell lung cancer. He received

leuprorelin and nivolumab for 2 years. Physical examination revealed rales in both basal areas, while chest CT showed bilateral ground-glass opacities (Figure 2A). The patient was started on methylprednisolone at a dose of 0.5 mg/kg, which was gradually tapered, resulting in clinical and radiological improvement. Radiological response was observed in follow-up imaging performed after 3 months of treatment (Figure 2B).

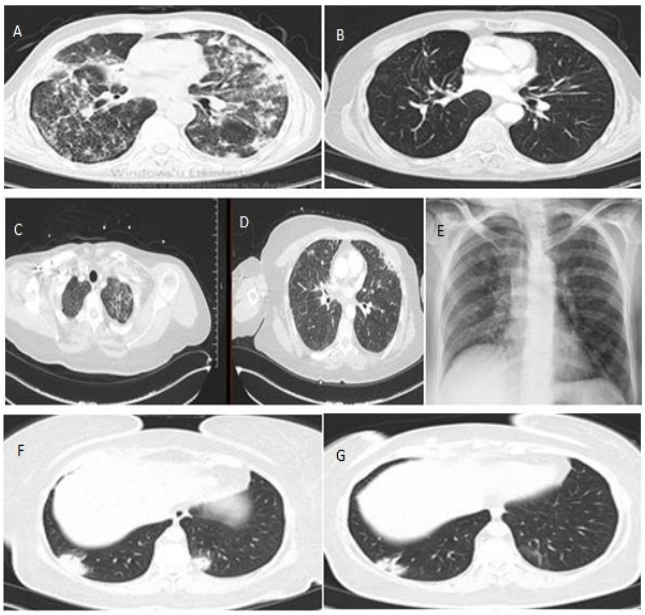

Figure 2: Diagnostic and follow-up thoracic CT slices of cases 4, 5, and 6. (A) Case 4 Thoracic CT at diagnosis, (B) Case 4 Thoracic CT two years after treatment, (C and D) Case 5 Thoracic CT at diagnosis, (E) Case 5 Posteroanterior chest X-ray two months after treatment, (F) Case 6 Thoracic CT at diagnosis, (G) Case 6 Thoracic CT two months after treatment.

Case 5: A 46-year-old female with a 30 pack-year smoking history and asthma presented with symptoms of dyspnea, cough, and sputum. She was diagnosed with locally advanced invasive breast carcinoma and treated with paclitaxel and tamoxifen for 1 year. Chest CT revealed a small number of bilateral ground-glass opacities (Figures 2C and D). Bronchoscopy was performed but no definitive diagnostic result was obtained. The patient was started on methylprednisolone at a dose of 0.5 mg/kg, which was gradually tapered, resulting in clinical and radiological improvement. Radiological response was observed in follow-up imaging performed after 3 months of treatment (Figure 2E).

Case 6: A 54-year-old female nonsmoker with no comorbidities and no reported symptoms was found to have metastatic malignant melanoma and was treated with temozolomide and nivolumab for 5 months. A consolidated area was identified in the right lower lobe adjacent to the pleura (Figure 2F). The patient was asymptomatic, and so chemotherapy was discontinued after drug-induced lung disease was diagnosed. Follow-up imaging 1 month later revealed that the lung findings had regressed, and the patient continued under observation without further treatment (Figures 2G).

Case 7: A 41-year-old female with a 15 pack-year smoking history presented with dyspnea and cough, and was subsequently diagnosed with metastatic invasive breast carcinoma and treated with ribociclib, denosumab, and letrozole for 7 months. Chest CT revealed bilateral ground-glass opacities (Figure 3A). The patient was started on methylprednisolone at a dose of 0.5 mg/kg, which was gradually tapered, resulting in clinical and radiological improvement. Radiological response was observed in follow-up imaging performed after 3 months of treatment (Figure 3B).

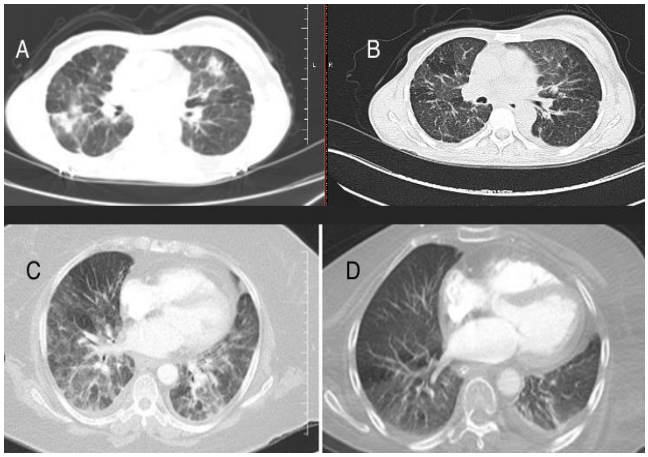

Figure 3: Diagnostic and follow-up thoracic CT slices of cases 7 and 8. (A) Case 7 Thoracic CT at diagnosis, (B) Case 7 Thoracic CT one month after treatment, (C) Case 8 Thoracic CT at diagnosis, (D) Case 8 Thoracic CT one year after treatment.

Case 8: A 54-year-old female nonsmoker with hypertension and diabetes presented with dyspnea. Her primary malignancy was glioblastoma, for which she underwent chemotherapy with temozolomide for 1 month. Chest CT revealed bilateral ground-glass opacities (Figure 3C). The patient declined bronchoscopy and was treated presumptively for CILD with concurrent pneumocystis pneumonia. The patient was started on methylprednisolone at a dose of 0.5 mg/kg, which was gradually tapered, resulting in clinical and radiological improvement. Radiological response was observed in follow-up imaging performed after 3 months of treatment (Figure 3D).

Demographic data of the patients is shown in Table 1.

DISCUSSION

CILD can clinically and radiologically mimic both opportunistic or widespread infections and interstitial lung diseases. These include infectious pneumonia, which can be viral (e.g., influenza, *Respiratory syncytial virus*, *Adenovi*

Table 1: Demographic Data of the Patients

Case	Gender	Age	Smoking History	Comorbidities	Symptom	Primary Malignancy	Chemotherapeutic Agent Received	Duration of Chemotherapy
1	F	70	Nonsmoker	Diabetes	None	Metastatic Invasive Breast Carcinoma	Letrozole and Ribociclib	5 months
2	F	68	Nonsmoker	None	Dyspnea	Adenocarcinoma of the Pancreatic Head	Gemcitabine	13 months
3	M	61	Nonsmoker	Diabetes	Cough and sputum	Rectal Adenocarcinoma	Pembrolizumab	4 months
4	M	65	50 pack/years	Chronic Obstructive Pulmonary Disease	Dyspnea	Metastatic Non-Small Cell Lung Cancer	Leuprorelin and Nivolumab	2 years
5	F	46	30 pack/years	Asthma	Dyspnea, cough and sputum	Locally Advanced Invasive Breast Carcinoma	Paclitaxel and Tamoxifen	1 year
6	F	54	Nonsmoker	None	None	Metastatic Malignant Melanoma	Temozolomide and Nivolumab	5 months
7	F	41	15 pack/years	None	Dyspnea, cough	Metastatic Invasive Breast Carcinoma	Ribociclib, Denosumab, and Letrozole	7 months
8	F	54	Nonsmoker	Hypertension and Diabetes	Dyspnea	Glioblastoma	Temozolomide	1 month

rus, COVID-19), bacterial (e.g., *Streptococcus pneumoniae*, *Staphylococcus aureus, Pseudomonas aeruginosa*), or opportunistic (e.g., *Pneumocystis jirovecii, Aspergillus spp*., *Cytomegalovirus*) in immunocompromised patients. Other conditions to consider are pulmonary edema, pulmonary embolism, radiation-induced pneumonitis, and progression or metastasis of the underlying malignancy. Distinguishing CILD from the above conditions requires careful assessment of the timing of symptom onset, imaging patterns, microbiological studies, and the patient's treatment history. Due to the challenges in differential diagnosis, simultaneous treatment for multiple possible causes may sometimes be necessary. Bronchoalveolar lavage (BAL) findings in CILD are nonspecific and may include increased levels of lymphocytes, neutrophils, and eosinophils. BAL should be performed to exclude infectious etiologies and to differentiate possible interstitial lung diseases based on CD4/CD8 cell ratios.

In a center in which 624 patients received chemotherapy, the medications of 18 symptomatic patients were discontinued after being evaluated as radiologically suspicious (4) and were followed up with a diagnosis of CILD. All 18 patients underwent transbronchial lung biopsy, revealing normal lung tissue in nine cases, nonspecific chronic alveolar interstitial inflammation in two cases, and organizing pneumonia in five cases, while the biopsy was considered diagnostically insufficient in two cases. Histopathologically verifiable abnormalities were identified in seven cases (38%). As demonstrated in the present study, lung biopsy can reveal pathological findings in both focal and diffuse parenchymal lung conditions in the diagnosis of chemotherapy-induced lung disease. It should be noted, however, that definitive results are not revealed in all cases and the risks associated with the procedure must be considered. While histopathological diagnosis is not mandatory for the confirmation of drug-induced lung disease, it can help in excluding other possible conditions.

CILD may become apparent early during treatment stages or may develop after prolonged use of chemotherapeutic agents. It may present during the initial treatment cycle, after subsequent cycles, or even years later, as is the case with carmustine-associated pulmonary fibrosis. A single chemotherapy agent may be associated with different lung injury patterns (5,6).

Pulmonary symptoms associated with chemotherapy-induced lung disease (CILD) are often nonspecific and may mimic other pulmonary conditions. Dyspnea is the most common presenting symptom, followed by cough and, less frequently, fever or chest pain (7). In many cases, respiratory complaints develop insidiously and may initially be mistaken for infection or disease progression, underscoring the importance of clinical suspicion and early radiological evaluation. The majority of our patients presented with shortness of breath.

The toxicity of some drugs correlates with cumulative dose levels; however, adverse reactions can occur even at low doses. CILD is diagnosed through exclusion and a multidisciplinary approach, and while lung injury may resolve with discontinuation of the offending agent, corticosteroid therapy may be required.

The management of CILD begins with cessation of the offending agent, followed by systemic corticosteroid therapy tailored to severity. In mild cases, approximately 0.5–1 mg/kg/day of prednisolone equivalent can be initiated, whereas moderate to severe cases may require 1–

2 mg/kg/day, with gradual tapering over 4–8 weeks depending on clinical and radiological improvement (8). Once a patient has shown complete clinical and radiographic recovery, the re-introduction of the causative therapy may be considered, but only after a careful risk-benefit assessment. Factors favoring rechallenge include full resolution of lung injury, absence of hypoxia, stable or improving pulmonary imaging, and the lack of an alternative safer regimen. If the event was life-threatening or recovery was incomplete, permanent discontinuation is recommended.

Previous studies vary in their assessment of whether targeted therapies or systemic chemotherapy regimens are more likely to induce CILD, reporting different results. Recent meta-analyses have shown that the incidence of CILD in oncology is associated with the treatment type. For example, a meta-analysis of patients with non-small cell lung cancer (NSCLC) treated with anaplastic lymphoma kinase (ALK) inhibitors reported a significantly increased risk of CILD (Peto OR ≈ 3.27) when compared with chemotherapy (9). Another comprehensive review reported that CILD may develop in patients receiving cytotoxic chemotherapy, targeted therapy and immunotherapy, but did not identify a consistent superiority of one over the other (3). Moreover, a pan-cancer retrospective study reported a 14.2 % cumulative incidence of ILD at 6 months among lung cancer patients treated with cytotoxic chemotherapy (10). Collectively, these findings suggest that while both chemotherapy and targeted therapies carry a risk of CILD, the incidence may be influenced by patient-specific factors, pre-existing lung conditions, and the type of agent used, highlighting the need for individualized risk assessment.

In a study based on FDA reports, it was observed that reported cases of drug-induced lung disease increased steadily each year from 2004 to 2021. The reasons for this rise are likely multifactorial, with the primary factor being the growing awareness of the condition among physicians, although the increased attention to adverse events by both patients and the pharmaceutical industry may also contribute. Antineoplastic agents represent the most frequently reported class of drugs associated with drug-induced lung disease to the FDA (11).

The presented cases demonstrate both similarities and differences when compared to previously reported cases in the literature on CILD. Consistent with the literature, most patients developed bilateral ground-glass opacities, often without severe respiratory symptoms, and responded favorably to corticosteroid therapy, particularly when the offending agent was discontinued. While radiological improvement is commonly reported within weeks, our cases showed variability, with improvements observed as late as 3 months. The sepsis-based mortality seen in two of our cases underscores the importance of monitoring for secondary infections, which is a complication less emphasized in earlier reports. Overall, our findings are largely in line with the literature, and highlight the potential for diverse clinical courses and the need for individualized management strategies.

CONCLUSION

The identification of new infiltrates on thoracic CT in patients receiving chemotherapy should raise suspicion for CILD, and differential diagnoses must be thoroughly evaluated. This is important to reduce the morbidity and mortality associated with drug-induced lung injury. A stepwise evaluation involving radiological imaging, bronchoscopy, and, when necessary, biopsy, is key to diagnosis. Most cases respond to discontinuation of the causative agent, while some may require short-term steroid therapy. Future pharmacogenomic studies may help identify subgroups of patients at risk of lung injury related to specific chemotherapeutic agents.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - C.D., O.S.D., S.S.O., H.A.T.Ö., İ.A., U.T., O.O.T., A.A.; Planning and Design - C.D., O.S.D., S.S.O., H.A.T.Ö., İ.A., U.T., O.O.T., A.A.; Supervision - C.D., O.S.D., S.S.O., H.A.T.Ö., İ.A., U.T., O.O.T., A.A.; Funding - C.D., O.S.D., S.S.O., A.A.; Materials - C.D., O.S.D., S.S.O., U.T., O.O.T., A.A.; Data Collection and/or Processing - C.D., H.A.T.Ö., İ.A.; Analysis and/or Interpretation - C.D., O.S.D., S.S.O., A.A.; Literature Review - C.D., O.S.D., S.S.O., A.A.; Writing - C.D.; Critical Review - C.D., O.S.D., S.S.O.

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Ultrasound Facilitated Catheter Directed Thrombolysis in the Treatment of Acute Pulmonary Embolism: A Case Series of Six Patients

Akut Pulmoner Embolizm Tedavisinde Ultrason Eşliğinde Kateter Yönlendirmeli Tromboliz: Altı Olguluk Bir Seri

Pervin Hancı[1], Başak Gönen[2], Osman Kula[3], Gökhan Karataş[3], Ethem Yıldız[2], İlker Yılmam[2], Osman Nuri Hatipoğlu[2]

Abstract

Pulmonary embolism (PE) is a potentially fatal cardiovascular emergency for which catheter-directed thrombolysis has emerged as an alternative therapy in cases where systemic thrombolysis is contraindicated, particularly when assisted by ultrasound (US-CDT). We present here the clinical characteristics, management, and outcomes of six patients with intermediate–high or high-risk PE treated with US-CDT in a tertiary care center. All patients were diagnosed based on CT pulmonary angiography and echocardiography findings and underwent ultrasound-assisted thrombolysis with EKOS catheters. Demographic, clinical, and hemodynamic data were collected, and outcomes were assessed based on echocardiographic parameters and clinical recovery. All patients presented with hemodynamic compromise and right ventricular dysfunction. US-CDT resulted in improvements in pulmonary artery pressures, right ventricular size and function, and oxygenation indices. No major bleeding complications occurred. US-CDT can be considered a safe and effective option in acute PE patients in whom systemic thrombolysis is contraindicated. Further studies are needed to evaluate long-term outcomes and improve patient selection.

Keywords: *Pulmonary embolism, catheter-directed thrombolysis, right ventricular dysfunction.*

Öz

Pulmoner emboli (PE), ciddi mortalite riski taşıyan bir kardiyovasküler acildir. Sistemik trombolitik tedavinin kontrendike olduğu durumlarda, özellikle ultrason destekli kateter yönlendirmeli tromboliz (US-CDT) giderek daha fazla tercih edilmektedir. Bu olgu serisi, orta-yüksek ve yüksek riskli PE tanısı alan ve US-CDT ile tedavi edilen altı hastanın klinik özelliklerini, tedavi sürecini ve sonuçlarını sunmayı amaçlamaktadır. Tüm hastalara BT pulmoner anjiyografi ve ekokardiyografik değerlendirme sonrası 'EKOS' kateteri ile US-CDT uygulandı. Demografik, klinik ve hemodinamik veriler toplandı, sonuçlar ekokardiyografi parametreleri ve klinik iyileşme üzerinden değerlendirildi. Tüm hastalarda sağ ventrikül disfonksiyonu ve hemodinamik bozulma mevcuttu. US-CDT sonrası pulmoner arter basıncı, sağ ventrikül boyutu ve fonksiyonları ile oksijenasyon parametrelerinde belirgin iyileşme sağlandı. Hiçbir hastada majör kanama komplikasyonu gözlenmedi. US-CDT, sistemik tromboliz için uygun olmayan seçilmiş PE hastalarında güvenli ve etkili bir tedavi seçeneği olabilir. Uzun dönem sonuçların değerlendirilmesi ve hasta seçiminin optimize edilmesi için ileriye dönük çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: *Pulmoner emboli, kateter yönlendirmeli tromboliz, sağ ventrikül disfonksiyonu.*

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Pulmonary embolism (PE) is the third most common cardiovascular emergency after myocardial infarction and stroke (1–3). The annual incidence of PE varies between 39 and 120 cases per 100,000 population, with a marked increase in older age groups (4,5). Management of PE has evolved with the development of new treatment options and multidisciplinary response teams (3,6). Despite the advances in diagnosis and treatment, PE continues to pose a significant challenge for physicians due to its potentially fatal nature and the bleeding risk linked to anticoagulant therapy (1).

