Vertical Transmission of COVID-19 in Children of Sero-positive Mothers to SARS-CoV-2 in Southeast Mexico: A Case Report

Güneydoğu Meksika'da SARS-CoV-2 Seropozitif Annelerin Çocuklarında COVID-19'un Vertikal Bulaşısı: Bir Olgu Sunumu

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Abstract
The clinical features of Covid-19 have been described in adults and infants younger than 1 year of age, although there is little data on the characteristics and the potential of intrauterine transmission in newborns. A case of infection was identified in a baby born in Cancún Quintana Roo, in a regional hospital at the beginning of the epidemic. The patient did not require intensive care, nor were there any serious complications. The mother was infected with SARS-CoV-2, showing mild respiratory symptoms. Although 10 mothers with symptoms of SARS-CoV-2 have been observed to date, only one case of a positive newborn has been identified in the hospital. In summary, newborns are susceptible to SARS-CoV-2 infection. The SARS-CoV-2 PCR-positive newborn had no symptoms, and so SARS-CoV-2 may be considered less severe in neonates than in adults. Vertical intrauterine transmission in women who develop COVID-19 pneumonia is possible, although evidence is still lacking in Latin America and around the world.

Key words: SARS-CoV-2, Covid-19, pregnancy, newborn.

Özet

Coronavirus disease (COVID-19), caused by SARS-CoV-2, was first detected in Wuhan, China in December 2019 (1). After the disease spread exponentially around the world, an international public health emergency was declared by the World Health Organization (WHO) on January 30, 2020 (2). Mexico reported a total of 74,560 confirmed cases and 8,134 deaths on 05/26/2020 (3). SARS-CoV-2 is a member of the coronavirus family, subtype Beta-Coronavirus, with an RNA genome, that has been shown to share the Angiotensin-Converting Enzyme receptor with SARS-CoV-2 (4-7), which has a mortality rate of 10% in the general population and up to 25% in pregnant women (5,6). To date, two forms of the virus have been identified: type L (accounting for 70% of cases) and type S (30% of cases) (7).

The human transmission of SARS-CoV-2 occurs through fomites, direct contact or aerosols, resembling the spread pathways of influenza. An incubation period of 14 days has been reported, with an average of 5.2 days, and it has been shown that symptoms tend to develop an average of 2.5 days after exposure to the virus (7).

The most common manifestations of coronavirus 19 are fever, cough, fatigue, myalgia, cough with expectoration and headache, associated from abnormalities identified in the laboratory with the presence of lymphopenia, the elevation of liver enzymes, DHL, VSG, PCR, D-dimer and a prolongation of clotting times (7).

Coronavirus 19 has a high infectivity rate and develops easily in a susceptible population, and pregnant women and their newborns are included in this group (6-8). Due to the lack of records of confirmed cases in the previously mentioned population group, there is a lack of information regarding its management and the existence of vertical transmission, and so maternal-fetal complications prevail (9,10). In Mexico, newborns with COVID-19 in the first 24 hours have not been reported.

We report here on a case of probable intrauterine vertical transmission involving a patient with COVID-19 infection.

CASE

We present here the case of a 28-year-old female hospital warehouse assistant with a history of hyperthyroidism under treatment with thiamazole, and with a penicillin allergy. O+ blood type, G4A0C2P1 previous cesarean section 11 and 6 years ago due to cord to neck circulation and uncertain fetal status, P1 9 years ago with death as a result.

Background of this pregnancy: I present six threats of abortion from the beginning of the pregnancy with treatment based on Indomethacin and Micronized progesterone. It carried on a preterm delivery at hospital in the 31st week of gestation with intrahepatic cholestasis conditioning. The patient was treated with ursodeoxycholic acid and indomethacin in three doses, as well as a pulmonary maturation scheme with Dexamethasone 4 doses.

Table 1 presents the analytical evolution of the patient, who experienced an increase in transaminase parameters during her stay, with a clinical diagnosis of cholestasis of pregnancy. The patient presented with fever, general discomfort, headache and a runny nose, and with a history of coming into contact with two co-workers who had tested positive for SARS CoV-2 PCR. The patient tested positive on 04/16/2020. Telephone follow-up begins with the results shown in Table 2. On April 28, she went again for presenting fetal hypomotility, having 34 SDG. It was decided to perform a cesarean section due to fetal hypomotility and the COVID-19 diagnosis, and a male child was born at 22:38 hours with APGAR 8/9, CAPUR-RO, after 37 weeks gestation, weighing 2,250 grams and 50 cm in height. The neonate was kept in joint accommodation, and received lactation via a mixed technique (mother with the use of an N95 face mask without valve), and remained afebrile and asymptomatic, without respiratory distress or any need for mechanical ventilation. A nasopharyngeal culture was taken at 24 hours and PCR was performed for COVID-19. The day after the pregnancy was resolved, the mother reported slight respiratory distress that she attributed to the use of N95 face mask, coupled with the presence of a decreased vesicular murmur in the right lung base. A chest X-ray of the mother revealed a glass-like opacity (Figure 1). The maternal biochemical parameters are presented in Table 3. A change in transaminase levels was observed from those taken during previous hospitalizations. Arterial Blood Gas: pH: 7.48, pO2: 149 mmHg, pCO2: 21 mmHg, HCO3: 15.6, FiO2: 21%. The patient’s situation improved, and the newborn remained asymptomatic for the duration of hospitalization, with no evidence of respiratory distress, and they were discharged. On May 5, the newborn recorded a positive PCR, and the mother was notified by telephone to bring the newborn to respiratory triage for assessment. At 17 days of age (May 15, 2020), the newborn was called to undertake second PCR for COVID-19, which was negative. The mother has reported the newborn being asymptomatic since the last evaluation. After the sample was taken, a chest radiograph was requested that revealed no change (Figure 2).
DISCUSSION
In China, Zhang et al. (11) reported on four cases of COVID-19 positive newborns with a maternal history of SARS-CoV-2 (respiratory symptoms, chest CT with compatible findings and positive PCR test) during the third trimester of pregnancy. The neonates presented positive PCR tests, and three underwent chest CT scans with findings indicative of COVID-19. All received supportive treatment, and none required mechanical ventilation. This study supports the presence of vertical transmission by excluding infection by contamination, although there is a lack of sufficient evidence to confirm this.

Chen et al. (12) reported on nine pregnant women in the third trimester of pregnancy with a positive COVID-19 PCR test, with no comorbidities and with mild respiratory symptoms. Of the nine, eight had multiple ground-glass opacities on chest tomography; four developed perinatal complications related to the SARS-CoV-2 infection, including fetal distress and a premature rupture of the membranes. Nine infants were born through Cesarean section, with APGAR scores of 8–9 in the first minute and 9–10 in the fifth minute, and with no respiratory symptoms. Oropharyngeal samples were taken, and in six cases samples of cord blood, placenta, amniotic fluid and breast milk were collected, all of which were negative in a PCR test for COVID-19. This systematic review is similar to our case, given the inclusion of mothers with SARS-CoV-2 infection in the third trimester of pregnancy, but differs when negative PCR are presented.

In two case reports, one from China and the other from Spain, two newborns were confirmed with COVID-19. The first was to a 34-year-old woman at 40 weeks of gestation who was being treated for hypothyroidism, who presented with fever, lymphopenia, ground glass opacities in the upper and lower left lobes on a chest CT, and a positive nasopharyngeal exudate PCR for SARS-CoV-2 (13). This case resembles the case in the present study in terms of the hypothyroidism, which leads us to believe there may be some relationship between pregnant patients with hypothyroidism and susceptibility to COVID-19.

Table 1: Biochemical parameters during hospitalization

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<th>Laboratory / Date</th>
<th>02/04/20</th>
<th>04/04/20</th>
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<tr>
<td>Glucose</td>
<td>71 mg/dL</td>
<td>156 mg/dL</td>
<td>68 mg/dL</td>
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<td>Urea</td>
<td>4 mg/dL</td>
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<td>Creatinine</td>
<td>0.3 mg/dL</td>
<td>0.3 mg/dL</td>
<td>0.4 mg/dL</td>
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<td>Total bilirubin</td>
<td>0.7 mg/dL</td>
<td>0.5 mg/dL</td>
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<td>Direct bilirubin</td>
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<td>Indirect Bilirubin</td>
<td>0.4 mg/dL</td>
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<td>Albumin</td>
<td>3.1 mg/dL</td>
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<td>ALT</td>
<td>50 UI/L</td>
<td>99 UI/L</td>
<td>93 UI/L</td>
<td>83 UI/L</td>
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<td>AST</td>
<td>37 UI/L</td>
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<td>DHL</td>
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<td>Hemoglobin</td>
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<td>Hematocrit</td>
<td>36.2 %</td>
<td>30.7 %</td>
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<td>Platelets</td>
<td>229 10^3µL</td>
<td>228 10^3µL</td>
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<td>White Blood Cells</td>
<td>7.0 10^3µL</td>
<td>8.8 10^3µL</td>
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<td>Lymphocytes (%)</td>
<td>29 10^3µL</td>
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<td>Fibrinogen Derived</td>
<td>619 mg/dL</td>
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The case reported in Spain was a 41-year-old woman with a 38-SDG pregnancy, a history of IVF and hypothyroidism under treatment. An urgent cesarean section was performed for pre-eclampsia, and the neonate was obtained with an APGAR score of 7/9, beginning with respiratory distress that merited a nasal CPAP (withdrawn at 2 hours), transfer to the neonatal unit and subsequent referral to joint accommodation. Three days after hospitalization, the mother developed fever and respiratory symptoms compatible with COVID-19, and with a chest X-ray suggestive of pneumonia. A nasopharyngeal exudate RT-PCR SARS-CoV-2 test was requested, which was positive. Later, the mother required admission to the intensive care unit, and the girl was separated from the mother. On the sixth day of life, a sample was taken from the neonate for COVID-19 testing, and was negative, but when repeated 8 days after birth, the test was positive. The girl presented with intermittent polypnea with lower chest retractions, while a chest radiograph showed ground glass opacity, predominantly in the right parahilar. After 24 hours the respiratory symptoms disappeared. On day 13 of life, the test for COVID-19 was still positive (14). This case, unlike ours, presented with respiratory symptoms after pregnancy resolution, which prevents the exclusion of the possibility of contamination of the neonate for positivity by COVID-19.

This case is relevant, as there are no previous records of newborns with positive PCR for SARS-CoV-2 at 24 hours of life, or maternal confirmations of COVID-19 by maternal antecedent PCR of COVID-19.

Although the patient was 18 days post onset of respiratory symptoms due to COVID-19 infection, she was managed as an at-risk patient, given previous reports of transmissibility of up to 45 days (15). It is important to highlight the increase in transaminases in this case, considering that the patient had no typical clinical data indicating COVID-19 infection. She did, however, have an increase in transaminases, which leads us to believe that there may be a relationship between early modifications of liver markers and COVID-19 infection, which can be considered an early marker of infection. This assumption should be determined in all of pregnant patients with suspected COVID-19 infection, since it is considered a serious factor in patients positive for COVID-19 infections (16).
Table 2: Home follow-up of the pregnant patient

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In the review by Zhang et al. (11) and the case report by Wang et al. (13), symptomatology in mothers begins two to three days before birth, and even after it, questioning whether the median incubation time is at 5.2 days, according to Li et al. (17). These data lead us to consider the possibility that the immunological state of pregnancy could produce a shortening of the median presentation of respiratory clinical data for SARS-CoV-2 infection in pregnant women, unlike in adults in the general population, by three days.

On the other hand, in our patient we could rule out the secretion contagion route, as the cesarean section was performed with all the required protective measures, the mother wore an N95 mouthpiece at all times and the sample was taken 24 hours after birth. Contrary to the case reported by Alonso et al. (14), in which a positive PCR was obtained at 8 days of life, with a negative result 6 days after birth, indicating horizontal transmission. This type of in utero infection has already been demonstrated in cases of viruses such as cytomegalovirus (18).

Viral load plays an important role at the time of detection of the virus by PCR, since in the first days of the incubation period it is low and may not be detected, being below the detection threshold (14). If our patient had been infected via horizontal transmission, it would have been assessed in the first hours of the incubation period, reducing the likelihood of viral detection in the nasopharyngeal exudate.

Due to the lack of information and studies on vertical transmission in COVID-19 positive mothers, it is not possible to completely determine its presence in this case. Making such a determination would require more specific tests, such as the presence of IgM in the blood, which was not taken in our patient. Accordingly, health systems must consider the IGM determination for SARS-CoV-2 within the study protocol package for such patients. No SARS-CoV-2 viral RNA tests of neonatal cord blood, placenta samples or amniotic fluid have been carried out to date. IgM and IgG in maternal and newborn blood have not been measured. The mother not used n95 mask with valve, and it was believed that the virus in the expiratory air mixed with the external environment and infected the baby. This is the first case of vertical transmission to be reported in Mexico, and strongly supports this theory, and so this study can be considered as the basis for the development of future research.
CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS

REFERENCES
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Spontaneous Pneumothorax in Severe COVID-19 Pneumonia: Interventional Treatment and Risk of Transmission

Mia Elhidsi, Prasenohadi, Dicky Soehardiman

Abstract
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2), or Coronavirus disease 2019 (COVID-19), is a highly contagious and rapidly-spreading disease. While pneumonia is a common finding, pleural space involvement, such as pneumothorax, occurs only in rare cases. Pneumothorax requires the immediate insertion of a chest tube. Thoracostomy procedures require prompt and precise management, but with caution to avoid the risk of transmission. We report here on a 49-year-old male patient who was admitted to the emergency ward with shortness of breath and oxygen desaturation. A physical examination and portable chest X-ray indicated a left pneumothorax. The patient underwent tracheal intubation followed by chest tube insertion, and the lungs inflated two hours after the procedure. The operators included two people, wearing personal protective equipment (PPE), including N95 masks, full eye protection, a face shield and a fluid-resistant gown. Two weeks following chest tube insertion, the operators underwent a SARS-CoV2 PCR examination, with negative results. This report discusses relevant findings in literature related to the current issue.