Acute pulmonary embolism (PE) management involves stratifying patients according to risk levels and adjusting treatment intensity accordingly (7). Risk evaluation considers the patient's hemodynamic stability, as well as the presence of any right ventricular dysfunction, and is based on the patient's estimated 30-day mortality risk. The Pulmonary Embolism Severity Index (PESI) is the most widely used clinical prediction tool in such cases (8). Echocardiography and CT angiography are the primary imaging modalities for the evaluation of right ventricular function, and the high negative predictive value of high-sensitivity cardiac troponin-I bolster its effectiveness in identifying patients who are less likely to experience adverse outcomes (9–11). High-risk PE patients exhibit hemodynamic instability, whereas those classified as intermediate-high risk may exhibit right ventricular dysfunction and biomarker abnormalities, yet remain hemodynamically stable. Nevertheless, early reperfusion therapies are recommended for these patients due to the potential for clinical deterioration and the high risk of mortality (12).

The currently available reperfusion therapies that have gained popularity in recent years include systemic thrombolytic therapy, surgical embolectomy, and catheter-directed thrombolysis (CDT). Among these, CDT aims to reduce the thrombus burden in the pulmonary arteries through the direct administration of thrombolytic agents at site and, in some cases, mechanical fragmentation of the thrombus. One potential benefit of CDT over systemic thrombolytic therapy is its ability to reduce the risk of systemic bleeding through the utilization of targeted therapy with lower doses of thrombolytic agents. This targeted approach is particularly advantageous among older adult patients or those with high bleeding risk, making it a significant area of research.

We present here the clinical characteristics, treatment processes, and outcomes of six patients with PE who were treated with ultrasound-facilitated CDT (US-CDT) to ascertain the effects of CDT on actual clinical practice and its contribution to patient management. The obtained findings may contribute to a better understanding of the role of CDT in the treatment of PE and inform the development of future patient selection criteria.

CASES

The patients in this case series were selected based on clinical necessity at a tertiary-care institution equipped with intensive care and interventional radiology units. All patients had a confirmed diagnosis of acute pulmonary embolism via computed tomography pulmonary angiography (CTPA) and underwent physiological assessment with transthoracic echocardiography. The patients' demographic characteristics, comorbidities, PESI score points, vital signs at ICU admission, arterial blood gas analysis results, cardiac biomarkers, electrocardiogram findings and outcomes are summarized in Table 1. Each case was reviewed and discussed by a multidisciplinary team (MDT) comprising pulmonology, cardiology, intensive care, and interventional radiology specialists. Indications for urgent reperfusion therapy and contraindications to systemic thrombolysis were evaluated during the MDT discussions.

Table 1: Characteristics of the patients upon ICU admission

	N=6
Age (years)	55 [34-80]
Gender, male, n(%)	4 (66.7)
Comorbidities n(%)	
Hypertension	2 (40)
Malignancy	3 (50)
Chronic cardiovascular disease	3 (50)
Chronic pulmonary disease	2 (33.3)
Intracranial mass	2 (33.3)
Pregnancy	1 (20)
PESI point	135 [54-208]
BOVA score	5 [4-7]
Heart rate (1/min.)	98 [80-124]
Respiratory rate (1/min)	30 [21-36]
Mean arterial pressure (mmHg)	85 [63-100]
pH	7.45 [7.41-7.48]
$PaCO_2$ (mmHg)	35 [25-39]
PaO_2 (mmHg)	92 [51-137]
HCO_3	16.5 [11-22]
Lactate (mmol/L)	9.5 [6-13]
PaO_2/FiO_2 (mmHg)	236 [103-370]
Hs-Troponin I (ng/L)	206 [133-279]
Brain natriuretic peptide (pg/ml)	428 [334-523]
ECG findings, n (%)	
Sinus tachycardia	5 (83.3)
T-wave abnormality	2 (33.3)
S1Q3T3	1 (16.7)
Right axis deviation	1 (16.7)
Deep venous thrombus (n,%)	2 (40)
Total administered t-PA dosage (mg)	18 [9-18]
Hospital mortality, n(%)	0 (0)

PESI: *Pulmonary Embolism Severity Index,* ***$PaCO_2$:*** *Partial arterial carbondioxide pressure,* ***PaO_2:*** *Partial arterial oxygen pressure, ECG: electrocardiogram,* ***t-PA:*** *Tissue plasminogen activator*

Data expressed as median [min-max] and n(%)

After institutional approval for the study was obtained, patients were transferred to the interventional radiology unit and provided informed consent for their inclusion in the study. Under sterile conditions, the femoral vein was punctured at two different levels using real-time ultrasound guidance, and separate catheters were advanced into the pulmonary arterial tree (Figures 1A and 1B). Depending on thrombus burden and anatomical distribution, ultrasound-assisted thrombolysis catheters (EKOS: Boston Scientific, Marlborough, MA, USA) were positioned in the right, left, or both pulmonary arteries (Figure 2).

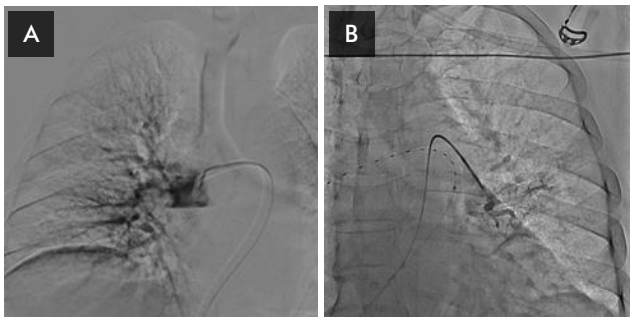

Figure 1: Pulmonary angiography images of Case 1. Right main pulmonary artery (A), left main pulmonary artery (B)

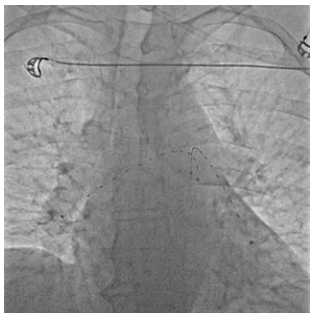

Figure 2: Ultrasound-assisted thrombolysis catheters (EKOS: Boston Scientific, Marlborough, MA, USA) positioned in the right and left pulmonary arteries.

Then, 1 mg of tissue plasminogen activator (tPA) was administered, followed by an additional 0.5–0.75 mg/h of tPA through each catheter over the next 16 hours. Hemodynamic parameters, gas exchange indices, and bleeding events were closely monitored in the intensive care unit (ICU). The echocardiography results of the six patients, before and 16–48 hours after the procedure, are presented in Table 2.

Table 2: The echocardiography results of the patients, before and 16-48 hours after the procedure

	Before US-CDT	After US-CDT
RV basal diameter (mm) (n=6)	43 [33-50]	30 [28-41]
RV/LV ratio (n=6)	0.9 [0.8-1.2]	0.7 [0.6-0.8]
Septal dyskinesia, n(%) (n=6)	5 [83.3]	1 [16.7]
TAPSE (mm) (n=5)	19 [15-22]	25 [20-28]
sPAP (mmHg) (n=6)	56 [30-73]	37 [25-55]

RV: right ventricle, LV: left ventricle, TAPSE: Tricuspid annular plane excursion, sPAP: systolic pulmonary arterial pressure.

Data expressed as Median [Min-Max]

Case 1: A 54-year-old male with no known comorbidities was admitted to our emergency room (ER) complaining of abdominal pain. A physical exam revealed tenderness in the right lower abdomen, and a computed tomography (CT) confirmed perforated appendicitis, and the patient was sent for emergency surgery. On the 6th day following surgery, the patient exhibited tachycardia, tachypnea, and desaturation, leading to his transfer to the Respiratory ICU. His vital signs on admission were: pulse, 90 beats per minute; respiratory rate, 30 breaths per minute; and SpO_2, 88% while the patient was on a 10 L/min oxygen diffuser mask. Non-invasive blood pressure was recorded at 130/80 mmHg, with a mean arterial pressure (MAP) of 90 mmHg. Electrocardiogram (ECG) demonstrated sinus rhythm. High-flow nasal oxygen therapy was started at a flow rate of 50 L/min and oxygen fraction (FiO_2) of 70%. CTPA revealed a filling defect in both main pulmonary artery branches, consistent with a distally extending saddle embolism (Figure 3).

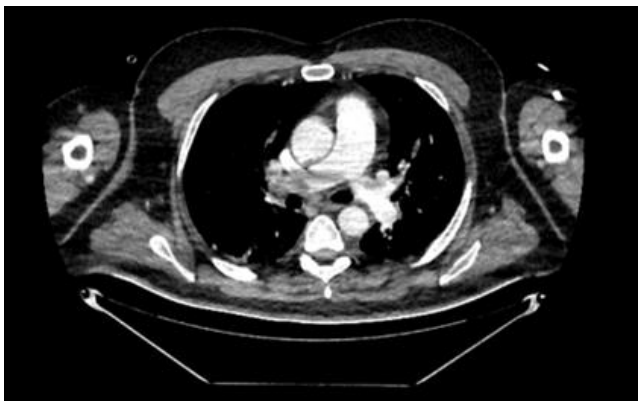

Figure 3: Saddle-shaped thrombus in computed tomography pulmonary angiography of Case 1.

Echocardiography results indicated an ejection fraction (EF) of 60%, normal contraction, and no evidence of septal dyskinesia or pericardial effusion. Tricuspid annular plane systolic excursion (TAPSE) was 19, right ventricular (RV) size ranged from 43 to 47 mm, and pulmonary artery pressure (PAP) was 30 mmHg, with mild tricuspid regurgitation. High-sensitivity troponin I (hsTrop I) levels were 137.2 ng/L. Ultrasonography of the lower extremities demonstrated absent venous flow and no compressibility in the right femoral vein, with an anechoic appearance proximally and a hyperechoic thrombus in the mid-to-distal segments. US-CDT was performed by interventional radiology due to the patient's high oxygen requirement, elevated cardiac biomarkers, elevated RV size, and recent surgical history. Treatment continued 12 hours after the conclusion of the thrombolytic infusion with low-molecular-weight heparin at a dose of 6000 U subcutaneously twice daily. The flow rate and FiO_2 were decreased after the patient's blood gas values improved,

and HFNO therapy was halted. On the 6th day in the ICU, the patient was moved to nasal cannula oxygen at 4 L/min. The patient was then transferred to the ward, initiated on warfarin as maintenance therapy, and discharged on the 20th day of hospitalization.

Case 2: A 60-year-old male patient with a medical history of hypertension and diabetes mellitus was under observation for lung adenocarcinoma after being diagnosed in 2021 subsequent to a wedge resection. His treatment history included a left lung lobectomy and radiotherapy (RT) for brain metastasis, and he completed one course of chemotherapy before choosing to discontinue treatment voluntarily. The patient presented to the ER with sudden-onset dyspnea, and was found to have hypotension (99/69 mmHg), rapid breathing (30 breaths/min), and low oxygen levels, with peripheral oxygen saturation 82% on room air. The patient had sinus tachycardia (130 beats/min) and T-wave inversion in the chest leads on ECG. Following the detection of hsTrop I, 122 and B type natriuretic peptide (BNP, 522), the patient underwent cardio evaluation, during which an echocardiogram revealed an ejection fraction of 50–55%, along with normal contractions. The RV diameter was measured at 47–52 mm, with evidence of septal dyskinesia resulting in a D-shaped left ventricle. The degree of tricuspid regurgitation was classified as grade 2. Hemodynamic findings included a PAP of 52 mmHg; tricuspid regurgitant velocity (TRV), 3.3 m/sec; and TAPSE, 15 mm. The inferior vena cava (IVC) diameter was 21 mm, with greater than 50% collapse observed. The CTPA showed a saddle-shaped massive embolism in the bilateral main pulmonary artery branches. The presence of brain metastases compelled the neurosurgeon to assess the risk of intracranial hemorrhage as high during systemic thrombolysis. Consequently, ultrasound-guided catheter-directed thrombolytic therapy was initiated by interventional radiology. The patient was transferred for follow-up in the ICU, beginning with a diffuser mask and oxygen support of 4 L/min. There was no need for inotropes. The state of consciousness was stable (GCS, E4M6V5). Low-molecular-weight heparin (LMWH) treatment was initiated at a therapeutic dose based on the control APTT result. Echocardiography performed on the 2nd day of treatment showed a right ventricular diameter of 37 mm, a PAP of 34 mmHg, and a TAPSE of 20 mm. Since the patient's clinical condition was stable, inotropic medications were deemed unnecessary, and the requirement for oxygen support diminished. He was moved to the ward on the third day of his hospitalization. The patient required no oxygen therapy in the ward, and was discharged with recommendations on the 8th day of hospitalization.

Case 3: An 80-year-old female with a history of hypertension who had undergone gallbladder and cataract surgeries within the past 6 months presented to the ER of an external facility complaining of chest pain and shortness of breath. Furosemide infusion was administered due to a suspicion of pulmonary edema, but produced no clinical response. Laboratory tests revealed increased troponin levels (from 261 to 279 ng/L), prompting her transfer to our hospital's ER with a suspected diagnosis of acute coronary syndrome. At the time of admission, her vital signs were as follows: blood pressure, 112/73 mmHg; pulse, 76 beats per minute; oxygen saturation, 83% on room air; respiratory rate, 20 breaths per minute; and thoracoabdominal breathing was observed. Sinus rhythm was detected, and no ST elevation or acute ischemic changes were observed on the ECG. Echocardiographic examination demonstrated an EF of 60%, with synchronized contractions, normal myocardial thickness, and indications of right heart strain, including a TAPSE of 22 mm, pulmonary artery pressure of 65 mmHg, a D-shaped septum, and a TRV of 3.7 m/sec. Laboratory investigations revealed a BNP level of 334 pg/ml. CTPA showed filling defects in the left and right main pulmonary arteries, along with lobar branches, as well as slight ground-glass opacities in the lung parenchyma on both sides. Furthermore, a subpleural nodular lesion measuring 11 mm in diameter was identified in the basal left lower lobe (Figure 4A). The patient was admitted to the ICU due to respiratory distress and was closely monitored for vital signs. Oxygen saturation levels ranged from 92% to 96%, while she received 12 liters per minute of oxygen therapy through a reservoir mask. US-CDT was performed due to her recent surgical history. The need for supplemental oxygen decreased during follow-up; and her saturation improved to above 90% with 2–4 L/min of oxygen delivered via nasal cannula. Due to a decrease in hemoglobin levels, a contrast-enhanced thoracoabdominal CT scan was performed 48 hours after intensive care, revealing no active bleeding. A regression of the filling defects consistent with embolism was noted in both main pulmonary arteries (Figure 4B). The patient was transferred to the ward on the 8th day of ICU admission and was discharged on the 20th day of hospitalization with a new-generation oral anticoagulant therapy (Apixaban 2 x 5 mg).

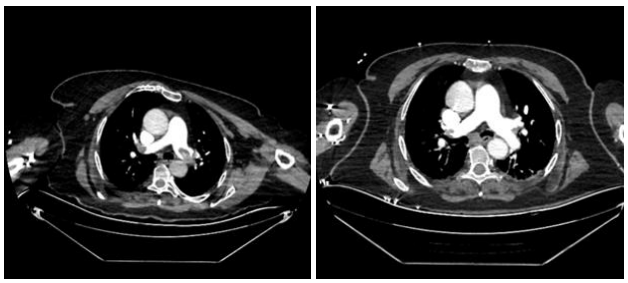

Figure 4: Computed tomography pulmonary angiography images of Case 3 before (A) and 48 hours after ultrasound-facilitated catheter-directed thrombolysis (B).

Case 4: A 34-year-old female who was 6 weeks pregnant following assisted reproductive technology, presented to the ER with complaints of chest pain and difficulty breathing. She reported experiencing several days of increasing fatigue and worsening dyspnea, along with newly onset chest pain, palpitations, and syncope after walking for 5–10 minutes. Her medical history included a heterozygous gene mutation linked to thrombophilia. In her family history, her father had a condition characterized by "blood thickening", suggesting a possible hereditary thrombophilic disorder. She was taking several medications as part of her in vitro fertilization regimen and thromboprophylaxis, including acetylsalicylic acid, folic acid, estradiol valerate/norgestrel, progesterone, and enoxaparin (0.4 ml once daily). She had tachycardia and hypotension upon admission. A bilateral venous Doppler ultrasound of the lower extremities revealed no signs of deep vein thrombosis. Electrocardiography showed sinus rhythm with an incomplete right bundle branch block. Transthoracic echocardiography indicated a preserved left ventricular EF of 55% with no regional wall motion abnormalities. The right ventricle measured 33 mm, and the right atrium measured 37 mm. There was moderate to severe tricuspid regurgitation, with a tricuspid regurgitation velocity (TRV) of 3.6 m/sec and an estimated pulmonary artery pressure (PAP) of 70 mmHg. TAPSE was measured at 12 mm, and TLSA at 11 mm. A D-shaped septum was noted, indicating right ventricular pressure overload. Laboratory tests revealed a high hsTrop I level of 1149 ng/L. The patient was transferred to the ICU for monitoring in room air under strict immobilization and a therapeutic dose of LMWH and intravenous fluid infusion were initiated. Due to the patient's hypotensive state, prolonged acquisition time, and the expected suboptimal image quality, no MR angiography was performed. After a comprehensive discussion with the patient and her family, the potential risks were thoroughly detailed, and written informed consent was obtained for a CTPA. The CTPA revealed a filling defect consistent with a massive PTE extending to the main pulmonary artery and middle lobar branch, causing near-total occlusion of the lower lobar branch in the right pulmonary artery. Additionally, a total occlusive thrombus was observed in the lower lobar branch of the left pulmonary artery. US-CDT was initiated, taking into account the location and size of the thrombi, the history of hypotension and syncope, and the risk of bleeding associated with the possibility of termination of pregnancy. Follow-up echocardiography performed 48 hours after hospitalization demonstrated a PAP of 40 mmHg and TAPSE of 20 mm. Swelling and bruising were observed in the right radial region during follow up, along with paleness in the fingers. The capillary refill time was measured at less than 2 seconds – findings that were consistent with a hematoma at the site of previous arterial blood gas sampling. An arterial Doppler ultrasound revealed no evidence of vascular compromise. Conservative management was initiated, which included elevating the affected area and the application of topical chondroitin polysulfate gel. The swelling, redness, and pallor of the right hand gradually regressed. She was moved to the ward on the 3rd day of ICU stay and was discharged on the 30th day of hospitalization.