Key words: Pneumothorax, COVID19, chest tube, thoracostomy, risk of transmission.

ÖZET

Anahtar Sözcükler: Pnömotorak, COVID 19, toraks tüpü, torakostomi, bulaşma riski.

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COVID19 is an infectious disease that primarily affects the respiratory system. First identified in Wuhan, China at the end of 2019, the condition spread globally, resulting in a global pandemic. Although most cases are mild and asymptomatic, the mortality risk is quite high in severe cases. The most commonly noted symptoms are cough, fatigue, phlegm, shortness of breath, myalgia, sore throat and headache (1,2). Typical radiological findings are bilateral multilobular ground-glass opacities (GGO) with predominance in the peripheral and posterior areas (3).

Pneumothorax as a clinical manifestation is rare. We report here on a thoracostomy chest tube insertion procedure on a patient with severe COVID19 complicated with pneumothorax and pneumomediastinum, and the subsequent follow-up PCR analysis of the assigned operators.

CASE

A 49-year-old male was admitted to the emergency room (ER) with progressive shortness of breath for the two days prior to admission. The patient complained of continuously tightness of the chest that was not induced by activity. There was no chest pain or fever for three days, and only rare coughing. The patient was conscious and with a respiratory rate of 34/minute; blood pressure, 130/90 mmHg; heart rate, 102/min; and oxygen saturation, 70% room air. The patient is a smoker, but with no comorbid factors. A physical lung examination revealed decreased breathing sounds in the left hemithorax accompanied by crepitations in the left hemithorax and neck. Blood examination WBC, 10.7 10^3/uL; Neu lymphocyte, 91.2%; HGB, 14.2 g/dL; HCT, 40.0%; PLT, 142 10^3/uL; blood glucose, 173 mg/dL; urea, 234 mg/dL; Creatinine, 14.0 mg/dL; ALT (SGPT), 43 U/L; AST (SGOT), 74 U/L; CRP, 115 mg/L; and procalcitonin, 1.91 ng/ml. Blood gas analysis, pH: 7.28; pCO2, 20.10 mmHg; pO2, 43.70 mmHg; HCO3, 9.70 mmHg; and SaO2, 73.70%. A radiograph and chest X-ray using portable machines revealed plural lines in the left hemithorax.

The patient’s severe respiratory distress led to intubation and invasive mechanical ventilation. A chest X-ray suggested progressing pneumothorax. The patient had chest tube inserted (thoracostomy) into the left chest using a 28Fr tube connected into the pleural drainage system in a negative-pressure room (Figure 1). Initially, a 10-cm undulation presenting with bubbles without fluid production was observed. The team comprised two members, i.e., one operator and one assistant, using protective equipment, including as fluid-resistant gown, safety goggles, gloves and N95 masks (Figure 2).

Following the chest tube insertion, oxygen saturation rose to 90% with a 100% fraction of inspired oxygen. A chest X-ray repeated two hours after the procedure revealed an inflating left lung. The medical team was evaluated two weeks after the procedure. Both they had no respiratory symptoms, and PCR analyses of nasopharynx swabs were negative for SARS-CoV2.

DISCUSSION

Pneumothorax is a rarely-encountered COVID19 complication (3,4). Studies in Wuhan reported that only 1 of 99 COVID19 patients experienced pneumothorax (4). A literature review was made of three databases, namely PubMed, ScienceDirect and Cochrane, on June 10, 2020. Medical subject headings (MesH terms) and text words in the title or abstracts were used to search the two subjects of interest, i.e., population and intervention. Both keywords were combined with Boolean operators such as “and” and “OR”. We avoided restrictions on language or article type, while averted is findings on unpublished articles and incorrect manuscripts. We obtained four case reports related to a total of 5 patients (Table 1). The majority of patients were male, in line with the gender distribution of those with COVID19 in general (5-8). Found literature reported left thoracic pneumothorax, but provided no biological or plausible explanation. No dominant side was noted to be affected by pneumothorax during the severe acute respiratory syndrome (SARS) outbreak in 2003 (9,10).

Pneumothorax is an emergency necessitating immediate management. As with other etiologies, a pneumothorax complicating COVID19 requires thoracostomy. In the case of tension pneumothorax, emergency measures involving needle chest decompression are necessary. The lung may re-inflate in a few hours or in up to two weeks. In different settings, pneumothorax may happen following the extensive use of a mechanical ventilator, in which excessive pressure and volumes become disruptive. In such cases, when accompanied by a persistent air leak, the optimum outcome will require an invasive procedure, i.e., thoracoscopy (8).
ACKNOWLEDGEMENT

Severe COVID-19 infection proceeds rapidly, according to the clinical finding and chest CT findings, although no effective drug has yet been identified. In such situations, the use of glucocorticosteroids may be clinically useful. The number of patients continues to increase worldwide, while data on the treatment and prognosis of the disease are still insufficient. Further research is warranted in the future.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS


YAZAR KATKILARI


REFERENCES


Bleomycin-Induced Fatal Lung Toxicity Misdiagnosed as Covid-19 Pneumonia: A Case Report

Covid 19 Pnömonisi ile Karşılan Bleomisine Bağlı Fatal Akciğer Toksitiseti: Olgu Sunumu

Murathan Köksal¹, Yasin Celal Güneş²

Abstract

Bleomycin is a chemotherapeutic agent that is preferred for the treatment of testicular cancer, lymphoma and some squamous cell carcinomas. Bleomycin-induced lung toxicity is a common, but rarely fatal side-effect, and the radiological image of which can be confused with other reasons which makes organizing pneumonia pattern. We report here on the case of a 40-year-old male patient with testicular cancer with bleomycin-induced fatal lung toxicity that was misdiagnosed as Covid-19 pneumonia. The patient suffered subsequent fatal spontaneous pneumomediastinum, pneumothorax, and pulmonary interstitial and subcutaneous emphysema, and died from respiratory failure.

Key words: Bleomycin, lung toxicity, covid-19, organizing pneumonia.

Özet


Anahtar Sözcükler: Bleomisin, akciğer toksitiseti, covid-19, organize pnömoni.
Bleomycin is a chemotherapeutic agent that has been isolated from Streptomyces verticillus, and that has been used successfully for the treatment of testicular cancer, lymphoma and squamous cell carcinomas. The main limitations of bleomycin therapy are dose-dependent lung toxicity and fibrosis. It can rarely cause fatal lung toxicity. Accordingly, early diagnosis and treatment, and the prevention of limiting toxicities such as bleomycin-induced lung injury, are important.