Case 5: A 48-year-old male was admitted to the ER with complaints of shortness of breath and fatigue for several days. The patient had been diagnosed with high-grade glioblastoma 4 months earlier, for which he had undergone a total of 30 sessions of RT and was on targeted chemotherapy. His last RT and chemotherapy sessions were 3 weeks prior. Neurological symptoms, including forgetfulness, delayed responses, and impaired cooperation, were reported by his relatives for the last 3 months. Upon admission, the patient's vital signs were recorded as follows: blood pressure, 139/70 mmHg; heart rate, 106 bpm; body temperature, 36.7°C; and SpO_2, 78% on room air. The respiratory rate was 34 breaths per minute. The GCS score was recorded as E4M6V4. Blood gas analysis indicated a pH of 7.440, a PaO_2 of 60.1 mmHg, a $PaCO_2$ of 28.1 mmHg, and SaO_2 at 93.5% on 7 L/min of oxygen via nasal cannula. His troponin I level was 127.3 ng/L. ECG revealed sinus tachycardia with S1Q3T3 findings. A bedside echocardiography revealed an EF of 60%, with normal segmental contractions, although interventricular septal dyskinesia was observed. The right ventricular to left ventricular ratio was greater than 1, tricuspid regurgitation was noted, while pulmonary artery pressure (PAP) could not be evaluated due to poor echogenicity. CTPA revealed filling defects consistent with PE extending from the right to the left main pulmonary arteries and involving the upper, middle, and lower lobar branches bilaterally. Ground-glass opacities and per-bronchial thickening were also noted, more prominently in the left lung, suggesting possible superimposed infection or pulmonary edema. Medical thrombolysis was deemed contraindicated due to the presence of intracranial masses. The patient was transferred to our ICU and started on HFNC treatment with FiO2, 50% and flow, 50 L/min. US-CDT was planned for the patient whose mean arterial pressure decreased below 65; tachypnea and high-dose oxygen requirement continued in the ICU follow-up. A thrombus was observed in the right main pulmonary artery; however, attempts to catheterize the left pulmonary artery were unsuccessful, and the procedure was terminated. LMWH was initiated at a therapeutic dose as maintenance therapy. Echocardiography performed at 48 hours of treatment was similar to the previous echocardiography. Oxygenation improved and the patient was normotensive, and he was transferred to

the ward on day 6 of hospitalization. A control echocardiography 4 weeks later demonstrated EF 59%, right ventricular diastolic diameter 30 mm, right atrium 33 mm, and PAP<25 mmHg. There were no signs of segmental akinesia or septal dyskinesia.

Case 6: A 57-year-old male patient was admitted to the ER with sudden-onset dyspnea. The patient had undergone a right pneumonectomy for lung cancer 2 months prior. A thrombus was detected in the main branches of both pulmonary arteries on thoracic computed tomography conducted to investigate the dyspnea. On admission, vital signs were as follows: blood pressure, 120/75 mmHg; respiratory rate, 30 breaths per minute; heart rate, 117 bpm; body temperature, 36°C; and oxygen saturation, 92% with 6 L of oxygen support under a nasal cannula. Cardiac ultrasonographic evaluation revealed a pulmonary artery pressure of 75 mmHg and enlarged right heart chambers. The high-sensitivity troponin I level was 345.66 pg/ml. The patient was classified as intermediate–high risk, and thrombolytic therapy was planned. Due to his recent surgical history, thrombolysis via a catheter with EKOS ultrasound was considered appropriate. The EKOS catheter was positioned, and 2 mg of tPA was administered through the left pulmonary artery, while the right pulmonary artery could not be catheterized, and so the procedure was terminated. The patient was followed up in the ICU after the procedure. Oxygen demand decreased following 4 hours of thrombolytic treatment, and the treatment was continued for 16 hours with 0.5 mg/h tPA. At the end of 16 hours, the patient's vital signs were as follows: blood pressure, 148/98 mmHg; heart rate, 114 bpm; respiratory rate, 21 breaths per minute; and oxygen saturation, 97% with a 2 L nasal cannula. The patient's complaint of dyspnea resolved and no complications were observed after the procedure. On control cardiac evaluation, pulmonary artery pressure was 55 mmHg, with persistent enlargement of the right heart chambers. Maintenance treatment was continued with LMWH. The patient was transferred to the ward on the 7th day of ICU admission.

DISCUSSION

This case series highlights the clinical use of US-CDT in six patients with acute PE who exhibited varying degrees of hemodynamic instability and oxygenation disturbances. Despite their different clinical backgrounds – including recent surgery, active malignancy, pregnancy, and intracranial issues – all patients experienced improvements in both oxygenation and hemodynamic status following CDT. Importantly, no major bleeding complications were reported. These findings suggest that US-CDT may be a viable therapeutic option for selected high-risk or intermediate–high-risk patients with PE, especially when systemic thrombolysis is contraindicated.

US-CDT is an advanced technique for the management of acute PE, particularly in patients at intermediate–high or high risk of mortality. Unlike systemic thrombolysis, in which there is a risk of significant bleeding, US-CDT allows for the localized delivery of low-dose thrombolytic agents directly into the thrombus. This method is combined with ultrasonic energy to break apart fibrin structures, thereby enhancing the dissolution of the clot. Such a targeted approach not only enables effective thrombolysis but also significantly reduces systemic exposure to fibrinolytic drugs, thereby minimizing the risk of bleeding complications.

The safety and efficacy of US-CDT have been consistently reported in numerous studies. In the ULTIMA trial, patients treated with US-CDT showed a greater reduction in the ratio of right ventricular to left ventricular (RV/LV) diameter at 24 hours compared to those receiving anticoagulation alone. It is worth noting that there was no increase in major bleeding events associated with US-CDT treatment (13). Additionally, pulmonary artery pressures and oxygenation levels exhibited significant improvements, highlighting the physiological benefits of early right ventricular unloading. The SEATTLE II study similarly reported that US-CDT led to substantial reductions in right ventricular dysfunction, pulmonary artery pressure, and thrombus burden. Notably, there was a 10% incidence of moderate to severe hemorrhage, but no cases of intracranial hemorrhage were reported (14). Kaymaz et al. (15) assessed the effectiveness and safety of US-CDT in patients diagnosed with high-risk and intermediate–high-risk PE through an analysis of data from 15 studies involving over 650 patients. The authors reported that US-CDT significantly improved key hemodynamic parameters, including reductions in pulmonary artery mean pressure, RV/LV ratio, and CT obstruction scores. Overall, the mortality rate was low at 3.2%, with cardiovascular mortality accounting for 2.2%. Furthermore, major bleeding complications were observed in only 5.5% of patients, a figure that is significantly lower when compared to traditional systemic thrombolysis. Recurrent PE was uncommon at 1.7%, further supporting the use of US-CDT as an effective alternative for critically ill patients with PE.

Another meta-analysis assessing the outcomes and bleeding risks associated with catheter-directed thrombolysis for patients with high and intermediate-high risk PE reported the following results: in high-risk patients, the 30-day mortality rate was 8%, and the major bleeding rate was 6.7%. In contrast, patients in the intermediate–high-risk group, the risk of major bleeding was lower, at 1.4%,

with no reported deaths (16). These findings underscore US-CDT as a promising therapeutic option for optimizing patient outcomes while minimizing bleeding risks in high-risk populations with PE.

Our results align with previous reports, demonstrating postprocedural improvements in right ventricular function, including normalization of pulmonary arterial pressure and an increase in TAPSE, along with better oxygenation metrics, as indicated by SpO_2 levels greater than 90% on room air or low-flow oxygen. Our study further highlights the efficacy of CDT in patients who are at an elevated risk of bleeding, such as those with brain metastases, recent surgical procedures, or older age. None of the patients in our series experienced clinically severe hemorrhage or needed blood transfusions, although one developed local swelling and bruising at the site of a radial puncture that was resolved through conservative treatment.

Current international guidelines support the selective use of catheter-based therapies. The European Society of Cardiology 2019 guidelines recommend catheter-directed reperfusion therapies for intermediate–high-risk patients with PE in whom systemic thrombolysis is contraindicated (Class IIa) (17). Similarly, the American College of Chest Physicians highlights the usefulness of catheter-based interventions as a substitute for systemic thrombolysis in carefully selected patients, especially those at increased risk of bleeding, those who fail to respond to systemic thrombolysis, or those in shock facing imminent death before systemic thrombolysis can have an impact (18). Our patient cohort fits well within these guideline-supported indications, as all cases were discussed in a multidisciplinary team setting and selected based on bleeding risk and clinical instability.

The findings suggest that US-CDT can be considered a promising therapeutic alternative for patients in whom systemic thrombolysis is contraindicated. This includes those with recent surgical histories, those with active malignancies, older adults, and pregnant women, all of whom face significant risks from traditional thrombolytic treatments. While the preliminary short-term outcomes for US-CDT are encouraging, indicating its usefulness in cases with acute thromboembolic events, there is a critical need for further prospective randomized trials. Such studies should evaluate the long-term efficacy of US-CDT, particularly in preventing the development of chronic thromboembolic pulmonary hypertension (CTEPH). Additionally, these trials should also assess improvements in functional outcomes for patients and explore optimal dosing strategies to maximize the therapeutic benefits while minimizing the potential risks.

Despite its promising clinical profile, US-CDT has significant methodological and logistical limitations. The procedure requires specialized operator experience, advanced interventional radiology infrastructures, and continuous intensive care monitoring. Furthermore, its limited availability in many centers and the high procedural and device-related costs restrict its widespread routine use. All of these factors should be carefully considered when determining the applicability of this technique in different healthcare systems.

Several significant limitations of this study must also be acknowledged. First, the small sample size ($n = 6$) inherently limits the statistical power and generalizability of the findings. Second, this is a single-center experience, which may not reflect broader real-world practice. Third, the study design (case series, observational) limits any causal inference. In addition, the follow-up period was relatively short, and outcomes were primarily assessed based on echocardiographic parameters rather than long-term clinical endpoints, such as recurrent PE, functional capacity, or development of chronic thromboembolic pulmonary hypertension (CTEPH). These factors may restrict the strength of the conclusions.

In conclusion, this case series adds to the growing evidence identifying US-CDT as a safe and effective reperfusion strategy in carefully selected patients with acute PE in whom systemic thrombolysis is contraindicated. While short-term hemodynamic and clinical improvements are encouraging, larger multicenter prospective randomized trials are required to define the optimal patient selection criteria, dosing protocols, long-term clinical outcomes, and cost-effectiveness of this advanced therapeutic modality.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - P.H., B.G., O.K., G.K., O.N.H., E.Y., İ.Y.; Planning and Design - B.G., P.H., O.N.H., İ.Y., E.Y., O.K., G.K.; Supervision - P.H., O.N.H., O.K., G.K., B.G., İ.Y., E.Y.; Funding - P.H.; Materials - E.Y., İ.Y., O.K.; Data Collection and/or Processing - B.G.; Analysis and/or Interpretation - P.H.; Literature Review - G.K., P.H.; Writing - P.H.; Critical Review - O.N.H.

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RESPIRATORY CASE REPORTS

The Effect of Colchicine on the Treatment of Recurrent Pleural Effusion with Unknown Etiology

Etiyolojisi Bilinmeyen Tekrarlayan Plevral Efüzyon Olgusunun Tedavisinde Kolşisinin Etkisi

Sinem Ersoy, Tibet Uğur Kurak, Erhan Ayan

Abstract

Pleural effusion is an abnormal accumulation of fluid in the pleural space that can result from a variety of etiological factors, ranging from benign to malignant. Despite investigations, the etiological cause remains undetermined in 20–25% of patients. In the case presented here, pleural fluid regressed with colchicine therapy in a patient with a history of recurrent pleural effusion, the etiology could not be determined, despite treatment with nonspecific antibiotic and non-steroidal anti-inflammatory drugs. The therapeutic benefit of oral colchicine therapy for the treatment of pleural effusions that occur after lung resection or conditions with known etiologies, such as pericarditis and Familial Mediterranean Fever (FMF), has been well documented in the literature. Its potential for the treatment of pleural effusions with unknown etiology has also been documented.

Keywords: *Pleural effusion, colchicine, thoracoscopy.*

Öz

Plevral effüzyon plevral boşlukta anormal sıvı birikimi olup benign sebeplerden malign sebeplere kadar birçok etiyolojik faktörden kaynaklanabilir. Bunun yanında tüm incelemelere rağmen %20-25'lik hastada etiyolojik sebep saptanamaz. Bu olgu sunumunda yapılan etiyolojik araştırmalara rağmen sebebi saptanamayan, verilen spesifik olmayan antibiyoterapi ve nonsteroid antiinflamatuvar tedavi rejimlerine rağmen tekrarlayan plevral effüzyon öyküsü mevcut hastada plevral sıvının kolşisin ile regrese olmasından bahsedilmektedir. Oral kolşisin tedavisinin; güncel literatürde akciğer rezeksiyonu sonrasında oluşan veya perikardit ve Ailevi Akdeniz Ateşi (FMF) gibi etiyolojik sebebi belli plevral effüzyonlarda terapötik rolü vardır. Bunlarla birlikte etiyolojisi bulunamayan plevral efüzyonlarda ise potansiyel olarak kullanım söz konusudur.

Anahtar Kelimeler: *Plevral efüzyon, kolşisin, torakoskopi.*

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Pleural effusion is characterized by the abnormal accumulation of fluid within the pleural space between the visceral and parietal pleura. It has many possible causes, including infective, malignant, and systemic inflammatory disorders, and congestive heart failure in particular. The accumulations of fluid can impair lung expansion during inspiration by preventing adequate lung expansion (1).

Pleural effusions can arise from a variety of causes, ranging from spontaneously resolving conditions to those with significant prognostic implications, such as cancer or congestive heart failure. Previous studies have reported 1-year mortality rates in the range of 25–57% in patients with non-malignant pleural effusions. Given the direct impact on treatment choice, identifying the underlying cause is vital (2). Pathophysiologically, effusions are generally classified as transudative or exudative. Transudative effusions are usually caused by systemic disturbances in fluid homeostasis (increased pulmonary capillary pressure or decreased plasma oncotic pressure), as seen in heart failure, nephrotic syndrome, and cirrhosis. In contrast, exudative effusions are usually associated with localized inflammatory (such as bacterial pneumonia and tuberculosis) or malignant processes (3).

The diagnostic approach to pleural effusion begins with clinical evaluation, as patients may be asymptomatic or present with symptoms such as dyspnea, cough, or chest pain. Physical examination may reveal dullness to percussion in the affected area, while auscultation may reveal decreased breath sounds. Diagnostic methods include chest radiography, thoracic ultrasonography, computed tomography, microbiological, and biochemical and cytological examinations of pleural fluid obtained by diagnostic thoracentesis, as well as histopathological examinations of pleural biopsy specimens. Thoracentesis, preferably performed under ultrasound guidance, is a valuable diagnostic procedure that also provides symptomatic relief. Standard analysis of aspirated pleural fluid includes tests such as protein and lactate dehydrogenase (LDH) levels, pH, gram stain and cytological examination, adenosine deaminase measurement, and culture. Light's criteria are systematically applied to differentiate pleural effusions based on pathophysiology (exudative/transudative). If initial tests are inconclusive, further investigations may be necessary, such as bronchoscopy, percutaneous pleural biopsy, or thoracoscopy (3). Treatments of benign pleural effusions are primarily directed at the treatment of the underlying systemic disease (4), while different treatment strategies exist for malignant pleural effusions (Table 1).

We present here the case of a 42-year-old female patient with left pleural effusion and a history of recurrent hospitalizations for which the underlying cause could not be found, despite all investigations, who was treated with colchicine.

Table 1: Therapeutic strategies for malignant pleural effusions (5)

Simple observation	
Systemic chemotherapy for underlying malignancy	
Repeated thoracentesis	
Chest tube drainage alone (tube thoracostomy)	
Pleurodesis	Physical Chemical Biological Mechanical
Pleural catheters	
Surgical method	Pleuroperitoneal shunt Pleurectomy
Other measures	Intrapleural chemotherapy Radiotherapy for chylothorax Intrapleural fibrinolytic agents for multiloculated effusions
Supportive and symptomatic	(oxygen, opiates, etc.)

CASE

A 42-year-old female presented with complaints of dyspnea and dry cough. She appeared morbidly obese and had normal vital signs. Breath sounds were absent at the base of the left hemithorax. Her heart rate and rhythm were normal. Abdominal examination revealed some hepatomegaly and splenomegaly. No clubbing or edema was observed in her extremities. Her hemogram, electrolyte, and coagulation parameters were normal, as were the results of liver, kidney, and thyroid function tests, and oncological markers were within the normal range. Rheumatological markers were negative.

A pleural effusion forming a Damoiseau line in the left hemithorax was identified on posteroanterior (PA) chest X-ray (Figure 1). After pleural effusion was confirmed by thorax CT, PET-CT imaging was conducted for malignancy investigation due to the patient's rural habitat, and her suspected exposure to pesticides and asbestos.

FDG PET imaging revealed a pleural effusion measuring 2.5 cm deep in the left hemithorax (Figure 2).

Detailed echocardiography and color Doppler examination revealed no cardiac pathology, no valvular pathology, and no signs of pulmonary hypertension. Abdominopelvic CT revealed enlargement of the liver and spleen and an umbilical hernia was present. Portosplenic color Doppler US revealed a liver measuring 180 mm and spleen measuring 130 mm craniocaudally.

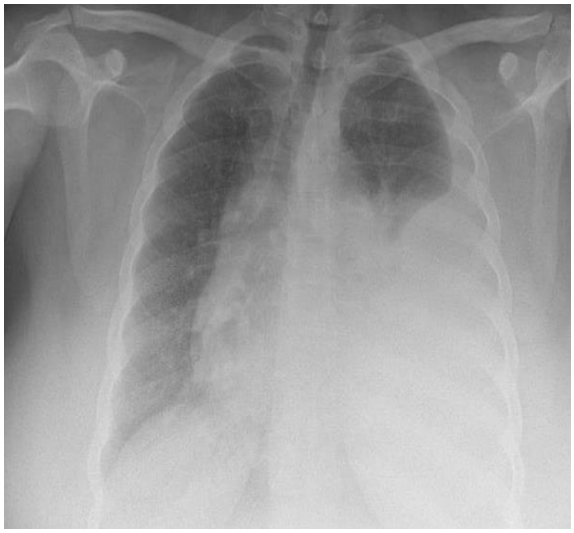


Figure 1: PA chest radiograph of the patient at the time of her initial presentation.