CASE
A 40-year-old male patient with a history of diabetes and testicular cancer was admitted to the emergency department of our hospital with dyspnea. A physical examination revealed blood pressure of 120/63 mmHg, oxygen saturation of 83%, body temperature of 36.8°C and a C-reactive protein level of 0.022 g/L (N: 0.005 g/L). Other blood test results were normal. Following a physical examination, the patient was referred to the Radiology Department for an anteroposterior chest radiograph. A chest X-ray showed increased reticular opacities in the upper and lower zones, left lung multifocal scattered opacities in the perihilar region. A subsequent chest computed tomography (CT) revealed an organized stage of Coronavirus Disease 2019 (COVID-19) pneumonia with diffuse fibrotic changes (Figure 1 and 2). Based on the results, the patient was hospitalized in the infectious disease inpatient clinic. Hydroxychloroquine, azithromycin ceftriaxone were started. In the first week of hospitalization, the polymerase chain reaction (PCR) test result for COVID-19 was twice negative, and the respiratory pathogen test result and sputum culture were also negative. The patient was not evaluated by bronchoscopy. When serologic test results came up negative, the patient was re-evaluated based on medical history, which revealed that he had undergone three cycles of an etoposide-bleomycin-cisplatin chemotherapy protocol, and had actually experienced shortness of breath for two months, since the last dose. Following this re-evaluation, the patient was diagnosed with bleomycin-induced pneumonitis. Other medications were stopped, and steroid treatment was started. On the eighth day of hospitalization, the patient’s partial pressure of oxygen (PaO₂) levels decreased suddenly and he was referred to the Radiology department for a further anteroposterior chest radiograph and chest CT, which revealed bleomycin-induced diffuse fibrosis, pulmonary interstitial pneumonia and spontaneous pneumomediastinum, pneumothorax and pulmonary interstitial emphysema (Figure 3 and 4). The patient was transferred to the intensive care unit and a chest tube was inserted. Despite the treatment protocol, the patient died from respiratory failure after a few hours.

DISCUSSION
Bleomycin, the most significant side effect of which is lung toxicity, is a chemotherapeutic agent that is preferred for the treatment of testicular cancer, lymphoma and some squamous cell carcinomas. Due to Bleomycin-induced lung toxicity (BILT), an endothelial and interstitial capillary edema, and an increase in surfactant overproduction and fibroblasts production were observed as a result of the mediators released by macrophages. These findings were consistent with the histological findings of diffuse alveolar damage, interstitial pneumonia and interstitial pulmonary fibrosis (1-3).

BILT presents with such clinical manifestations as fever, dyspnea, pleurisy and substernal pain. Patient older than 70, cumulative doses higher than 450 mg, renal insufficiency, administration path, oxygen treatment, smoking, granulocyte colony-stimulating factor (G-CSF) administration and bleomycin hydrolase activity are some of the predisposing factors (4-8).

A BILT diagnosis is based on exclusion, and is often excluded through microbiological and laboratory testing such as culture, gram staining of sputum and PCR. Pneumocystis jiroveci pneumonia (PJP) in particular should always be investigated (9).
Bleomycin lung toxicity is well established, and can be detected as bleomycin-induced pneumonitis (10). In chest high resolution computed tomography (HRCT) it can appear as diffuse alveolar damage, pulmonary fibrosis, organizing pneumonia pattern (OP) or nonspecific interstitial pneumonia pattern (NSIP). The HRCT features that imply underlying pulmonary fibrosis are a honeycomb pattern, traction bronchiectasis and reticulation. Diffuse alveolar damage is associated with ground-glass opacities and consolidations. The OP pattern manifests as bilateral multifocal ground glass opacifications and/or consolidations with peribronchial or subpleural distribution (9). CT findings of COVID-19 have enabled the diagnosis of the most common pattern-resembled OP (11).

COVID-19 typically presents with ground glass opacities with or without consolidation, with a peripheral, posterior, and diffuse or lower lung zone distribution. Crazy paving pattern, reverse halo sign and other findings of OP patterns seen later in the disease are also typical signs (12). Primary or secondary organizing pneumonia, such as drug toxicity, connective tissue disease, some viral pneumonias and acute lung injury patterns are the main differential diagnoses of COVID-19 pneumonia.

The mortality rate associated with BILT is 1–2% (13). Spontaneous pneumomediastinum, pneumothorax and pulmonary interstitial emphysema are very rare fatal complications of the treatment, as identified in our case study, as well as in a few studies in literature (14–17).

CONCLUSION
The radiology of BILT can be confusing, and so patients may be misdiagnosed as COVID-19. During the ongoing pandemic, the history and follow-up of the patient, as well as the radiological images, must serve for correct diagnoses, as in our case.

CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
Concept - M.K., Y.C.G.; Planning and Design - M.K., Y.C.G.; Supervision - M.K., Y.C.G.; Funding -; Materials -; Data Collection and/or Processing -; Analysis and/or Interpretation -; Literature Review - Y.C.G.; Writing - M.K., Y.C.G.; Critical Review - M.K.
REFERENCES


A Case of Chronic Eosinophilic Pneumonia Confused with Covid-19 Pneumonia

Covid-19 Pnömonisi ile Karışan Kronik Eozinofilik Pnömoni Olgusu

Selvi Aşker¹, Hanifi Yıldız¹, Nevzat Esen¹, Müntecep Aşker²

Abstract

The etiology of chronic eosinophilic pneumonia (CEP) is not precisely known, although its characteristic features include eosinophilia, involving alveoli or blood; subacute or chronic respiratory and general symptoms; while chest radiological imaging shows peripheral pulmonary infiltrates. Many cases of pneumonia associated with the new coronavirus (2019-nCoV) were detected in Wuhan, China starting in December 2019. HRCT is a highly sensitive and convenient screening tool for 2019-nCoV. The radiological appearance of the new coronavirus pneumonia is not very different from that of the common viral pneumonia, but it has some unique features. It usually manifests with patchy or punctuate opacities resembling ground glass (85.7%), and patchy consolidation (19.0%), and the lesions are mainly located in the subpleural area. Here we present a case of CEP who presented with shortness of breath, cough, fever, and a clinical and radiological picture similar to COVID-19.

Key words: Chronic eosinophilic pneumonia (CEP), SARS-CoV-2, Computed Tomography, Ground Glass Opacity.

Özet


Anahtar Sözcükler: Kronik eozinofilik pnömoni (CEP), SARS-CoV-2, Bilgisayarlı Tomografi, Buzlu Cam Opasitesi.

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Chronic eosinophilic pneumonia (CEP) is a rare disorder, the etiology of which is not exactly known. Its characteristic features are eosinophilia involving alveoli or blood; subacute or chronic respiratory and general symptoms; and a chest radiological imaging with peripheral pulmonary infiltrates (1). Females are affected by CEP twice as often as males, and it is commonly seen in asthmatic patients (2).

A history of asthma is seen in two-thirds of patients, and nearly half of the patients have a history of atopia, ranging from eczema and nasal polyposis to urticaria (3). The symptoms begin silently, and the most frequent are cough, dyspnea, fatigue, weight loss and fever. There are no clear-cut diagnostic criteria for CEP, although eosinophilia of the peripheral blood is usually present. In bronchoalveolar lavage (BAL), the percentage of eosinophils is elevated, in the 12–95% range, with a mean of 58% (3). There may also be increases in IgE levels, erythrocyte sedimentation rate and C-reactive protein. Chest-X-rays of the original CEP series revealed peripheral opacities that resembled “photographic negatives” of pulmonary edema. Although there may be varying patterns, peripherally distributed patchy airspace consolidations may be seen in computed tomographies (CT) of the chest (2). Alveolar infiltrates are bilateral in 97% of cases, but can also be unilateral (3). Such opacities are usually found at the periphery of the upper lobes, and the appearance may be ground glass or consolidation. The higher sensitivity of CT better reveals pulmonary features and more accurately defines CEP. Both pleural effusions and radiographic cavitations are rare manifestations of CEP (2).

Prior to making a CEP diagnosis, eosinophilia due to infections, toxic etiologies or drugs should be excluded. Treatment mainly involves corticosteroids, and treatment response is rapid. Despite corticosteroid treatment, the asthma accompanying CEP may be progressive and often severe (3). Many patients have good long-term prognosis, but relapses may occur, especially during the tapering process of oral corticosteroid therapy. Up to half of the patients may relapse, and some patients may experience multiple recurrences.

| Table 1: Similar and Different Radiologic Features of CEP and COVID-19 pneumonia |
|---------------------------------|-------------------------------------------------|
| **COVID-19**                    | **Chronic Eosinophilic Pneumonia**               |
| Multifocal and particularly the lower lobes distribution, subpleural and peripheral patchy ground glass opacities | Non-segmental, Migratory peripheral airspace ground-glass opacities, mainly the upper lobes |
| Intralobular and interlobular reticulations, resulting in a crazy paving pattern | Longitudinal bands coursing vertically parallel to the pleural surface |
| Reversed halo sign             | -                                               |
| Alveolar consolidation         | Consolidation with peripheral lung distribution, photograph negative appearance of pulmonary edema |
| Widespread ground glass opacities with ARDS | -                                               |
| After treatment, residual pulmonary fibrosis may be identified in some patients | After treatment, residual pulmonary fibrosis may be identified in some patients |
| Endobronchial mucoid impaction | Endobronchial mucoid impaction                   |
| Centrilobular pulmonary nodules may be present, sometimes with a tree-in-bud pattern reflecting small airways involvement | Centrilobular pulmonary nodules may be present, sometimes with a tree-in-bud pattern reflecting small airways involvement |
| Pleural effusions and cavitation are rare | Pleural effusions and cavitation are rare |
Many cases of pneumonia associated with the new coronavirus (2019-nCoV) were detected in Wuhan, China starting in December 2019, and the disease then spread rapidly around the world (4). High-resolution computed tomography (HRCT) of the chest is a highly sensitive and feasible screening tool for 2019-nCoV (5). Although the radiological appearance of COVID-19 pneumonia resembles common viral pneumonia, it has also some unique characteristics, such as patchy ground-glass opacities (85.7%) and patchy consolidations (19.0%), which are mostly seen in sub-pleural locations (4). For the diagnosis of COVID-19, a chest CT has high sensitivity (Table 1). In epidemic areas where the pre-test probability of the disease is high, a chest CT may be used for the screening, evaluation and follow up of COVID-19. Positive CT findings still suggest COVID-19 in epidemic areas, even if a RT-PCR is negative (5). The CT findings in COVID-19 coincide with other pulmonary diseases. Bronchoalveolar lavage (BAL) is used for the diagnosis and follows up of many pulmonary diseases, and is carried out to identify cellular characteristics in interstitial lung diseases, and to define the etiological agent in patients in whom diagnosis and treatment could not be made. In patients with strong suspicions of Coronavirus, BAL may identify the agent when it cannot be isolated by any other means. IDSA recommends performing lower respiratory tract sampling in patients whose initial upper respiratory tract samples are negative (6). In viral infections, lymphocytes are expected to dominate in the early days of infection when bacterial infections are not accompanying. However, cellular features may change later due to superinfections or cytokine storm, and BAL findings may also change (7). We present here a case whose radiological imaging suggested COVID-19 pneumonia, although the subsequent diagnosis was CEP.

CASE

A 24-year old female patient was admitted to the COVID-19 clinic with shortness of breath, cough and fatigue. She had no overseas travel history, although her contact history was suspicious. The patient, who had a previous asthma diagnosis, had a fever of 37.5°C; systolic blood pressure of 110 mmHg; and diastolic blood pressure of 60 mmHg. The pulse rate was 88 beats/min, and the respiration rate was 24. Breathing sounds were normal. A chest X-ray revealed a suspicious infiltration in all zones of both lungs, with prominent air-filled areas at the periphery. CT showed ground-glass densities, most prominently in the upper regions of both lungs, adjacent to the pleura (Figure 1).

Nasopharyngeal and oropharyngeal swabs were obtained for COVID-19 assessment, and the patient was hospitalized in a ward accepting suspicious COVID-19 patients. Her blood count is presented in Table 2. Her hospital records revealed high eosinophil numbers at the time of previous assessments. A CT record was found from 2016 and compared, and the lesions seen in 2020 were more intense (Figure 2). A tuberculin skin test was negative; and serological tests were negative for Mycoplasma pneumonia, Chlamydia pneumonia, Adenovirus, Legionella, Aspergillus, Cryptosporidium and Candida. Both serological tests and stool exams were negative for parasites, and there were negative results for antinuclear antibodies, anti-double-stranded DNA, anti-mitochondria, anti-LKM antibodies, c-ANCA and p-ANCA, ruling out autoimmune diseases. There are various known causes of eosinophilic lung disease (ELD), including allergic bronchopulmonary aspergillosis, drug reactions, parasitic infections and eosinophilic vasculitis (Churg-Strauss syndrome). Allergic bronchopulmonary aspergillosis, parasitic infections and drug-induced eosinophilic pneumonia (EP) were excluded; and the absence of cutaneous vasculitis or other multiorgan involvements ruled out Churg-Strauss syndrome. Echocardiography revealed no cardiac pathology. A previous bronchoalveolar lavage, the eosinophils percentage was 25% (Table 3). Steroid treatment was initiated at the center at which the tests were performed, but the patient terminated treatment voluntarily, and did not attend any follow up visits. The patient was taking salmeterol, fluticasone propionate, and montelukast regularly. COVID-19 PCR tests were performed twice, and both were negative. Upon the diagnosis of CEP, prednisolone 1 mg/kg was initiated, and the patient was discharged.
**Table 2: Laboratory data of the patient (2020)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range</th>
<th>On Arrival, Emergency Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit (%)</td>
<td>41.0–53.0</td>
<td>42.1</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13.5–17.5</td>
<td>13.6</td>
</tr>
<tr>
<td>White-cell count (per μl)</td>
<td>4500–11,000</td>
<td>11,600</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>28–78</td>
<td>62.8</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>17–57</td>
<td>19.7</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>0–10</td>
<td>13.3</td>
</tr>
<tr>
<td>Platelet count (per μl)</td>
<td>130,000–400,000</td>
<td>313,000</td>
</tr>
<tr>
<td>Carbon dioxide (mmol/l)</td>
<td>23–38</td>
<td>36.8</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.60–1.50</td>
<td>0.55</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>70–110</td>
<td>78</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/liter)</td>
<td>10–55</td>
<td>22</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/liter)</td>
<td>10–40</td>
<td>38</td>
</tr>
<tr>
<td>C-reactive protein (mg/liter)</td>
<td>8–25</td>
<td>13.6</td>
</tr>
<tr>
<td>Lactate dehydrogenase (U/liter)</td>
<td>125–220</td>
<td>138</td>
</tr>
<tr>
<td>Sedimentation</td>
<td>1–20</td>
<td>23</td>
</tr>
<tr>
<td>D-Dimer</td>
<td>0–0.5</td>
<td>0.43</td>
</tr>
<tr>
<td>Total IgE (IU/ml)</td>
<td>0–100</td>
<td>71.5</td>
</tr>
</tbody>
</table>