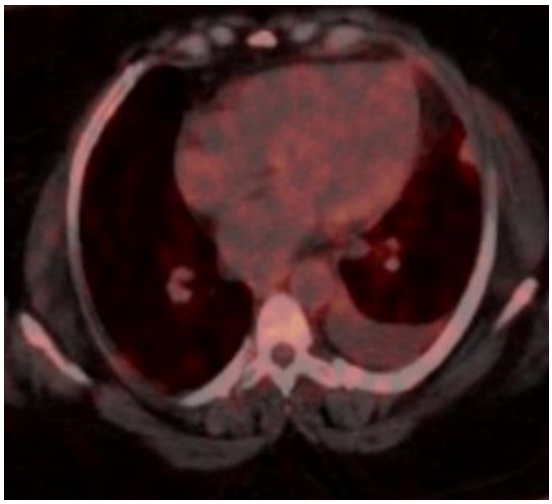


Figure 2: Left pleural effusion identified on PET-CT performed to rule out malignancy (SUVmax, 3.5).

Cell count analysis of the pleural fluid sample obtained from the patient revealed 800 erythrocytes and 300 leukocytes per mm^3. Biochemical analysis of the pleural fluid showed an LDH level of 90 U/L, glucose 95 mg/dL, total protein 41 g/dL, and albumin 28 g/dL. Simultaneously obtained peripheral blood samples demonstrated a LDH level of 169 U/L, total protein 60 g/dL, blood glucose 76 mg/dL, and albumin 38 g/dL. Light's criteria applied to the pleural effusion and serum samples indicated that the fluid was exudative. Pleural tuberculosis culture and Acid-fast bacilli (AFB) staining were negative, as were pleural fluid and other cultures. The patient was monitored with a pleural catheter that was terminated upon the cessation of drainage and the patient was discharged. The patient presented with similar complaints 1 month later, when chest radiograph revealed an increase in the left pleural effusion, and video-assisted thoracoscopic surgery (VATS) was performed. The biopsy revealed no evidence of malignancy or inflammation. Despite all treatments and tests, the patient's pleural effusion recurred, and the etiology remained unknown. The patient was started on a non-steroidal anti-inflammatory drug (NSAID) containing ibuprofen at a dose of 600 mg twice daily. After continuing this treatment for approximately 5 months, the pleural effusion showed progression again. The patient was given 2 grams of intravenous ceftriaxone twice a day intermittently during hospitalization for surgical prophylaxis. Colchicine therapy was started at a dose of 0.5 mg twice daily as the etiology of the condition could not be determined, despite cytological, biochemical, and pathological examinations and the lack of response to NSAID therapy. The oral colchicine treatment continued for 3 months, after which the patient's pleural effusion was found to have completely resolved, and there was no recurrence (Figure 3). The patient was followed for a total of 5 months with intermittent hospitalizations, and subsequently for an additional 4 months through outpatient clinic visits.

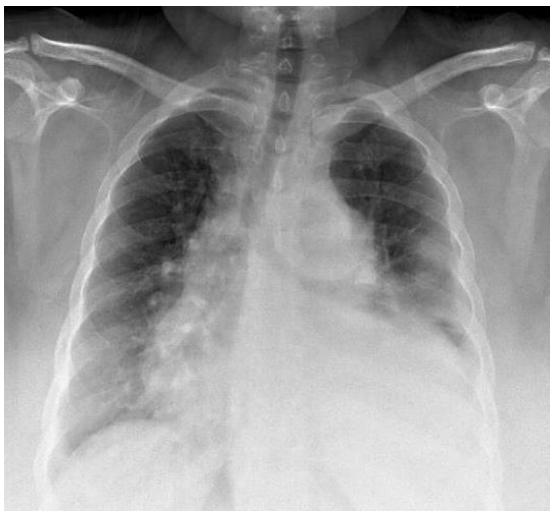


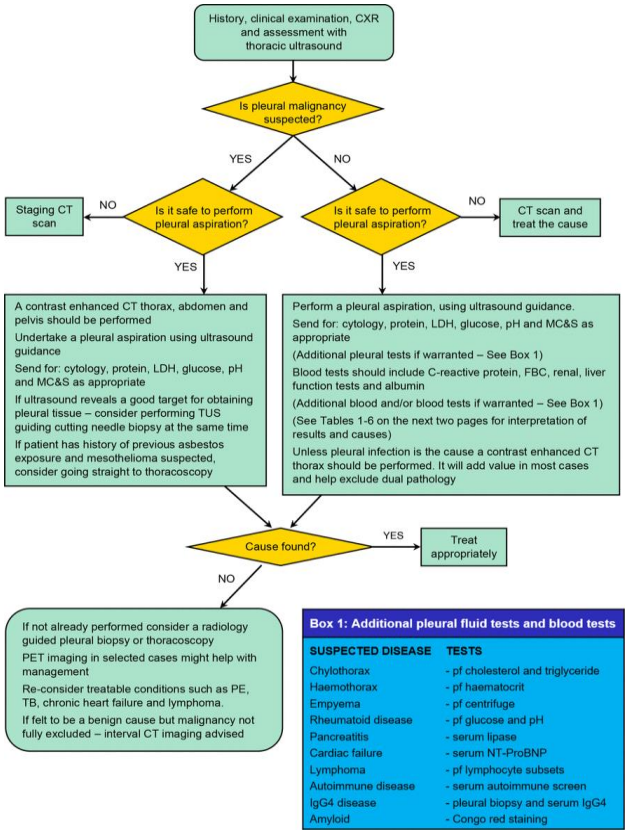
Figure 3: PA chest radiograph after oral colchicine treatment.

DISCUSSION

Pleural effusion is a common condition encountered in daily life, and determining its etiology is crucial for monitoring and treatment. In a significant number of patients, a definitive etiology can remain undetermined, despite comprehensive examinations that include biochemical and microbiological tests, cytological examinations of pleural fluid, and thoracic computed tomography (CT). This diagnostic uncertainty often necessitates invasive procedures such as VATS for the thorough direct examination and biopsy of the pleural space, although the findings of such interventions may still be insufficient for a specific diagnosis (5,6). A wide range of etiological causes exist that include both benign and life-threatening conditions. Practical challenges may also arise if the invasive and non-invasive tests required for etiological diag-

nosis are not readily available in primary care settings. Consequently, patients may require symptomatic treatment before the underlying cause of the effusion is identified to facilitate prompt intervention. Although evidence-based guidelines, such as those published by the British Thoracic Society in 2010, are helpful in structuring the assessment of unilateral pleural effusions (Table 2), there remains a paucity of data guiding clinical decision-making in many areas (7).

Table 2: British Thoracic Society Guidelines for Pleural Disease: Unilateral Pleural Effusion Diagnostic Pathway



In the present case, a systematic and comprehensive investigation was undertaken to identify the cause of the effusion. The most common etiologies were methodically excluded. Congestive heart failure was ruled out following a cardiology consultation, which included an echocardiogram and a pro-B-type natriuretic peptide (ProBNP) level of 45 pg/mL, and the exudative nature of the fluid further argued against this diagnosis. Pneumonia was deemed unlikely due to the atypical clinical presentation, the absence of infiltrates on radiological imaging, and non-supportive laboratory and cytological findings. Potential systemic causes were also investigated. Subsequently, cirrhosis was excluded based on normal liver function test results and the lack of intra-abdominal ascites, despite the presence of hepatosplenomegaly. Tuberculosis was also ruled out after acid-fast bacilli (AFB) stains and cultures from both pleural fluid and tissue samples yielded negative results. Similarly, renal pathology and nephrotic syndrome were not considered, given the patient's normal urea, creatinine, albumin, total protein, and urinalysis levels, estimated glomerular filtration rate (eGFR), and normal renal ultrasonography.

Further investigations for less common causes also proved unrevealing. To evaluate for Meigs syndrome, tumor markers (CA-125, CA-19.9, CA-15.3, CEA, AFP) were measured and an abdominopelvic CT was performed, and all results were negative. Other malignancies were considered unlikely based on negative oncological markers. Yellow nail syndrome, rheumatological diseases, and hypothyroidism were systematically excluded based on physical examination and normal laboratory results. The possibility of a pesticide-induced effusion was discounted, as the fluid accumulation progressed even after the cessation of exposure. Despite this range of tests, cytological examinations, biochemical and microbiological examinations, and two separate pleural biopsies performed in accordance with the guidelines in our patient, no specific etiology was detected. An estimated 20–25% of pleural effusions remains undiagnosed, even after thorough biochemical, microbiological, cytological, and pathological evaluation, and is subsequently termed idiopathic or nonspecific. This clinical dilemma is well documented in the literature. In a large study of 3,077 patients with pleural effusions in Spain, no underlying cause could be identified in 94 cases (8). Similarly, a Belgian study reported that 25% of cases evaluated by thoracoscopy were diagnosed with nonspecific pleuritis, and no specific etiology was found within a 1-year follow-up period (9).

Given the refractory and idiopathic nature of our patient's effusion, a literature review was conducted to investigate alternative anti-inflammatory treatments. Studies reporting the successful use of colchicine for the resolution of pleural effusions in patients with underlying inflammatory conditions such as pericarditis, Familial Mediterranean Fever (FMF), and Postcardiac Injury Syndrome were identified in the review. For example, a randomized pilot study published in the European Journal of Cardio-Thoracic Surgery involving 100 patients undergoing lobectomy reported that colchicine administration significantly reduced daily pleural drainage volume when compared with a placebo group (10). Case reports further support its effectiveness, including one detailing a 16-year-old female with FMF and recurrent pleural effusion whose condition resolved completely after the initiation of oral colchicine therapy (11). In a case in Taiwan, an 82-year-old female with postpericardiotomy syndrome and severe steroid-resistant pleural and pericardial effusions entered rapid remission after starting treatment with a combination of colchicine and steroids, with no recurrence report-

ed after 2.5 months of treatment and 1 year follow-up (12).

Colchicine exerts its therapeutic effect by inhibiting microtubule polymerization in leukocytes, leading to the suppression of neutrophil migration and activation, the down-regulation of inflammasome (e.g. NLRP3)-mediated IL-1β and other pro-inflammatory cytokine releases, and the reduction of endothelial activation/permeability.

As a result, capillary permeability decreases and exudative fluid formation in serosal cavities becomes less likely — an effect clearly demonstrated during the treatment and prevention of acute and recurrent pericarditis, where colchicine significantly reduces symptom duration and recurrence risk.

For pleural effusion, these same anti-inflammatory mechanisms suggest a potential benefit, particularly in cases with an inflammatory (exudative) basis – for example, idiopathic, post-surgical or inflammatory pleural effusions.

Moreover, beyond the pleura and pericardium, colchicine has also been used to treat recurrent serositis involving other serosal surfaces (e.g. peritoneum) in which the suppression of inflammasome-mediated cytokine releases and neutrophil recruitment may similarly reduce pathological serous fluid accumulation (13-15).

To the best of our knowledge there have been no studies to date reporting the use of colchicine for the treatment of idiopathic pleural effusions with an uncertain etiology, despite all biochemical, microbiological, cytological, and pathological investigations. In our clinic, colchicine had not previously been used for therapeutic purposes in any patient with unknown etiology of pleural effusion. In this case report, colchicine therapy was administered for the first time in the mentioned patient.

There is a lack of prospective data in the literature quantifying the success rate of colchicine in the treatment of benign pleural effusions prior to pleurectomy, with available evidence being limited to small series and case reports on specific inflammatory conditions. These include familial Mediterranean fever and idiopathic recurrent serositis, in which colchicine has been reported to be effective in resolving pleural effusions and preventing recurrence. It should be noted that colchicine is not currently recommended as a standard therapy for benign pleural effusions in major guidelines, and its use in our patient was therefore off-label and individualized.

CONCLUSION

Pleural effusions are a common clinical condition that, if left untreated, can be associated with significant morbidity and mortality. Treatments for effusions of known etiology generally involve the treatment of the underlying disease, the options for idiopathic pleural effusions are quite limited. Given its known anti-inflammatory mechanism and documented efficacy in other inflammatory diseases that cause pleural effusions, oral colchicine therapy should be considered as a potential treatment option for patients with recurrent idiopathic pleural effusions.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.E., T.U.K., E.A.; Planning and Design - S.E., T.U.K., E.A.; Supervision - S.E., T.U.K., E.A.; Funding -; Materials -; Data Collection and/or Processing - S.E., T.U.K., E.A.; Analysis and/or Interpretation - S.E., T.U.K., E.A.; Literature Review - S.E., E.A.; Writing - S.E., T.U.K., E.A.; Critical Review - S.E., T.U.K., E.A.

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A Case of Leptospirosis Causing Pulmonary Hemorrhagic Syndrome

Pulmoner Hemorajik Sendroma Neden Olan Leptospiroz Olgusu

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Abstract

Leptospirosis is a zoonotic infection caused by Leptospira spirochetes. We present here the case of a 31-year-old male with alveolar hemorrhage, renal, and hepatic dysfunction who reported abdominal pain and weakness after cleaning out a warehouse containing rats 2 weeks earlier. Physical examination revealed abdominal tenderness but no other significant findings. As his clinical condition worsened, he developed cough and shortness of breath. Chest radiography revealed bilateral consolidation, and computed tomography (CT) of the chest revealed ground-glass opacities. Bronchoalveolar lavage pathology identified hemosiderin-laden macrophages. Leptospirosis testing confirmed antibodies against L. icterohaemorrhagiae with a titer of 1/800. The patient was placed on antibiotic therapy, corticosteroids, and plasmapheresis. Following treatment, his symptoms and laboratory results improved, and he was discharged.

Keywords: *Pulmonary hemorrhage, leptospirosis, Weil Disease.*

Öz

Leptospiroz, leptospira cinsi spiroketlerin neden olduğu zoonotik bir hastalıktır. Bu yazıda, alveoler hemoraji, böbrek ve karaciğer fonksiyon bozukluğu olan bir olgu sunuldu. Otuz bir yaşında erkek hasta, karın ağrısı ve halsizlik şikayeti ile başvurdu. Anemnezinden 2 hafta öncesinde farelerin bulunduğu bir depoyu temizlediği öğrenildi. Fizik muayenesinde batında hassasiyet dışında bulgu saptanmadı. Klinik, radyolojik ve laboratuvar parametrelerinin takibi sırasında hastada öksürük ve nefes darlığı şikayetleri ortaya çıktı. Bilgisayarlı toraks tomografisinde her iki akciğerde dağınık yamasal buzlu cam dansiteleri saptandı. Bronkoalveolar lavaj patolojisinde hemosiderin yüklü makrofajlar izlendi. Hastadan leptospiroz için gönderilen tetkik sonucunda L. icterohaemorrhagiae antikoru 1/800 titrede pozitif saptandı. Multisistemik tutulumu olan hastanın tedavisinde antibiyoterapi, kortikosteroid ve plazmaferez uygulandı. Tedaviler sonrasında hastanın semptomları ve laboratuvar değerlerinde düzelme sağlanarak hasta taburcu edildi.

Anahtar Kelimeler: *Pulmoner hemoraji, leptospirozis, Weil Hastalığı.*

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Pleural effusion is characterized by the abnormal accumulation of fluid within the pleural space between the visceral and parietal pleura. It has many possible causes, including infective, malignant, and systemic inflammatory disorders, and congestive heart failure in particular. The accumulations of fluid can impair lung expansion during inspiration by preventing adequate lung expansion (1).

Leptospirosis is a zoonotic disease caused by spirochetes of the Leptospira genus. It is commonly observed in tropical regions and in our country (1). Infection typically occurs as a result of direct contact with infected animals or contaminated water or soil. The disease is most frequently seen among farmers, soldiers, miners, veterinarians, and sewer workers (2). The clinical presentation of leptospirosis can range from asymptomatic or mild cases in 90% of cases to severe forms such as Weil's disease or pulmonary hemorrhagic syndrome (PHS) with multi-organ involvement in the remaining 10%. Pulmonary hemorrhagic syndrome is one of the leading causes of death in leptospirosis and has a mortality rate of 40–60% (3). We present here a case of leptospirosis characterized by pulmonary hemorrhagic syndrome that was treated with plasmapheresis and high-dose steroids. Written informed consent was obtained from the patient prior to the preparation of this report.

CASE

A 31-year-old male patient presented to the emergency department with complaints of abdominal pain and weakness. No significant findings were noted in the patient's medical history. A detailed anamnesis revealed that the patient, who is a refugee in our country, had been employed to clean out a warehouse in which rats were present 2 weeks prior to the onset of symptoms.

Physical examination revealed no findings other than abdominal tenderness. Laboratory tests performed in the emergency department produced the following results: urea, 239.3 mg/dL (17–43); creatinine, 6.31 mg/dL (0.67–1.17); AST, 50.3 U/L (0-50); ALT, 52.3 U/L (0–50); CRP, 249.8 mg/L (0–5); WBC, 1900/mm^3; Neutrophils, 1500/mm^3; Hb, 15.2 g/dL (12–17); and Platelets, 39,000/mm^3. Arterial blood gas analysis indicated metabolic acidosis. After initial assessment, the patient underwent hemodialysis and was started on empirical ceftriaxone therapy. Following initial assessment and acute management in the emergency department, the patient was transferred to the Infectious Diseases Department for further inpatient care. While monitoring the clinical, radiological, and laboratory parameters, the patient developed cough and shortness of breath, along with elevated total bilirubin levels and decreased platelet count, leading to the administration of plasmapheresis. Therapeutic plasma exchange was conducted within the Infectious Diseases inpatient service throughout the patient's admission (Table 1).