**Table 3: Bronchoalveolar lavage results**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range</th>
<th>On Arrival, chest disease Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils (%)</td>
<td>50–80</td>
<td>44</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>0.5</td>
<td>25</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>25–50</td>
<td>23.7</td>
</tr>
<tr>
<td>CD4 (%)</td>
<td>34–56</td>
<td>0.5</td>
</tr>
<tr>
<td>CD8 (%)</td>
<td>18–36</td>
<td>13.4</td>
</tr>
<tr>
<td>Tuberculosis culture</td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Covid -19 RT(PCR)</td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>PCP culture</td>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td>Sputum cytology</td>
<td></td>
<td>Inflammation rich from eosinophilic leukocytes</td>
</tr>
</tbody>
</table>
A Case of Chronic Eosinophilic Pneumonia Confused with Covid-19 Pneumonia | Aşker et al.

DISCUSSION

CEP, first described by Carrington et al. (8) in 1969, is a rare disorder children aged 2–5 years, although the actual incidence and prevalence are unknown. In the adult population, women are more frequently affected than men. Onset is insidious with non-specific general symptoms, including cough, dyspnea, night sweats, weight loss, fever, wheezing and sputum production, although these symptoms may easily be misdiagnosed as an infectious illness, contributing to a delay in diagnosis and treatment (8). Chronic eosinophilic pneumonia can be differentiated from acute eosinophilic pneumonia based on the prolonged symptom duration, history of asthma, the occurrence of relapse and radiologic features of subpleural consolidation (9). Chronic eosinophilic pneumonia (CEP) is a rare disorder that responds well to corticosteroids, although there is a lack of consensus on the initial dose and treatment duration with corticosteroids. The most significant complication is recurrence, which develops during the tapering process. The patient in the present study experienced recurrence after terminating her treatment. It is likely that the intermittent use of steroids for the treatment of her asthma prevented relapse, although as the recurrence amid the COVID pandemic, led to diagnostic confusion due to the similarities in radiological involvement.

The new coronavirus, which first appeared in Wuhan, China, has been named officially COVID-19 by WHO. The disease was initially local, but then spread around the entire world (4). It is hard to differentiate between the radiological features of COVID-19 pneumonia and those of common viral pneumonia, although there are some specific imaging features. Patchy or punctate opacity resembling ground glass (GGO) is the most frequent radiologic presentation, although there may also be a patchy consolidation (4). The findings of a previous study have emphasized the use of chest CT for diagnoses of COVID-19 in patients with negative RT-PCR test results, as chest imaging may play a key role in diagnosis when RT-PCR gives negative results at an early stage. For rapid diagnosis, changes in radiological appearance should be clearly identified. CT findings alone are usually not enough to differentiate COVID-19 from other viral pneumonias, although a high-resolution CT (HRCT) of the chest may be used when RT-PCR yields negative results (10). Radiologists will encounter more patients as the number of 2019-nCoV cases increases. A detailed travel and exposure history should be obtained before considering the disease, and radiologists should suspect 2019-nCoV in patients with bilateral ground-glass opacities or consolidation. RT-PCR for 2019-nCoV may yield negative results for some patients with positive chest CT findings (11). Previous studies have found that CT images in the majority of cases showed GGO or mixed GGO and consolidation. Pneumonia due to 2019-nCoV is likely to present with a peripheral distribution, and to involve the lower lungs bilaterally (12). As a non-invasive imaging modality, chest CT offers high accuracy and speed. Recent studies have reported characteristic CT findings such GGOs with or without crazy-paving sign, multifocal organizing pneumonia and peripheral architectural distortions. In the present study, 60% of patients had typical CT features at the time of, or prior to, the initial positive RT-PCR results (13). Furthermore, in almost all patients, a chest CT yielded positive results before or within six days.
of the initial positive RT-PCR results. These results suggest that CT imaging may be very useful for detecting cases of suspected COVID (5). The rate of confirmed RT-PCR assays in the present study (97%) was higher than in a previous study conducted by Kanne et al. (76.4%) (11). The first study, which demonstrated higher rates for the concordance of CT imaging, was conducted in the largest hospital in Wuhan, China. As this city was the center of the COVID-19 outbreak, radiologists may have had a high index of suspicion, and may have more readily diagnosed COVID-19 when encountering typical CT features. These results suggest that the sensitivity of chest CT for COVID-19 is high, and that chest CT may be used for screening, comprehensive evaluation and follow up purposes COVID-19 outbreak areas, and where the pre-test probability of the disease is high (5). In another trial, the clinical features and chest CT characteristics of six patients were evaluated, and a decreased eosinophil count was found to be helpful in the diagnosis of the disease in an early period. The study also identified a variety of new CT manifestations on CT. Lesions may appear as round nodular-like GGOs in the central region of the lung lobe, different to the patch-like lesions in the subpleural area noted in many previous trials (14).

In conclusion, computed tomography is used as routinely in the current COVID-19 pandemic, and some physicians regarded all patients as if COVID-19 pneumonia. This situation caused cases whose tomographic appearance was confused with COVID-19 pneumonia. A detailed anamnesis, previous radiological images, and clinical, biochemical and microbiological data should be evaluated together for an accurate diagnosis.

CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS

YAZAR KATKILARI

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A Rare Case of Pulmonary Infection: Endobronchial Actinomycosis

Nadir Bir Akciğer Enfeksiyonu Olgusu: Endobronşiyal Aktinomikoz

Serhat Özgün¹, Büşra Yaprap Bayrak², Tuba Çifçi Küsbec³, Ahmet Ilgazlı⁴

Abstract

Pulmonary actinomycosis is a bacterial disease that can be difficult to diagnose due to its nonspecific clinical and radiological findings caused by actinomycetes. A 59-year-old female patient presented with a history of coughing and white sputum for the last one year. Here, we present a rare case of endobronchial actinomycosis with an endobronchial lesion obstructing the basal segments of the right lower lobe, diagnosed from a transbronchial biopsy taken during a fiberoptic bronchoscopy.