Table 1: *Laboratory findings according to the patient's hospitalization days*

Lab Findings	Admission	Day 3	Day 5	Day 8	Day 10	End of therapy
HB (g/dL)	15.2	10.1	9.9	10.1	8.6	9.7
WBC (/mm^3)	1900	7820	12600	20500	9100	10600
Neutrophil (/mm^3)	1500	4800	8300	17000	7660	6500
Thrombocyte (/mm^3)	39000	27000	31000	305000	541000	374000
Urea (mg/dL)	239	132	129	26	36	35
Creatinine (mg/dL)	6.31	2.6	2	0.7	0.6	0.8
AST (U/L)	50	33	35	55	31	42
ALT (U/L)	52	41	39	55	56	73
Total Bilirubin (mg/dL)	2.64	10.6	14.6	25.4	6.6	2.8
CRP (mg/L)	249	137	43.6	31	7.8	4.1

Serological tests, including direct and indirect Coombs, Anti-HAV IgM, Anti-HCV, Anti-HIV, HBsAg, Brucella IgG, IgM, Anti-CMV IgM, and EBV IgM, were all negative. Peripheral blood examination showed no plasmodium infection. Cultures of blood, urine, sputum, and bronchoalveolar lavage revealed no growths. The bronchoalveolar lavage culture was negative for acid-fast bacilli. Reverse transcription PCR and a respiratory virus panel also returned negative results.

In the radiological findings, a chest X-ray at the time of admission was evaluated as normal, while a follow-up chest X-ray on the 5th day after the onset of respiratory symptoms revealed consolidation areas in all bilateral lung zones (Figure 1). A chest computerized tomography (CT) revealed scattered patchy ground-glass densities in both lungs (Figure 2).

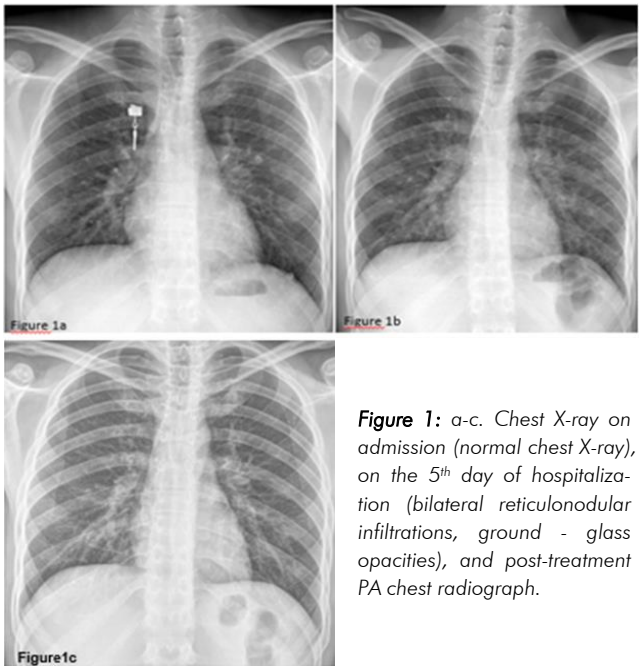

Figure 1: *a-c. Chest X-ray on admission (normal chest X-ray), on the 5th day of hospitalization (bilateral reticulonodular infiltrations, ground - glass opacities), and post-treatment PA chest radiograph.*

Magnetic resonance cholangiopancreatography (MRCP) was normal. Bronchoscopy revealed no endobronchial lesions, while hemosiderin-laden macrophages were noted in bronchoalveolar lavage pathology. The leptospirosis test results showed a positive antibody titer of 1/800 for *L. icterohaemorrhagiae*. The analysis was performed using the ELISA method.

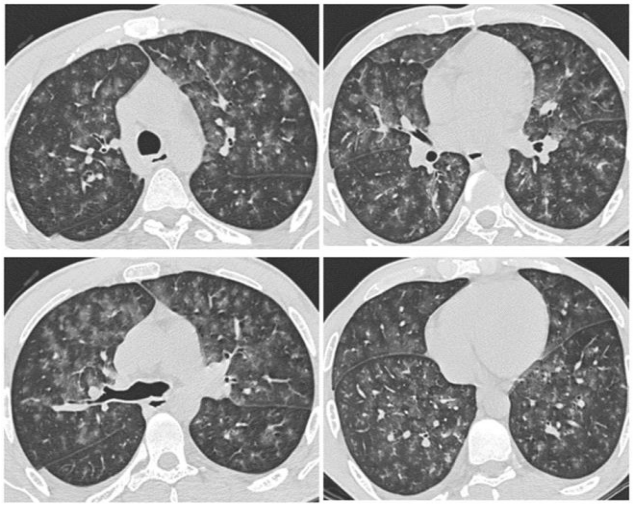

Figure 2: *Bilateral ground-glass opacities seen on thorax CT on the 5th day of hospitalization*

Alveolar hemorrhage due to leptospirosis was suspected based on anamnesis, clinical, laboratory, and radiological findings, for which the patient was started on ceftriaxone therapy. The patient was referred to the Pulmonology Department due to respiratory symptoms and radiologic abnormalities observed on chest imaging. After bronchoscopic lavage, high-dose methylprednisolone (500 mg/day) was added to the treatment, and the dosage was gradually reduced every 3 days, ultimately being discontinued after 15 days. Ceftriaxone therapy was completed to a total duration of 14 days and subsequently discontinued.

On the 3rd day of methylprednisolone treatment, the patient's respiratory symptoms started to decrease, bilirubin levels dropped, and platelet count returned to normal. Following treatment, the patient was discharged in a stable condition.

DISCUSSION

In cases of leptospirosis, pulmonary involvement may present with mild respiratory symptoms or pulmonary hemorrhage and acute respiratory distress syndrome (ARDS), accompanied by high fever, thrombocytopenia, renal failure, and jaundice (4,5). Clinical manifestations, including cough, dyspnea, and hemoptysis, typically emerge after the 4th day of illness. In pulmonary leptospirosis, reticular and nodular consolidations in the bilateral lower lung zones are revealed by chest radiography (6). High-resolution computed tomography (HRCT) typically demonstrates diffuse areas of consolidation with ground-glass opacities affecting all pulmonary lobes (7). In our patient, thrombocytopenia, hyperbilirubinemia, and renal failure were evident from the onset of illness. From the 5th day onward, pulmonary manifestations and radiographic abnormalities became more prominent, in line with previously reported findings in the literature. Clinical, laboratory, and radiological findings of leptospirosis are nonspecific and can be observed in many other diseases, and so differential diagnosis includes numerous infectious diseases, including influenza, HIV during the seroconversion period, dengue fever, viral hemorrhagic fevers, typhoid fever, malaria, brucellosis, rickettsioses, viral hepatitis, infectious mononucleosis, encephalitis, poliomyelitis, hantavirus infections, and respiratory infections such as viral pneumonia, bronchopneumonia, and tuberculosis (8). Leptospira infection is typically linked to exposure to contaminated water and may show jaundice and conjunctival suffusion, which are useful distinguishing signs. Hantavirus infection is associated with inhalation of rodent excreta and is characterized by either severe pulmonary edema (cardiopulmonary syndrome) or prominent renal involvement with thrombocytopenia (hemorrhagic fever with renal syndrome). Rickettsial infections are transmitted by ticks or lice and often present with an eschar or a petechial rash due to endothelial vasculitis. Differences in exposure history, presence of rash or eschar, and the pattern of organ involvement are central to the differentiation of these infections in clinical practice. In our case, the differential diagnosis from other diseases was established based on serological methods and cultures.

For the treatment of leptospirosis, antibiotic therapy should be initiated early to shorten the duration of symptoms, reduce morbidity and mortality, and decrease the urinary excretion of the microorganism. In addition to antibiotic therapy, patients should be closely monitored for such life-threatening complications as dehydration, hypotension, severe hemorrhage, and prolonged renal failure, and supportive treatments should be initiated.

In mild cases, oral doxycycline, azithromycin, and amoxicillin are preferred, while severe cases will require the parenteral administration of such agents as penicillin G, doxycycline, ceftriaxone, or cefotaxime (9–11). Previous studies in the literature include case reports documenting the use of corticosteroids, plasmapheresis, and extracorporeal membrane oxygenation (ECMO) for the management of leptospirosis-associated pulmonary hemorrhagic syndrome and acute respiratory distress syndrome (ARDS) (12–14).

Publications have reported that mortality can be reduced in affected patients through the early administration of high-dose methylprednisolone when respiratory symptoms become prominent, and plasmapheresis performed in conjunction with corticosteroid therapy (1,12,15). Our case was started on ceftriaxone for antibiotic therapy and underwent plasmapheresis. Subsequently, high-dose methylprednisolone was administered due to the development of pulmonary hemorrhage. Following treatment, a prompt resolution of clinical manifestations, radiological abnormalities, and laboratory findings was observed.

In conclusion, although rare, leptospirosis can cause pulmonary hemorrhagic syndrome with high mortality. In the presence of a relevant history and appropriate clinical and laboratory findings, the early initiation of antibiotic therapy is recommended. When respiratory symptoms develop, the addition of corticosteroids and plasmapheresis to the treatment should be considered as they may reduce mortality.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - E.A.A., L.Ö., S.G., M.U., O.G.; Planning and Design - L.Ö., E.A.A., S.G., M.U., O.G; Supervision - O.G, E.A.A., S.G., M.U., L.Ö.; Funding -; Materials - S.G., M.U., O.G; Data Collection and/or Processing - S.G., M.U.; Analysis and/or Interpretation - E.A.A.; Literature Review - E.A.A., L.Ö.; Writing - E.A.A.; Critical Review - L.Ö.

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Isolated Diffuse Alveolar Hemorrhage as the Initial Presentation of Microscopic Polyangiitis: A Case Report

İzole Alveoler Hemoraji ile Başlayan Mikroskobik Polianjiit: Olgu Sunumu

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Abstract

Microscopic polyangiitis, a necrotizing small-vessel vasculitis, typically presents with renal involvement and pulmonary-renal syndrome, while diffuse alveolar hemorrhage (DAH) as the sole initial presentation without concurrent glomerulonephritis is exceedingly rare and diagnostically challenging. We present here the case of a 68-year-old female with massive hemoptysis, hypoxemia, and radiologic evidence of bilateral ground-glass opacities, in whom bronchoalveolar lavage confirmed DAH. Coagulation parameters were within normal limits and infectious and cardiogenic causes were excluded. Despite initially preserved renal function, the presence of MPO-ANCA positivity established the diagnosis of microscopic polyangiitis. The patient exhibited rapid clinical improvement following high-dose corticosteroids and cyclophosphamide, although renal dysfunction developed during follow-up. This case underscores the need to consider ANCA-associated vasculitis in patients with isolated pulmonary hemorrhage. Early immunologic evaluation and bronchoscopic confirmation are critical for timely diagnosis and therapeutic intervention, even in the absence of extrapulmonary findings.

Keywords: *Microscopic Polyangiitis, Diffuse Alveolar Hemorrhage, ANCA-associated Vasculitis, Bronchoalveolar Lavage.*

Öz

Mikroskobik polianjiit (MPA), genellikle böbrek tutulumuyla seyreden nekrotizan bir küçük damar vaskülitidir ve sıklıkla pulmoner–renal sendrom tablosu ile tanı alır. Ancak yalnızca akciğer tutulumu ile başlayan olgular oldukça nadirdir ve tanının gecikmesine neden olabilir. Bu olguda, hemoptizi ve hipoksemi ile başvuran ve toraks bilgisayarlı tomografide bilateral buzlu cam opasiteleri olan, bronkoalveoler lavaj ile alveoler hemoraji tanısı konulan 68 yaşındaki bir kadın hasta sunulmaktadır. Koagülasyon testleri normal saptanmış, enfeksiyöz ve kardiyojenik nedenler dışlanmıştır. Yüksek MPO-ANCA düzeyleri ile MPA tanısı kesinleşmiş, kortikosteroid ve siklofosfamid tedavisine hızlı klinik yanıt alınmıştır. Başlangıçta böbrek fonksiyonları korunmuş olsa da takipte renal disfonksiyon gelişmiştir. Bu olgu, böbrek bulguları olmaksızın başlayan mikroskobik polianjiitin tanıda göz ardı edilebileceğini göstermektedir. Alveoler hemoraji ile başvuran hastalarda ANCA ilişkili vaskülitler, sistemik tutulum olmasa da erken dönemde mutlaka değerlendirilmelidir.

Anahtar Kelimeler: *Mikroskobik Polianjiit, Diffüz Alveoler Hemoraji, ANCA ilişkili Vaskülit, Bronkoalveoler Lavaj.*

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Diffuse alveolar hemorrhage (DAH) is a life-threatening condition characterized by acute hypoxemia, hemoptysis, and radiologic infiltrates, resulting from disruption of the alveolar-capillary membrane (1,2). Autoimmune diseases – particularly ANCA-associated vasculitides – are among the leading causes of DAH, among which microscopic polyangiitis (MPA) is the subtype most commonly associated with pulmonary involvement, often presenting concurrently with glomerulonephritis (3,4). In rare cases, MPA may present with isolated pulmonary involvement, limited exclusively to alveolar hemorrhage without any renal manifestations (5,6). The absence of systemic findings in such cases frequently results in delayed diagnosis. For this reason, once infection, cardiogenic pulmonary edema, and drug-induced toxicity are excluded in patients presenting with hemoptysis, immunologic etiologies should be considered. Notably, ANCA-associated vasculitides should remain a central component of the differential diagnosis, even in the absence of renal involvement (2,4). We present here a rare case of MPA with isolated pulmonary involvement, underscoring its relevance in the differential diagnostic process.

CASE

A 68-year-old female presented to the emergency department with progressively worsening dyspnea over the past week and the expectoration of approximately 200 mL of blood-tinged sputum. Her medical history included atrial fibrillation treated with rivaroxaban, hypertension, and prior radioactive iodine (RAI) therapy for thyrotoxicosis. Notably, she had been hospitalized 2 months earlier due to a gastrointestinal hemorrhage associated with anticoagulant therapy. She had no history of tobacco use or substance abuse.

The patient was alert, cooperative, and oriented at the time of presentation. Vital signs revealed a heart rate of 112 beats per minute, blood pressure of 92/58 mmHg, respiratory rate of 26 breaths per minute, and a body temperature within normal limits. Her oxygen saturation (SpO_2 85%) indicated hypoxemia in room air, which improved to 92% with 2 L/min of supplemental oxygen via nasal cannula. Pulmonary auscultation revealed diffuse bilateral crackles across all lung fields. Cardiac and other systemic examinations were unremarkable. Physical examination also revealed +1 bilateral pretibial edema.

Laboratory evaluation revealed a hemoglobin level of 7 g/dL with no evidence of leukocytosis, eosinophilia, lymphopenia, or thrombocytosis. C-reactive protein (CRP) was elevated at 31 mg/L (reference range, 0–5 mg/L). Blood urea nitrogen and serum creatinine were 33 mg/dL and 1.36 mg/dL, respectively. Urinalysis showed 3 RBCs/HPF and 14 WBCs/HPF, with no proteinuria, and no dysmorphic erythrocytes or casts observed on microscopic examination. Liver function was within normal limits. The patient was receiving rivaroxaban therapy for atrial fibrillation, and her international normalized ratio (INR) was 1.38.

Posteroanterior chest radiography performed in the emergency department revealed bilateral, centrally distributed consolidations extending toward the periphery, most prominently involving the middle lung zones. Pulmonary computed tomography (CT) angiography showed no filling defects suggestive of acute pulmonary thromboembolism, but revealed bilateral pleural effusions, each measuring approximately 2 cm in depth. Additionally, diffuse ground-glass opacities and areas of consolidation were observed in both lungs, predominantly in the lower lobes and extending from central to peripheral regions (Figure 1).

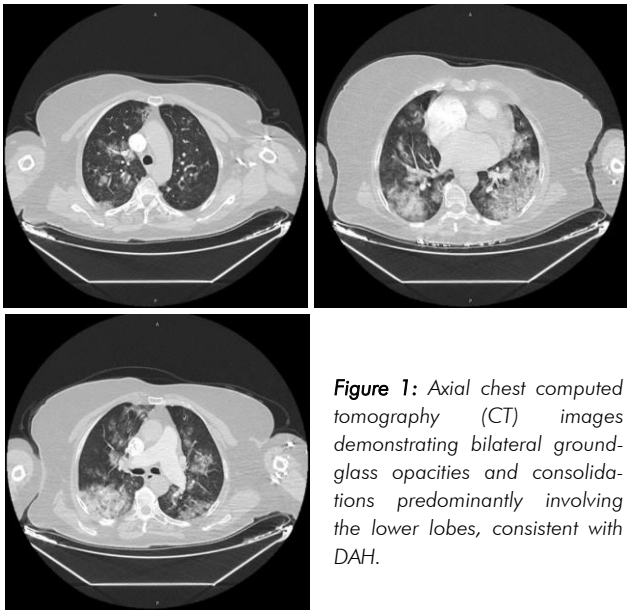

Figure 1: Axial chest computed tomography (CT) images demonstrating bilateral ground-glass opacities and consolidations predominantly involving the lower lobes, consistent with DAH.

Based on these findings, the patient was admitted to the inpatient unit with a presumptive diagnosis of alveolar hemorrhage, and urgent fiberoptic bronchoscopy was planned. Bronchoscopic examination revealed all lobar and segmental bronchial orifices to be bilaterally patent, and diffuse hemorrhagic foci in both lungs. During bronchoalveolar lavage (BAL), a progressive increase in hemorrhagic content was noted in sequential samples. The overall findings were considered consistent with alveolar hemorrhage. Infectious etiologies were excluded, and a respiratory viral panel performed on BAL fluid was negative.

In light of the clinical, laboratory, and radiological findings, the differential diagnosis included drug-induced toxic lung injury, infection-associated alveolar hemorrhage, and DAH secondary to autoimmune vasculitides

Table 1: Clinical Course and Management Timeline

Day / Time	Clinical Findings	Diagnostic Workup	Lab / Imaging	Treatment
Day 0 (Admission)	Hemoptysis, dyspnea, SpO_2 85% room air → 92% with 2lt/dk O_2	CXR, CT angio, bronchoscopy planned	Hb 7 g/dL, Cr 1.36, BUN 33, CRP 31, INR 1.38, Urinalysis: 3 RBC/HPF, 14 WBC/HPF, no proteinuria, bilateral consolidations, pleural effusions, ground glass opacity	Rivaroxaban stopped, O_2, IV piperacillin–tazobactam, PRBC planned
Day 1	Persistent hemoptysis	Bronchoscopy + BAL	Progressively hemorrhagic BAL, viral panel negative	Antibiotics continued, PRBC transfusion
Days 2–3	Ongoing hemoptysis, anemia	Autoantibody panel	Hb decline, MPO-ANCA >200, Lupus anticoagulant (+)	IV MP 1 g/day x 3
Days 4–7	Clinical/radiologic improvement	Follow-up labs	Hb stable, renal function worsening	Steroid taper (500 → 250 → 100 mg)
2nd week	Renal dysfunction, stable lungs	Lab monitoring	Cr 2.50 mg/dL	IV cyclophosphamide 1 g, MP 60 mg/day, enoxaparin after hemoptysis resolved
Post-stabilization	Stable respiratory status	—	—	Transferred to rheumatology clinic for further management

or connective tissue diseases. On admission, the patient was treated with rivaroxaban for atrial fibrillation. Rivaroxaban was discontinued due to DAH, while anticoagulation was withheld during the acute bleeding period. Empirical intravenous piperacillin-tazobactam (3 × 4.5 g) was initiated in light of her recent hospitalization and elevated CRP levels. The transfusion of two units of packed red blood cells was planned in view of her profound anemia.

To investigate possible autoimmune vasculitis, a rheumatology consultation was requested, and a comprehensive autoantibody panel was ordered, including c-ANCA, p-ANCA, rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP), anti-glomerular basement membrane (anti-GBM), antinuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), complement components C3 and C4, anti-tissue transglutaminase (anti-tTG), anti-endomysial IgA, anticardiolipin antibody, anti-β2 glycoprotein I, and lupus anticoagulant.

Persistent hemoptysis and a progressive decline in hemoglobin levels during follow-up, despite the red blood cell transfusion, prompted re-evaluation in consultation with the rheumatology team. Based on clinical judgment, intravenous methylprednisolone was initiated at a dose of 1 g/day, which the patient received for three consecutive days, followed by a tapering regimen of 500 mg, 250 mg, and 100 mg/day. Marked clinical and radiological improvement was achieved during corticosteroid therapy (Figure 2); however, the patient experienced progressive deterioration in renal function, with rising levels of blood urea nitrogen and serum creatinine, the latter reaching 2.50 mg/dL.

The autoantibody panel revealed a markedly elevated myeloperoxidase (MPO)-ANCA level (>200), consistent with MPA, along with a positive lupus anticoagulant. The results were reviewed by a multidisciplinary team that included rheumatology and pulmonary medicine specialists. The lupus anticoagulant positivity was deemed clinically insignificant, and the patient was subsequently managed under a diagnosis of MPA. Based on a consensus decision, treatment continued with intravenous cyclophosphamide (1 g) and systemic methylprednisolone at a dose of 60 mg/day. After stabilization and resolution of hemoptysis, therapeutic-dose enoxaparin was initiated and maintained during immunosuppressive induction. In the subsequent follow-up phase, the patient was transferred to the rheumatology clinic for continued management and monitoring. The chronological clinical course is summarized in Table 1.

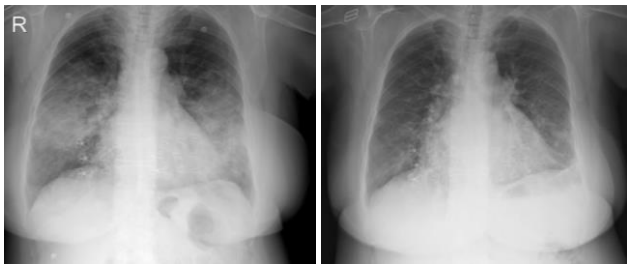

Figure 2: Posteroanterior chest radiographs at initial presentation (left) and at discharge (right). The admission image demonstrates bilateral perihilar and lower zone consolidations, consistent with DAH.

DISCUSSION

DAH is defined as bleeding from the pulmonary microvasculature – including alveolar capillaries, arterioles, and/or venules – and is clinically characterized by hypoxemia, alveolar infiltrates on imaging, and, in some cases, hemoptysis (3–7).

DAH is a clinical condition associated with high morbidity and mortality if not diagnosed promptly (2). Although it can occur in all age groups, it is most frequently diagnosed between the ages of 30 and 50 years, with a predominance among male patients (2,8). Notably, the present case deviates from these typical demographic patterns, as the patient is female and falls outside the usual age range.

The clinical presentations of DAH can vary widely. The most frequently reported symptoms include dyspnea, hemoptysis, cough, and hypoxemia, although such classical findings may not always be present, with hemoptysis in particular occurring in only approximately two-thirds of cases (2,9). It should thus be kept in mind that some patients may exhibit an atypical course, characterized solely by progressive hypoxemia or anemia (8). In the presented case, dyspnea, hemoptysis, and hypoxemia were all evident at the time of admission. On physical examination, fine diffuse crackles may be heard, as in the presented case, although this finding is nonspecific (3). Radiologically, chest X-rays frequently reveal bilateral, patchy, or diffuse infiltrates, which – similar to our case – may be more prominent in the lower lobes and exhibit rapid temporal changes. CT, particularly high-resolution CT (HRCT), offers greater diagnostic sensitivity, with the most common radiologic finding being ground-glass opacity, often accompanied by areas of consolidation. In some cases, a crazy-paving pattern may also be observed (10).

The underlying etiologies of DAH are highly heterogeneous and are generally classified into two main categories: immune-mediated, and non-immune (2,3). Immune-mediated mechanisms are more common and primarily include ANCA-associated vasculitides (e.g., granulomatosis with polyangiitis and MPA), connective tissue diseases (e.g., systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis, and dermatomyositis), and anti-glomerular basement membrane disease, also known as Goodpasture syndrome (3,9). In contrast, non-immune causes include coagulopathies, cardiogenic conditions such as mitral stenosis, and exposure to various drugs – most notably anticoagulants, cocaine, amiodarone, and nitrofurantoin – as well as radiation therapy, sepsis, and hematologic malignancies (2,10). Among the immune-mediated causes, ANCA-associated vasculitides are the most frequently encountered. In particular, MPA should be considered a prominent diagnosis in the differential diagnosis of DAH (2,3).

MPA typically presents as part of pulmonary-renal syndrome. Pulmonary involvement is reported in 25–50% of cases, while renal involvement occurs in 80–90% (11–13). That said, there are records of cases with isolated pulmonary manifestations in the absence of renal involvement (14). This atypical presentation may contribute to delayed diagnosis, late initiation of treatment, and a higher risk of complications (4,5). Pulmonary involvement most commonly presents as DAH (9), with reported prevalences in the range of 10–50% (15). Less commonly, pulmonary patterns such as interstitial lung disease, nodular infiltrates, pleural effusion, and pulmonary hypertension have been described (16,17).

The most striking feature of the presented case is the exclusive presence of pulmonary manifestations at the time of admission, with no evidence of renal involvement. Classically, MPA presents as pulmonary-renal syndrome, and diagnosis most commonly established based on signs of glomerulonephritis (3). In some cases, however, alveolar hemorrhage may be the initial – and occasionally the sole – manifestation of the disease, potentially leading to delays in diagnosis (5,6). Establishing a diagnosis can be particularly challenging when patients present with severe hemoptysis but with preserved renal function and normal urinalysis, without such findings as hematuria or proteinuria. In our case, renal function was preserved on admission, and only alveolar hemorrhage was evident, which suggested that the vasculitic process was initially localized to the lungs, with systemic involvement emerging later in the disease course (5). Delays in the diagnosis and the initiation of immunosuppressive therapy in such cases may contribute to increased morbidity. For this reason, in patients presenting with severe alveolar hemorrhage and preserved renal function, ANCA-associated vasculitis should be considered early in the differential diagnosis (1,2).

In the presented case, anticoagulant-associated hemorrhage was initially considered due to the patient's history of rivaroxaban use. However, several findings supported a vasculitic etiology, including a normal INR, progressively increasing hemorrhagic content during BAL, and a marked clinical response to corticosteroid therapy (2,3,5). In addition, anticoagulation management represented a critical challenge due to the coexistence of atrial fibrillation and DAH. Rivaroxaban was discontinued at admission, and anticoagulation was reintroduced with enoxaparin after stabilization. Low-molecular-weight heparin was preferred due to its shorter half-life, reversibility, and flexibility in the event of re-bleeding, which is consistent with the current consensus on the management of DOAC-associated bleeding (18). Overall, while anticoagulant-associated bleeding could not be entirely excluded, the overall clinical context favored ANCA-associated vasculitis as the primary cause of DAH.

Lupus anticoagulant positivity was also a notable finding in our case. According to the revised Sapporo (Sydney)

classification criteria, confirmed APS requires both persistent laboratory positivity (≥12 weeks apart) for lupus anticoagulant, anticardiolipin, or anti-β2 glycoprotein I antibodies, and at least one clinical manifestation, such as arterial/venous thrombosis or pregnancy morbidity (19). In our patient, lupus anticoagulant was detected once, while anticardiolipin and anti-β2 glycoprotein I antibodies were negative. Repeat testing at 12 weeks could not be performed due to the acute disease course. Clinically, there was no history of thrombosis, obstetric morbidity, or thromboembolic events during hospitalization. Although APS could not be fully excluded in the absence of follow-up testing, the lack of supporting laboratory and clinical features made this diagnosis unlikely. In addition, previous reports have shown that lupus anticoagulant positivity in the context of autoimmune vasculitis – particularly during periods of active inflammation – may be transient and not necessarily indicative of APS (6). Overall, the constellation of MPO-ANCA positivity, renal dysfunction, and DAH was more consistent with ANCA-associated vasculitis.

Bronchoscopic evaluation plays a central role in the diagnosis of DAH, with two main goals: to confirm the presence of alveolar hemorrhage through BAL, and to rule out alternative sources of bleeding within the airways, as well as concomitant conditions such as infection. In our case, alveolar hemorrhage was confirmed bronchoscopically via BAL; however, progressively hemorrhagic BAL aliquots, while diagnostic of DAH, are not specific for MPA or other etiologies. In our patient, the vasculitic cause was inferred from the overall clinical, serologic, and radiologic constellation rather than from BAL findings alone.

The use of high-dose intravenous methylprednisolone followed by cyclophosphamide is the recommended treatment protocol for DAH secondary to ANCA-associated vasculitis. In our case, a rapid clinical response to corticosteroid therapy was observed; but immunosuppressive treatment was escalated with the addition of cyclophosphamide due to the subsequent development of renal involvement (3,5). Favorable outcomes with such immunosuppressive regimens have also been reported in the literature, including cases with isolated pulmonary involvement in MPA (5). As the patient was transferred to a specialized center after stabilization, cumulative cyclophosphamide exposure, maintenance therapy, and prophylactic measures (e.g., *Pneumocystis jirovecii* pneumonia and osteoporosis prevention) were not initiated in our department. This represents a limitation of the present report, as detailed long-term therapeutic data could not be provided.

CONCLUSIONS

We describe here a rare case of isolated pulmonary MPA who presented exclusively with pulmonary involvement and without renal manifestations at the time of admission. The diagnosis was supported by MPO-ANCA positivity, characteristic findings on BAL, and a favorable clinical response to immunosuppressive therapy. Contributing to the existing literature, this case highlights the possibility of delayed systemic involvement in MPA and emphasizes that diagnosis should not rely solely on renal findings. Early ANCA testing and prompt bronchoscopic evaluation should thus be considered critical components of the diagnostic workup in patients presenting with DAH.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - B.Y.K., O.E.T., G.Ç.A., S.U.D.; Planning and Design - B.Y.K., O.E.T., G.Ç.A., S.U.D.; Supervision - B.Y.K., O.E.T., G.Ç.A., S.U.D.; Funding -B.Y.K., O.E.T., G.Ç.A., S.U.D.; Materials - B.Y.K., O.E.T.; Data Collection and/or Processing - B.Y.K., O.E.T.; Analysis and/or Interpretation - B.Y.K., O.E.T., G.Ç.A., S.U.D.; Literature Review - B.Y.K., O.E.T.; Writing - B.Y.K., O.E.T.; Critical Review - B.Y.K., O.E.T., G.Ç.A., S.U.D.

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Acute Eosinophilic Pneumonia as a Rare Cause of Acute Onset Respiratory Failure

Akut Başlangıçlı Solunum Yetmezliğinin Nadir Bir Nedeni Olarak Akut Eozinofilik Pnömoni

Mustafa Nadir Tantay, Kutay Arkoc, Damla Serçe Unat, Ahmet Emin Erbaycu

Abstract

Acute eosinophilic pneumonia (AEP) is a rare but life-threatening pulmonary disease characterized by the acute onset of respiratory symptoms, hypoxemia, and diffuse pulmonary infiltrates. Its clinical presentation is often mistaken for pneumonia or acute respiratory distress syndrome, leading to diagnostic delay. We report the case of a 59-year-old female who presented with a 3-week history of dyspnea and cough and was initially treated with antibiotics for presumed pneumonia. During follow-up, progressive peripheral eosinophilia, eosinophils in bronchoalveolar lavage, histopathological findings, and radiological progression supported the diagnosis of AEP. Spirometry performed before discharge demonstrated an obstructive pattern with significant bronchodilator reversibility; however, clinical and physical findings did not support asthma. Subsequently, the reversible obstruction was attributed to transient airway inflammation associated with AEP. Methylprednisolone (1 mg/kg) was initiated, resulting in rapid and dramatic clinical improvement. This case highlights the importance of considering AEP in the differential diagnosis of antibiotic-refractory pneumonia, the diagnostic value of spirometry findings, and the effectiveness of corticosteroid therapy.

Keywords: *Acute eosinophilic pneumonia, hypereosinophilia, bronchoalveolar lavage, corticosteroid.*

Öz

Akut eozinofilik pnömoni (AEP), ani başlangıçlı solunum semptomları, hipoksemi ve yaygın akciğer infiltrasyonları ile seyreden, nadir fakat mortal seyirli bir akciğer hastalığıdır. Klinik tablo sıklıkla pnömoni veya akut solunum sıkıntısı sendromu (ARDS) ile karıştırılabilir ve bu durum tanıda gecikmeye yol açabilir. Burada üç haftadır devam eden dispne ve öksürük yakınmaları ile başvuran, başlangıçta pnömoni tanısı alarak antibiyotik tedavisi başlanan 59 yaşında kadın hasta sunulmaktadır. Takipte artan periferik eozinofili, bronkoalveoler lavajda eozinofil varlığı, histopatolojik bulgular ve radyolojik progresyon ile AEP tanısı desteklenmiştir. Taburculuk öncesi yapılan spirometride obstrüktif patern ve bronkodilatör sonrası anlamlı reversibilite saptanmış; ancak klinik ve fizik muayene bulguları astımı desteklememiştir. Bu bulgular, akut eozinofilik pnömoni sürecinde gelişen geçici hava yolu inflamasyonu ve obstrüksiyona bağlanmıştır. Hastaya 1 mg/kg dozunda metilprednizolon başlanmış ve kısa sürede dramatik klinik iyileşme sağlanmıştır. Bu olgu, antibiyotik tedavisine yanıtsız pnömonilerde AEP'nin ayırıcı tanıda akılda tutulması gerektiğini, spirometrik bulguların tanısal katkısını ve kortikosteroid tedavisinin etkinliğini vurgulamaktadır.

Anahtar Kelimeler: *Akut eozinofilik pnömoni, hipereozinofili, bronkoalveoler lavaj, kortikosteroid.*

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Acute eosinophilic pneumonia (AEP) is a rare but severe lung disease characterized by acute onset of respiratory symptoms, hypoxemia, and diffuse pulmonary infiltrates. It was first described by Allen et al. in 1989 (1). AEP typically occurs in young, previously healthy individuals and is often associated with the recent initiation of cigarette smoking or exposure to inhaled agents. Clinically, it is characterized by rapidly progressive nonspecific symptoms, including fever, cough, dyspnea, chest pain, and fatigue. As a result of this presentation, it is often mistaken for community-acquired pneumonia or acute respiratory distress syndrome (ARDS). Peripheral blood eosinophilia is usually absent at disease onset or appears in later stages, which makes diagnosis more challenging (2). Radiologically, bilateral ground-glass opacities, consolidation, and frequently pleural effusion are observed. On chest computed tomography (CT), interlobular septal thickening and prominence of bronchovascular structures are also typical (3). Systemic corticosteroids are the mainstay treatment, and most patients show rapid clinical response within 24–48 hours. Delays in treatment may result in severe respiratory failure and mortality. Relapse is uncommon and is usually associated with re-exposure to the triggering agent (4). We present here a rare case of AEP to contribute to the literature and to increase clinical awareness.

CASE

A 59-year-old female was admitted to the emergency department with complaints of dyspnea and cough persisting for approximately 3 weeks. She had previously been hospitalized in the pulmonology department with a diagnosis of pneumonia and type 1 respiratory failure, where she received intravenous antibiotic therapy, followed by oral antibiotics upon discharge. After discharge, her dyspnea, cough, and pleuritic chest pain worsened, leading to multiple visits to the emergency room, after which she was discharged with symptomatic treatments.

The patient had no history of respiratory complaints until 3 weeks before her latest presentation. Her past medical history was notable only for hyperlipidemia, with no history of smoking, organic or inorganic exposure, or significant family history. She was housewife.

On admission, her vital signs were as follows: blood pressure, 101/60 mmHg; heart rate, 92 bpm; body temperature, 36.4°C, and oxygen saturation, 91% on room air. She was alert and cooperative. Chest auscultation revealed bilateral rhonchi in the middle and lower lung zones, while other systemic examination results were unremarkable.