Key words: Actinomycosis, endobronchial, bronchoscopy.

ÖZET

Pulmoner aktinomikozis, aktinomiçes türlerinin neden olduğu, nonspesifik klinik ve radyolojik bulguları olması nedeni ile tani konulmasında güçlük yaşanan bakteriyel bir hastalıktr. Elli dokuz yaşında kadın hasta, son bir yıl kadar devam eden öksürük ve beyaz renkli balgam şikayetleri ile başvurdu. Burada, fiberop tik bronkoskopide sağ alt lob bazal segmentleri obstrükte eden, endobronşiyal lezyon görülen ve transbronşiyal biyopsi ile tani konulan endobronşiyal aktinomikoz olgusu, nadir görülmeyi nedeniyle sunuldu.

Anahtar Sözcükler: Aktinomikoz, endobronşiyal, bronkoskopı.

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Actinomycosis is a rare chronic and infectious disease caused by bacteria known as actinomyces. It is a non-acid resistant gram-positive anaerobic bacterium of the Actinomyceataceae family. Pulmonary actinomycosis is an endogenous infection that likely develops as a result of aspiration of oropharyngeal or gastrointestinal secretions, occurring as a result of the actinomyces in the normal flora entering the damaged mucosa (1-3). All systems in the body may be affected, but the most common form of the disease is the cervicofacial type. The pulmonary involvement has been reported to be around 15% in all cases (4). Its resemblance to tuberculosis, lung abscess and lung cancer, both clinically and radiologically, may lead to misdiagnosis and delay in diagnosis (5). Here, we present a 59-year-old woman with endobronchial actinomycosis with complaints of cough and sputum, despite treatment for pneumonia.

CASE

A 59-year-old female patient was admitted to our clinic with cough and white sputum for the last one year. Intermittent antibiotic treatment led to a partial response. The patient was admitted to our clinic after the complaints continued. The patient was subfebrile, with no complaints of hemoptysis, chest pain or night sweats. She had been using oral antidiabetic agents for the treatment of type II diabetes mellitus for 5 years. There was no smoking history. A physical examination revealed her general status to be good and her vital signs to be stable. A chest examination identified crackles over the right lower lobe. The laboratory values at admission included a white blood cell count of 5.1×10³/μL, an erythrocyte sedimentation rate of 18 mm/h, a hemoglobin value of 11.7 g/dL, a hematocrit value of 38% and a mean corpuscular volume value of 80 (MCV) fL. In the biochemical analysis, an abnormal C-reactive protein value of 22.46 mg/L (normal value <5 mg/L) was recorded. A chest X-Ray revealed a nonhomogeneous density beat in the right lower zone (Figure 1). The patient, who lost 4 kg in the last year, was examined by fiberoptic bronchoscopy for tuberculosis and lung cancer. Bronchoscopy revealed an endobronchial lesion obliterating the basal segments of the right lower lobe (Figure 2). Bronchoalveolar lavage and bronchial biopsies were taken, and a pathological examination revealed characteristic sulfur granules of Actinomyces admixed with neutrophils and numerous neutrophil-laden histiocytes (Figure 3). Fungal, bacterial and mycobacterial smears were negative in the bronchoalveolar lavage. The patient was diagnosed with actinomycosis, and was started on intravenous sulbactam-ampicillin 4x1 g treatment. In the first month of treatment, the complaints of cough and sputum resolved. The treatment was continued for 4 weeks. Oral amoxicillin-clavulanate 2x1 g treatment was started after intravenous sulbactam-ampicillin treatment. The patient’s symptoms and radiological findings regressed in the third month of treatment (Figure 4), and having benefited from the treatment, the patient is in the third month of follow-up with continued oral treatment as an outpatient.

Figure 1: Chest X-ray displaying a nonhomogeneous density beat in the right lower zone

Figure 2: Fiberoptic bronchoscopy showing an obstruction of the basal segments of the right lower lobe with an exophytic endobronchial lesion
DISCUSSION
Pulmonary actinomycosis continues to be a significant problem for clinicians, as symptoms are non-specific, and the disease resembles other chronic suppurative chest diseases and malignancies. Fever, cough, sputum, shortness of breath, weakness, weight loss, night sweats, chest pain and hemoptysis are the main symptoms (2,6). Our case presented with complaints of a cough and sputum for the last one year. Chronic respiratory diseases such as emphysema, chronic bronchitis, bronchiectasis and alcoholism, poor oral hygiene, periodontal disease and surgery, facial trauma and diabetes mellitus are all predisposing factors for the disease (7). The leading risk factor in our patient was uncontrolled type 2 diabetes mellitus with hyperglycemia. The laboratory findings of the disease are nonspecific, as normochromic anemia, leukocytosis with polymorphonuclear leukocyte dominance and low C-reactive protein increase can be observed (7). Among these, high levels of C-reactive protein were present in our patient. In Kim et al.’s (8) study of 94 cases diagnosed between 2000 and 2010, 44 were reported to have never smoked, while an evaluation of radiological images revealed that all but six cases had been misdiagnosed initially, with the most common diagnosis being cancer, accounting for 35.1%. Our case never smoked. A bronchoscopy was planned following a diagnosis of malignancy and tuberculosis in the patient indicating that she had been weakened by 4 kg for the last year and did not pass his complaints despite her intermittently antibiotic use. The optimum approach to the diagnosis of actinomycosis is the pathological examination of specimens taken by biopsy and the production of microorganisms in culture (9). Bronchoscopy may reveal an exophytic mass with purulent exudate and a characteristic histology with sulfur granules (6). Our case was diagnosed from a biopsy following bronchoscopy. Actinomycosis was first treated with penicillin in the 1940s, and this approach still prevails (10). Beta-lactam antibiotics are frequently preferred as a treatment approach, and the duration of treatment is long (9). Alternatives are tetracycline, erythromycin, chloramphenicol, clindamycin and imipenem, especially in patients with penicillin allergies (7,11-13). Surgical treatment can be particularly helpful for complications such as pulmonary abscesses and empyema, in situations where fistula and sinuses need to be drained, or for the control of life-threatening hemoptysis (14,15). We started treatment with intravenous sulbactam-ampicillin 4x1 g, and switched to oral amoxicillin-clavulanate 2x1g treatment at the end of the first month following clinical and radiological improvement.

CONCLUSION
Pulmonary actinomycosis is still a significant problem for clinicians. Fiberoptic bronchoscopy is an important diagnostic tool, as it can lead to the avoidance of surgical procedures. We present this case to suggest pulmonary actinomycosis be kept in mind as a differential diagnosis in late response pneumonia or recurrences.