Laboratory findings showed leukocytosis (14,000/mm^3); CRP, 12 mg/L; and marked peripheral eosinophilia (2,950/mm^3). Arterial blood gas analysis revealed pH, 7.409; pO_2, 62.4 mmHg; pCO_2, 36.9 mmHg; HCO_3, 22.9 mmol/L; and oxygen saturation, 92.7%. A retrospective review of prior records revealed an eosinophil count of 740/mm^3 during the patient's initial hospitalization for pneumonia which had risen to 2,120/mm^3 at an emergency visit 1 week earlier last hospitalization.

Thoracic CT demonstrated patchy ground-glass opacities and consolidation in both upper lobes, similar to the CT obtained 3 weeks earlier. However, the lesions in the right lung had progressed, and a new lesion had appeared in the left lung (Figure 1). A viral swab was taken to exclude possible viral infections, but revealed no causative agent. Despite continued moxifloxacin therapy, her respiratory symptoms persisted, and she was re-admitted due to unresolved pneumonia and worsening hypoxemia, with differential diagnoses of unresolved pneumonia or eosinophilic lung disease.

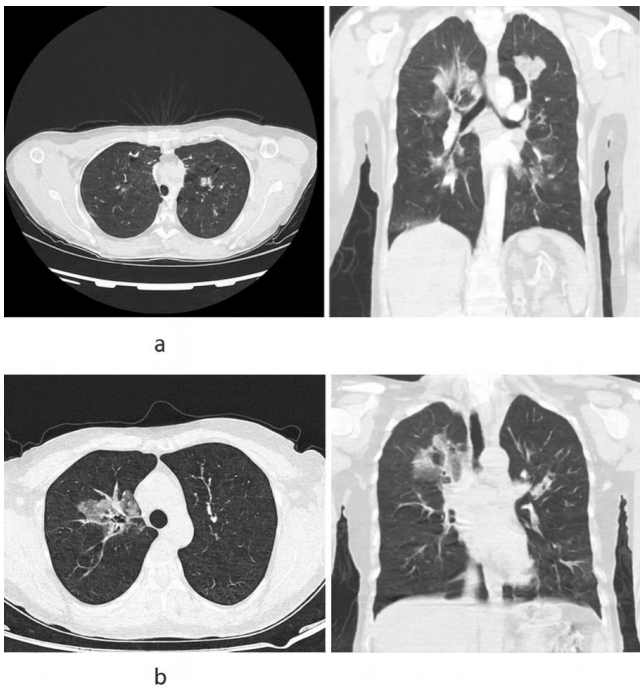

Figure 1: Imaging during follow-up under the diagnosis of pneumonia. Chest radiograph and thorax CT obtained during follow-up following a provisional diagnosis of bacterial pneumonia (a). Chest CT and radiograph before hospitalization after repeated emergency admissions, consistent with the diagnosis of acute eosinophilic pneumonia (b).

No drug exposures that could be associated with eosinophilia were identified. Total serum IgE was 42.91 IU/mL, and Aspergillus-specific IgE was <0.10 IU/mL. Stool examination was unremarkable. Rheumatologic evaluation excluded vasculitis and other systemic diseases. Consultation with the allergy and immunology department excluded ABPA and hypereosinophilic asthma.

Spirometry performed prior to the patient's discharge after her symptoms resolved revealed an FEV_1/FVC ratio of 52.7%; FEV_1, 550 mL (22% predicted); and FVC,

1050 mL (33% predicted). Post-bronchodilator values were FEV_1/FVC, 65.4%; FEV_1, 790 mL (32% predicted); and FVC, 1210 mL (38% predicted), with significant reversibility in FEV_1. Clinical and physical examination findings did not support asthma. The reversibility observed during pulmonary function tests was attributed to transient airway inflammation and obstruction that developed during acute eosinophilic pneumonia.

Hematology consultation showed leukocytosis with 25% eosinophils on peripheral blood smear. Bone marrow aspiration was performed to exclude hypereosinophilic syndrome. The bone marrow was normocellular (75%) and showed mature granulocytic forms, prominent eosinophilic lineage, dysplastic changes in megakaryocytes, and decreased erythroid series.

Fiberoptic bronchoscopy revealed BAL cytology with 60% neutrophils, 10% eosinophils, 10% alveolar macrophages, and 10% epithelial cells. Biopsy specimens demonstrated 10–15 eosinophils within the bronchial epithelium.

A diagnosis of AEP was made considering the patient's clinical presentation; laboratory and radiological findings; and the exclusion of other causes. She was started on methylprednisolone at 1 mg/kg, leading to a rapid improvement of respiratory symptoms.

At follow-up, her symptoms had resolved, chest X-ray demonstrated regression (Figure 2), and spirometry showed significant improvement: FEV_1/FVC, 74%; FEV_1, 1650 mL (66% predicted); and FVC, 2220 mL (70% predicted). Corticosteroid therapy was tapered and discontinued, and the patient remains stable under joint follow-up by the pulmonology and allergy departments.

DISCUSSION

Acute eosinophilic pneumonia (AEP) is a rare pulmonary disorder characterized by rapid-onset dyspnea, cough, diffuse pulmonary infiltrates, and eosinophilic inflammation that typically responds dramatically to corticosteroid therapy. It often mimics infectious pneumonia, leading to delays in diagnosis (5). Patients are commonly treated with antibiotics without improvement, as in our case. Our patient's progressive clinical course, increased eosinophil counts, worsening ground-glass opacities on chest CT, and BAL findings supported the diagnosis.

Although the presence of ≥25% eosinophils in bronchoalveolar lavage (BAL) fluid is regarded as a classical diagnostic criterion, recent studies have demonstrated that AEP can be diagnosed even when the eosinophil percentage is lower, provided that clinical and radiological features are strongly supportive (6).

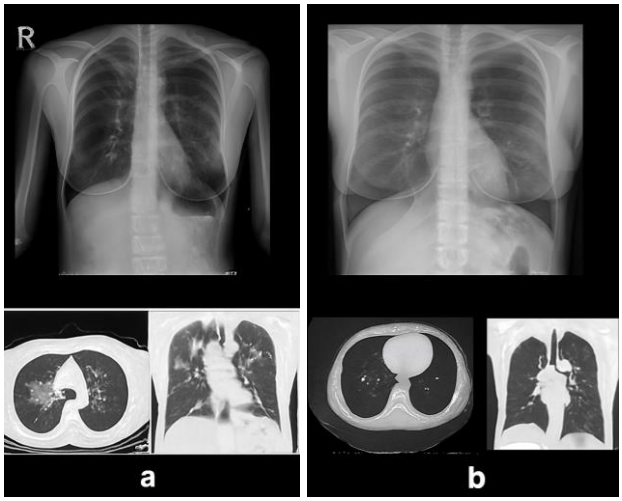

Figure 2: Thoracic imaging obtained before the initiation of steroid therapy (a). Thoracic imaging obtained following steroid therapy (b).

In our case, the patient had a 3-week history of dyspnea and cough refractory to antibiotics, bilateral patchy ground-glass opacities, and marked peripheral eosinophilia (2,950/mm^3). Despite the BAL eosinophil proportion being only 10%, the presence of 10–15 intraepithelial eosinophils in bronchial biopsy specimens, the exclusion of infectious and systemic causes, and the rapid improvement with corticosteroid therapy supported the diagnosis of AEP.

The diagnostic criteria proposed by Allen et al. (1) included acute febrile respiratory illness, bilateral infiltrates, BAL eosinophilia >25 %, exclusion of infection and asthma, and a prompt response to corticosteroids. Philit et al. (7) later modified these criteria by extending the symptom duration to ≤1 month and removing hypoxemia as a mandatory component. De Giacomi et al. (6) emphasized that AEP can still be diagnosed when BAL eosinophils fall below 25 %, provided that compatible clinical and radiologic findings are present.

The timing of BAL sampling, prior antibiotic or corticosteroid use, and an early predominance of neutrophilic inflammation may all contribute to a lower measured eosinophil percentage. Thus, AEP should not be excluded solely on the basis of BAL eosinophil count.

In our case, BAL contained 10% eosinophils, but bronchial biopsy and bone marrow findings confirmed the diagnosis.

The pathogenesis of AEP is yet to be completely understood; however, epithelial and endothelial injury leading to the release of type 2 cytokines such as IL-33, IL-5, and IL-13 is believed to trigger eosinophil recruitment and activation within the lung parenchyma. The predominance of neutrophils in the early phase, followed by eosinophilic infiltration, reflects the dynamic immunologic course of the disease. In our case, neutrophil predomi-

nance in BAL and intraepithelial eosinophilic infiltration in biopsy specimens supported this transitional pattern (6).

The differential diagnosis of eosinophilic lung diseases includes ABPA, hypereosinophilic syndrome, EGPA, parasitic infections, and allergic asthma (8). Comprehensive clinical, immunological, parasitological, and pathological evaluations in our patient excluded these conditions.

In the differential diagnosis of eosinophilic lung diseases, non-infectious etiologies also play an important role. Drug-induced pulmonary eosinophilia is an increasingly recognized cause of eosinophilic lung disease. Several medications – including antidepressants and certain antibiotics – can trigger both acute and chronic eosinophilic pneumonia; therefore, obtaining a thorough medication history is essential in the evaluation of all eosinophilic lung syndromes, including AEP (9–11). In our patient, an extensive medication history was obtained, and drug-related pulmonary eosinophilia was not suspected.

Chronic eosinophilic pneumonia (CEP) may clinically and radiologically resemble AEP but typically follows a more subacute course progressing over weeks to months. CEP is characterized by peripheral and upper-lobe predominant consolidations, a high relapse tendency, more pronounced FeNO elevations, and prolonged corticosteroid requirements, whereas AEP presents with abrupt onset, hypoxemia, diffuse ground-glass opacities, and a dramatic steroid response. CEP has a high recurrence risk, while AEP is usually monophasic, and so the temporal pattern of symptoms is a crucial determinant in distinguishing AEP from CEP (11).

Fractional exhaled nitric oxide (FeNO) has emerged as a non-invasive biomarker in both asthma and eosinophilic lung diseases, contributing to the improved phenotyping of type 2 (T2) inflammation. Elevated FeNO levels have been frequently reported in patients with eosinophilic pulmonary syndromes, particularly in CEP and EGPA, reflecting a T2-high phenotype and providing utility in monitoring disease activity and treatment response (9). In a study of non-asthmatic eosinophilic disorders accompanied by persistent eosinophilia, higher FeNO levels were closely associated with airway obstruction and symptoms such as cough and wheezing, while no significant correlation was found between peripheral blood eosinophils and FeNO (10). These findings suggest that FeNO assessment may serve as a complementary tool for detecting T2 inflammation and identifying bronchial involvement in AEP and other eosinophilic lung syndromes (9,10).

Additionally, an eosinophilic inflammatory pattern has been demonstrated in a significant subset of COPD exacerbations. Eosinophilic COPD exacerbations are associated with lower infectious burden, reduced CRP levels, less oxygen requirement, and shorter hospital stays compared with non-eosinophilic exacerbations, and this phenotype appears to respond more favorably to corticosteroids (12). These data indicate that eosinophilic inflammation represents a shared downstream pathway not only in AEP, CEP, and hypereosinophilic syndromes, but also in such chronic airway diseases as COPD, suggesting that peripheral eosinophil count may serve as a valuable biomarker for personalizing treatment strategies across this spectrum (9,12).

Within this broad spectrum of eosinophilic inflammation, AEP stands out as the most acute and rapidly steroid-responsive form.

The cornerstone of AEP treatment is the elimination of the potential trigger and the administration of systemic corticosteroids. De Giacomi et al. (6) reported marked clinical improvement within 24–48 hours of the initiation of corticosteroid therapy and complete radiologic resolution within approximately 1 month. Similarly, our patient showed rapid clinical and spirometric improvement following methylprednisolone 1 mg/kg, with no recurrence observed after the discontinuation of therapy.

CONCLUSION

Acute eosinophilic pneumonia should be considered in cases presenting with acute or subacute respiratory failure unresponsive to antibiotics, particularly when peripheral eosinophilia or radiologic findings suggest an eosinophilic process. Our case underscores that BAL eosinophilia below 25% does not exclude the diagnosis when histopathologic, clinical, and radiologic features are supportive. Comprehensive evaluation – including the exclusion of infectious, systemic, and drug-related causes – remains essential for accurate diagnosis. Early recognition is critical, as the prompt initiation of corticosteroid therapy leads to rapid clinical and radiologic improvement and prevents unnecessary antimicrobial exposure. This case contributes to the growing understanding of the heterogeneous spectrum of eosinophilic lung diseases and highlights the importance of integrating clinical, laboratory, and histopathologic data in distinguishing AEP from other eosinophilic pulmonary syndromes.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - M.N.T., K.A., D.S.U., A.E.E.; Planning and Design - M.N.T., K.A., D.S.U., A.E.E.; Supervision - M.N.T., K.A., D.S.U., A.E.E.; Funding -; Materials -; Data

Collection and/or Processing - K.A.; Analysis and/or Interpretation - D.S.U., M.N.T.; Literature Review - D.S.U., M.N.T.; Writing - M.N.T., K.A.; Critical Review - A.E.E., D.S.U.

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Infectious Masquerade: Mucinous Adenocarcinoma of the Lung Presenting as Pneumonia

Enfeksiyöz Maskeli Balo: Akciğerin Pnömoni Şeklinde Görülen Müsinöz Adenokarsinomu

Ashok Arbat, Diti Gandhasiri, Sweta Chourasia, Swapnil Bakamwar, Parimal Deshpande

Abstract

A 63-year-old postmenopausal Asian woman with a history of breast cancer, hypertension, diabetes, and hypothyroidism presented with persistent respiratory symptoms, including chronic dry cough and exertional dyspnea. Despite multiple courses of antibiotics for presumed pneumonia, imaging revealed a non-resolving consolidation in the left lower lobe with central necrosis and air bronchogram. Given her oncological background and family history of lung cancer, malignancy was suspected. High-resolution CT and PET/CT scans revealed progressive consolidation with increased metabolic activity, raising concerns for a neoplastic process. Bronchoscopy with transbronchial cryobiopsy was performed, and subsequent histopathological examination demonstrated glandular architecture with abundant intracytoplasmic mucin and basally located nuclei, consistent with invasive mucinous adenocarcinoma of the lung. This case highlights the importance of considering underlying malignancy in patients with non-resolving pneumonia, especially in patients with a prior cancer history. Early histological confirmation is crucial for accurate diagnosis and timely oncologic management.

Keywords: *Pulmonary mucinous adenocarcinoma, non-resolving pneumonia, lung cancer, transbronchial lung cryobiopsy.*

Öz

Meme kanseri, hipertansiyon, diyabet ve hipotiroidi öyküsü olan 63 yaşında, postmenopozal Asyalı bir kadın; kronik kuru öksürük ve eforla ortaya çıkan nefes darlığı gibi solunum semptomları ile başvurdu. Tekrarlayan pnömoni düşünülerek birçok kez antibiyotik tedavisi uygulanmasına rağmen akciğer görüntülemelerinde sol alt lobda santral nekroz ve hava bronkogramı içeren, düzelmeyen bir konsolidasyon saptandı. Onkolojik öyküsü ve ailesinde akciğer kanseri bulunması nedeniyle malignite olasılığı güçlü şekilde düşünüldü. Yüksek çözünürlüklü BT ve PET/BT'de artmış metabolik aktivite gösteren progresif konsolidasyon izlendi ve bu durum neoplastik bir süreci düşündürdü. Bronkoskopi ile transbronşiyal kriyobiyopsi yapıldı. Histopatolojik inceleme; bol miktarda intrasitoplazmik müsin ve bazal yerleşimli çekirdekler içeren glandüler yapılar gözlendi ve akciğerin invazif müsinöz adenokarsinomu ile uyumlu bulundu. Bu olgu, özellikle kanser öyküsü olan ve düzelmeyen pnömonisi bulunan hastalarda altta yatan malignitenin mutlaka akılda tutulması gerektiğini vurgulamaktadır. Erken histolojik doğrulama, doğru tanı ve zamanında onkolojik tedavi için kritik öneme sahiptir.

Anahtar Kelimeler: *Pulmoner müsinöz adenokarsinom, rezolüsyon olmayan pnömoni, akciğer kanseri, transbronşiyal akciğer kriyobiyopsi.*

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Pulmonary mucinous adenocarcinoma (PMA) is a rare subtype of adenocarcinoma, the most common pathological form of lung cancer (1). It is a type of non-small cell lung cancer characterized by the excessive production and secretion of a viscous, gel-like substance called mucin, and differs from other lung adenocarcinomas in clinical presentation, treatment strategy and response, along with molecular characteristics and prognosis (2). It often presents with pneumonia-like symptoms with similar radiological findings and can therefore be diagnostically challenging. We report here on a rare case of PMA that had been misdiagnosed as pneumonia, leading to a delayed diagnosis.

CASE

A 63-year-old postmenopausal Asian woman with hypertension, diabetes, and hypothyroidism presented with chronic respiratory complaints. She had been diagnosed with breast cancer 10 years earlier, at which time she underwent mastectomy, chemotherapy (8 cycles) and radiotherapy (25 sessions), followed by maintenance oral letrozole. Her family history included lung cancer in her father and sister.

The patient had developed fever and dry cough 1 year prior to presentation, when imaging revealed a heterogeneous consolidation in the basal left lung. Symptoms partially improved with antibiotics but recurred within two months. The consolidation persisted despite intravenous therapy, prompting pulmonary referral to our center.

At presentation, she reported a year-long dry cough and exertional dyspnea for 3–4 months. Spirometry with diffusing capacity of the lungs for carbon monoxide (DLCO) revealed mild restriction. High-Resolution Computed Tomography (HRCT) revealed a large left lower lobe consolidation with air bronchograms, central necrosis, and posterobasal volume loss, initially favoring infection. Given her oncologic history and family predisposition, malignancy was also considered, but the patient declined invasive testing and was managed conservatively.

The patient re-presented 2 months later with productive cough and whitish sputum. Repeat HRCT showed an increase in the extent of consolidation (Figure 1); and she was admitted. Left basal crackles and bronchial breath sounds were noted on examination, raising suspicion for necrotizing bacterial pneumonia. The provisional diagnosis was chronic bronchitis with left-sided necrotizing non-resolving pneumonia, with possible underlying malignancy. Erythrocyte Sedimentation Rate (ESR) was 34 mm/h, and C-reactive protein (CRP) was 49.99 mg/L, while other routine labs were normal. Bronchoscopy with lavage and transbronchial lung cryobiopsy was performed. Bronchoalveolar Lavage (BAL) cultures and Gene-Xpert

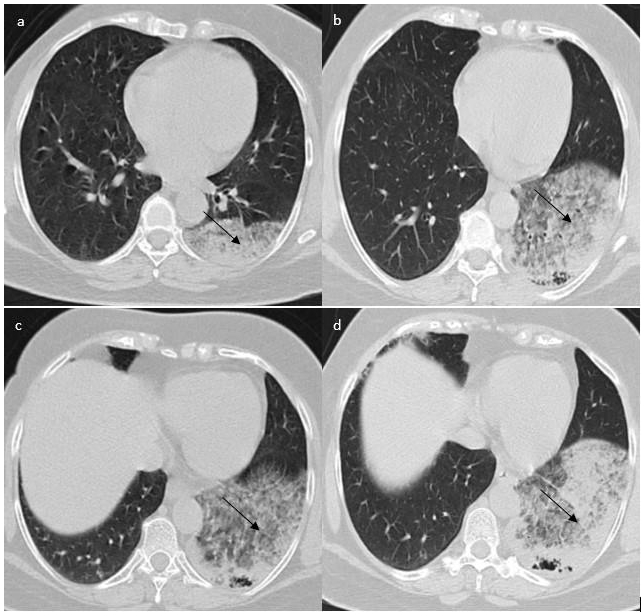

Figure 1: HRCT axial cut showing large airspace consolidation in the superior and basal segments of the left lower lobe with areas of breakdown. Interval increase in the size and density of the consolidation noted over a period of 2 months. (a) Large patchy consolidation in the left lower lobe, involving the superior segment (first consult), (b) Chest CT showing an increase in patchy consolidation and apical segments (at the time of hospitalization), (c) Large patchy consolidation in the left lower lobe involving the basal segments (first consult), (d) Increase in consolidation – basal segments (at the time of hospitalization)

were negative. Histopathological examination of the biopsy specimen revealed fragments of lung parenchyma infiltrated by glands lined with columnar epithelial cells. Intracellular mucin was abundant, being present in more than 90% of the tumor cells, and the surrounding stroma showed mixed inflammatory cell infiltrate. These findings were consistent with mucinous adenocarcinoma of the left lower lobe of the lung (Figure 2).

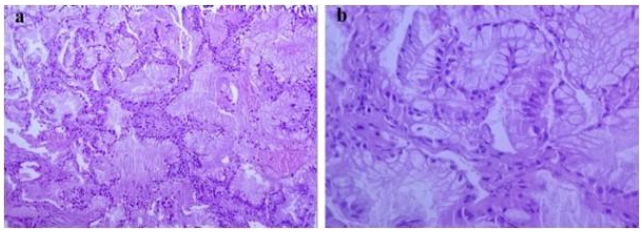

Figure 2: Histopathological examination of the cryobiopsy sample of the left lung lower lobe. (Hematoxylin and eosin, 10X and 40X). Tumor cells exhibiting goblet and columnar morphology with abundant intracytoplasmic mucin and basally located nuclei, consistent with mucinous differentiation.

Following the malignancy diagnosis, Positron Emission Tomography-Computed Tomography (PET/CT) revealed Fludeoxyglucose (FDG)-avid diffuse collapse-consolidative changes in the left lower lobe, along with minimal left-sided pleural effusion. Additionally, metabolically active circumferential soft tissue thickening, measuring 1.3 cm in thickness and approximately 4.3 cm in

length (Maximum Standardized Uptake Value [SUVmax], 13.45), was noted involving the thoracic upper esophagus and abutting the trachea. The combined findings raised concern for possible regional metastasis. The patient was diagnosed with mucinous adenocarcinoma of the lung, initially mimicking necrotizing pneumonia. The patient was referred to oncology for immunohistochemistry and systemic staging to guide treatment.

DISCUSSION

Pulmonary mucinous adenocarcinoma (PMA) is a rare subtype of lung cancer, accounting for about 5% of all adenocarcinomas (1). Its clinical and radiological similarity to infectious pneumonia represents a major diagnostic challenge (3). This case highlights how overlapping features can delay diagnosis, as the patient had been repeatedly treated with antibiotics for presumed pneumonia before malignancy was confirmed.

PMA often presents with nonspecific symptoms such as chronic cough, dyspnea, hemoptysis, and weight loss, all of which are commonly seen in other pulmonary diseases. Excessive mucus production may mimic bronchitis or pneumonia, complicating diagnosis. Our patient's persistent respiratory symptoms were initially attributed to infection, delaying recognition of PMA. Similar diagnostic difficulties have been described by Cabrera Charleston et al. (3), Daoud et al. (4), and Zirkiyeva et al. (5), where lung adenocarcinoma closely resembled pneumonia or inflammatory lung disease.

Radiology is vital, but can be misleading. PMA typically presents as lobar consolidation on chest X-ray, which is a common finding in pneumonia. HRCT provides more detail, revealing nodular and, more commonly, pneumonia-like patterns (6). Features include consolidation with ground-glass opacity, air bronchograms, or the "falling snowflake" sign described by Rossi et al. (7). Studies report solitary nodules in 43%, localized pneumonia in 40%, and diffuse pneumonia in 18% of PMA cases, correlated with varying mucus production according to Han et al. (8).

Definitive diagnosis requires histopathology. In the presented case, persistent consolidation with negative microbiological tests prompted biopsy, confirming PMA. Diagnostic tools include bronchoscopy with cryobiopsy, CT-guided aspiration, endobronchial ultrasound (EBUS)-guided sampling, thoracentesis, and surgical biopsy (9). PET/CT is crucial for staging and assessing spread (2), and revealed metastatic disease in the presented case.

Prognosis depends on tumor stage, cavitation, and the extent of metastasis. Cavitary lesions, present in 40–70% of cases, are associated with a poor outcome. While early disease without metastasis fares better, advanced PMA carries poor prognosis. Zhao et al. identified early diagnosis as critical for better management and prognosis (10).

CONCLUSIONS

Non-resolving pneumonia should not be attributed only to infection, particularly in patients with oncological risk factors. The presented case underscores the need for a multidisciplinary approach when non-resolving pneumonia is encountered, integrating imaging, histopathology, and clinical judgment to avoid misdiagnosis and improve outcomes.

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CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - A.A., D.G., S.C., P.D., S.B.; Planning and Design - A.A., D.G., S.C., P.D., S.B.; Supervision - A.A., D.G., S.C., P.D., S.B.; Funding -; Materials - A.A., D.G., P.D., S.B.; Data Collection and/or Processing - S.C., D.G.; Analysis and/or Interpretation - A.A., D.G., S.C., P.D., S.B.; Literature Review - A.A., D.G., S.C.; Writing - A.A., S.C., D.G.; Critical Review - A.A., D.G., S.C., P.D., S.B.

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Postoperative Chest Pain Unmasking a Subcarinal Mediastinal Lipoma

Postoperatif Göğüs Ağrısı ile Saptanan Subkarinal Mediastinal Lipom

Feyza Tulek[1], Abdullah Tunçez[2], Mustafa Koplay[3], Baykal Tulek[4]

Abstract

Mediastinal lipomas are rare lesions that are often missed on chest radiographs. A healthy 45-year-old male (ASA I) developed acute chest pain with palpitations in the post-anesthesia care unit after uncomplicated renal surgery. Examination, chest radiograph, and biomarkers were normal and ECG showed sinus tachycardia. The symptoms resolved with low-flow oxygen. CT/MRI the following day revealed a subcarinal fat-density mass (~6 × 5 × 8 cm) causing mild left-atrial compression. Bronchoscopy was normal; needle aspiration confirmed mature adipose tissue, consistent with lipoma. Surgery was advised but declined. This case underscores a structural cause of postoperative chest pain and the value of early cross-sectional imaging when initial evaluation is nondiagnostic.

Keywords: *Mediastinum Neoplasms, Postoperative Pain, Sinus Arrhythmia, Lipoma.*

Öz

Mediastinal lipomlar nadirdir ve akciğer grafisinde sıkça gözden kaçar. Sorunsuz bir renal cerrahi sonrası, 45 yaşındaki (ASA I) erkek hastada post-anestezi bakım ünitesinde çarpıntı ile akut göğüs ağrısı gelişti. Muayene, akciğer grafisi ve biyobelirteçler normaldi; EKG sinüzal taşikardi gösterdi ve semptomlar düşük akımlı oksijen ile geriledi. Ertesi gün BT/MR'da, sol atriyuma hafif bası yapan ~6×5×8 cm subkarinal yağ yoğunluklu kitle saptadı. Bronkoskopi normaldi; iğne aspirasyonu olgun adipöz doku lipomunu doğruladı. Cerrahi önerildi ancak hasta kabul edilmedi. Bu olgu, postoperatif göğüs ağrısında yapısal nedenleri ve tanısal olmayan durumlarda erken kesitsel görüntülemenin değerini vurgulamaktadır.

Anahtar Kelimeler: *Mediasten Tümörleri, Postoperatif Ağrı, Sinüs Aritmisi, Lipom.*

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Mediastinal lipomas account for <2% of all mediastinal tumors and are often discovered incidentally; symptoms – when present – arise from the compression of adjacent structures and include dyspnea, chest pain, palpitations, and dysphagia (1–3).

Postoperative chest pain is common and clinically important; while musculoskeletal and gastrointestinal etiologies predominate, a substantial minority is myocardial infarctions, warranting routine troponin screening in postsurgical patients with chest pain (4).

CASE

A 45-year-old male with no known comorbidities was evaluated in the pre-anesthesia clinic and was classified as ASA I prior to an elective renal operation. Intraoperative and immediate postoperative courses were uneventful.

The patient developed sudden retrosternal chest pain with palpitations in the postanesthesia care unit. Cardiovascular and respiratory examinations and the chest radiograph (Figure 1) were normal, while ECG showed sinus tachycardia without ischemic changes. Cardiac enzymes and D-dimer were within normal limits. Multidisciplinary evaluation by cardiology and pulmonary teams revealed no acute cardiopulmonary pathology. The symptoms resolved within approximately 60 minutes with 2–3 L/min nasal oxygen and no additional therapy.

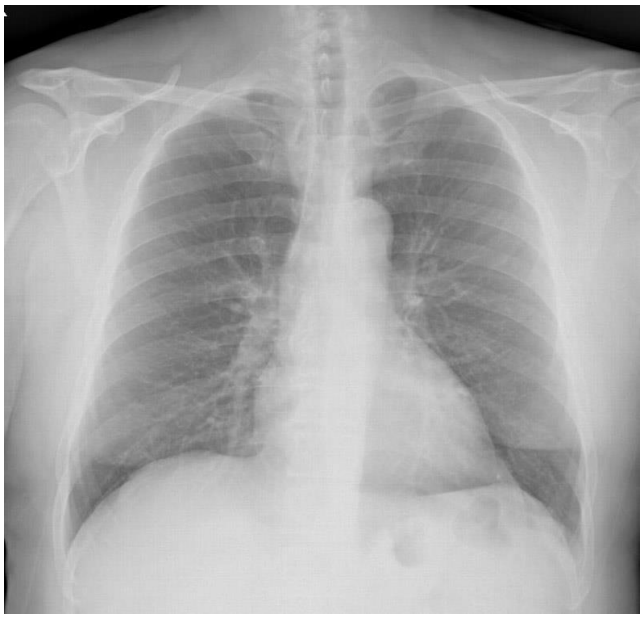

Figure 1: Chest radiograph (posteroanterior) with no remarkable radiologic features.

Given the atypical presentation, thoracic CT and cardiac MRI were obtained on postoperative day 1. Imaging revealed a well-circumscribed, subcarinal mass of homogeneous fat signal/density, measuring approximately 6×5×8 cm, compatible with lipoma, with mild extrinsic compression of the left atrium and impression on the pulmonary veins (Figures 2 and 3).

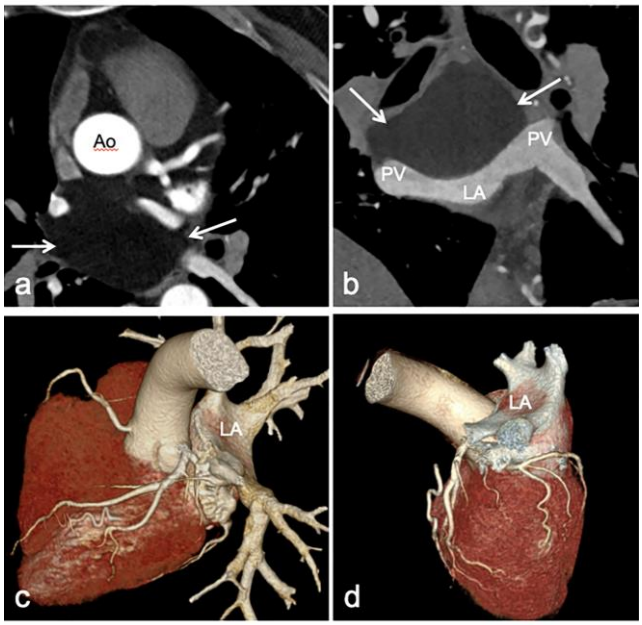

Figure 2: Coronary CT angiography. Axial (a) and coronal (b) images showing a well-circumscribed, homogeneous fat-attenuation mass consistent with lipoma. Coronal imaging (b) and 3-D volume-rendered reconstructions (c and d) demonstrate pronounced mass effect on the pulmonary veins and left atrium (Ao, aorta; PV, pulmonary veins; LA, left atrium).

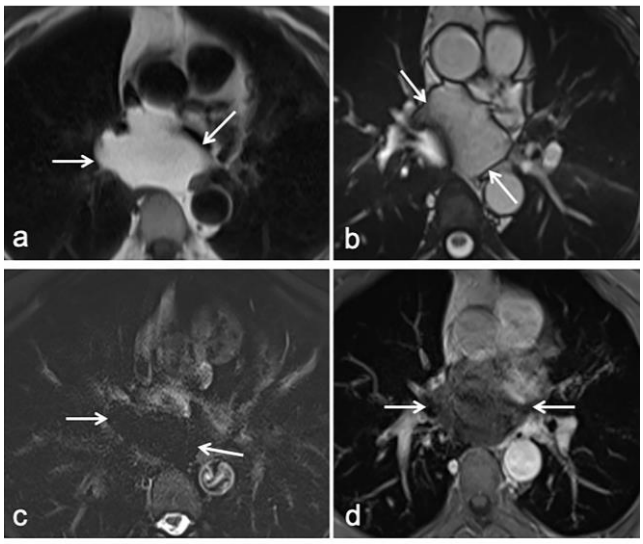

Figure 3: Cardiac MRI. Axial T1-weighted (a) and T2-weighted (b) images revealing a well-circumscribed hyperintense mass. On fat-suppressed axial T1 (c), the lesion becomes hypointense with marked signal drop, consistent with fat. The mass measures approximately 6 × 5 × 8 cm. Postcontrast axial T1 (d) revealing no pathological enhancement, supporting the diagnosis of lipoma.

Flexible bronchoscopy revealed no endobronchial lesions, while subcarinal needle aspiration yielded mature adipose tissue elements, consistent with benign lipoma. Surgical resection was recommended due to cardiac compression; however, the patient declined, citing minimal

day-to-day symptoms. A plan for clinical surveillance and interval imaging was agreed upon.

DISCUSSION

We report here an unusual cause of postoperative chest pain with sinus tachycardia: a subcarinal mediastinal lipoma compressing the left atrium. Most mediastinal lipomas are asymptomatic, but symptoms arise from mass effect. Published reports describe chest pain, dyspnea, palpitations, and dysphagia depending on the compartment and size of the tumor (2,3). Critically, routine chest radiography may miss fat-density lesions due to overlapping mediastinal silhouettes and radiolucent composition, necessitating CT/MRI for detection and characterization, as in our patient (1).

Our patient's postanesthesia care unit episode resolved rapidly with oxygen alone, and the cardiac work-up was negative. Our approach aligns with perioperative guidance advocating troponin testing in cases with postsurgical chest pain to detect occult myocardial injury/MI, which carries substantial morbidity and mortality if missed (4). The discovery of a sizable fat-density mediastinal mass with left atrial indentation provided a plausible mechanistic explanation for sinus tachycardia/palpitations via atrial stretch – an association echoed in case reports of cardiac/mediastinal lipomas compressing the left atrium and presenting with sinus tachycardia or arrhythmia (5,6).

Regarding management, contemporary series and case reports favor surgical excision when symptoms, rapid growth, or compression of cardiac/airway structures are present, although watchful waiting with serial imaging may be considered given the benign nature and low recurrence after resection (1). Multidisciplinary decision-making with cardiology, thoracic surgery, and anesthesia is essential, particularly in cases with cardiac chamber or pulmonary venous compression, even if symptoms are intermittent or mild.

CONCLUSION

Subcarinal mediastinal lipoma is a rare but noteworthy structural cause of postoperative chest pain and palpitations. Normal biomarkers/ECG do not preclude a compressive mediastinal etiology; CT/MRI can define fat-density masses that may be missed on routine chest radiographs. Multidisciplinary evaluation should balance the benign histology against potential cardiac compression, guiding individualized decisions between excision and surveillance.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - F.T., A.T., M.K., B.T.; Planning and Design - F.T., A.T., M.K., B.T.; Supervision - F.T., A.T., M.K., B.T.; Funding - F.T., A.T., M.K., B.T.; Materials - F.T., A.T., M.K., B.T.; Data Collection and/or Processing - F.T., A.T., M.K., B.T.; Analysis and/or Interpretation - F.T., A.T., M.K., B.T.; Literature Review - F.T., A.T., M.K., B.T.; Writing - F.T., A.T., M.K., B.T.; Critical Review - F.T., A.T., M.K., B.T.

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