CONFLICTS OF INTEREST
None declared.
AUTHOR CONTRIBUTIONS

YAZAR KATKILARI

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A Case of Severe H1N1 Pneumonia Complicated with Spontaneous Pneumomediastinum and Pneumothorax

Spontan Pnömomediastinum ve Pnömotoraksla Komplike Olan Ağır H1N1 Pnömonisi Olgusu

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Abstract

Cases of spontaneous pneumomediastinum and spontaneous pneumothorax related with influenza A (H1N1) infection in adults are quite rare. The case presented here was a 33-year old female patient admitted to the emergency room with high fever, severe dyspnea, cough and altered consciousness. Pneumomediastinum and bilateral pneumothorax were detected on a chest roentgenogram and thoracic computerized tomography imaging. The H1N1 virus was identified in a nasal smear and in tracheal aspirate samples. Clinicians should be aware of this rare complication of the Influenza A virus that has started to be seen in literature.

Key words: H1N1 virus, pneumothorax, pneumomediastinum.

Özet


Anahtar Sözcükler: H1N1 virüs, pnömotoraks, pnömomediastinum.

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The Influenza A (H1N1) virus mostly causes acute, infectious respiratory tract infections (1). It is one of the leading causes of the seasonal epidemics that result in serious disease and even death almost every year (2). Spontaneous pneumomediastinum (SPM) is a very rare complication of an H1N1 infection (3). The rare cases of SPM related with Influenza A infections are reported mostly in pediatric cases (4). The early initiations of antiviral medication along with an appropriate antibiotic regime for possible co-infections are strongly recommended (5). We present here a case with H1N1 virus accompanied by both SPM and spontaneous pneumothorax.

CASE
A 33-year old female patient was brought to the emergency department with severe dyspnea, cough, high fever and altered consciousness. Her general condition was poor, and her vital signs were: blood pressure: 80/60 mmHg, heart rate: 126/min, respiration rate: 28/min, SPO2: 84% and body temperature: 38.7°C. There were no abnormal findings on physical examination other than bilateral extensive rales. The laboratory results of the patient were WBC: 29,560, Hb: 12.2 g/dL, Htc: 37.7%, Plt: 376,000, CRP: 345 mg/L, AST: 70 U/L, ALT: 100 U/L, BUN: 8 mg/dL, creatinine: 0.53 mg/dL, Na: 138 mmol/L, K: 3.2 mmol/L, Ca: 7.6 mg/dL and Cl: 97 mmol/L. An arterial blood gas analysis showed pH: 7.14, PCO2: 84.5 mmHg, PaO2: 65.2 mmHg, SO2: 86.2%, HCO3: 21.1 mEq/L and lactate 3 mmol/L. Bilateral and partly intensified extensive infiltration zones and linear air density at the edge of mediastinum were identified in the patient’s chest roentgenogram (Figure 1). A subsequent chest computerized tomography imaging revealed parenchymal infiltration accompanied by pneumomediastinum and bilateral pneumothorax (Figure 2 and 3). The patient was admitted to the intensive care unit, and was simultaneously intubated and subjected to a bilateral tube thoracostomy (Figure 4). The vital signs of the patient after intubation were BP: 80/60 mmHg, HR: 124/min, SPO2: 99% and body temperature: 37.8°C. An arterial blood gas analysis showed pH: 7.17, PCO2: 87.5 mmHg, PaO2: 141 mmHg and HCO3: 32.8 mEq/L. There were rough sounds and rales upon physical examination. A fiberoptic bronchoscopy revealed intensive mucosal edema, inflammation and hyperemia; after which a nasal smear and tracheal aspirate samples were obtained. The H1N1 virus was identified in the obtained samples, and antiviral treatment (oseltamivir phosphate) was initiated in the early period. Empirical antibiotherapy was added to the treatment for the treatment of possible secondary bacterial infections (imipenem-cilastatin sodium combined with vancomycin). There was no air leakage from either chest tube. The left chest tube was removed on the third day and the right one was removed on the fifth day. The patient was extubated on the eighth day of follow-up, and was discharged on the 15th day with healing (Figure 5 and 6).

Figure 1: The appearance of pneumomediastinum on an anteroposterior roentgenogram of the patient at the first application. Black arrows indicate the edge of the paracardiac air densities

Figure 2: A coronal chest multidetector CT view of the lung window upon the first application of the patient. Inflammatory consolidated parenchyma areas can be seen. The black arrows indicate the edges of the bilateral pneumothorax, and the black circle shows the boundary of the pneumomediastinum
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DISCUSSION

Clinical presentations of H1N1 infections may begin as an upper respiratory tract infection with fever. They may cause such severe clinical conditions as pneumonia, pneumomediastinum and ARDS with secondary bacterial infections (1). There have been few studies to date describing radiological findings in patients with H1N1 admitted to the ICU. Rohani et al. (6) reported that the most common radiological findings of patients with severe H1N1 pneumonia admitted to the ICU were ground-glass opacities, consolidation and a reticular pattern. Less frequently, pleural effusion and mediastinal lymph node enlargement have been described. It is known that H1N1 pneumonia can cause pneumomediastinum and pneumothorax, although they are rare complications in H1N1 infections. In a study by Valente et al. (7), eight of 50 patients with a severe clinical course of H1N1 infection had pneumothorax, and four of those had pneumomediastinum. That said the presence of SPM and pneumothorax together, or whether or not the pneumothorax was bilateral was not clearly apparent in the text. SPM as a complication of Influenza A infection was first reported in a Mexican patient, and then in three cases in Ottawa (Canada) and one case in India. All of the cases detailed in literature came from the pediatric population (3). The present case was an adult with severe H1N1 pneumonia complicated with SPM and bilateral pneumothorax. To the best of our knowledge, this is the first case report detailing concomitant bilateral pneumothorax and SPM in global literature (4).

There is a lack of any definitive information or descriptions of the development mechanism of pneumomediastinum secondary to H1N1 infection in literature. In our case, we observed a clinical presentation that started as upper respiratory tract infection, that progressed rapidly and that caused pneumonia. We believed that the destructive inflammation caused by the H1N1 virus and the co-infections caused by the impaired immune response of the host caused alveolar and respiratory tract injuries, while also promoting pneumomediastinum and pneumothorax. Although we did not observe a major tracheal or bronchial injury during our evaluation with a flexible bronchoscopy, we concluded that the observed intensive inflammation and edema could also cause direct air leakage from the trachea.
The H1N1 virus is seen frequently as an infection causing pandemics in our country and around the world, causing mortalities. The identification of the virus in body fluids can be difficult in underdeveloped and developing countries. The early initiation of antiviral treatment, if the parameters of the infection suggest a viral infection, and even adding empirical antibiotic treatment for possible secondary infections in cases requiring hospitalization, are necessary. Being aware of all complications that H1N1 infections may cause is important. Diagnoses of spontaneous pneumomediastinum are based on imaging (4,5). Although a linear air image in the paracardiac area on a chest roentgenogram is diagnostic, a definitive diagnosis is made from computerized tomography imaging.

CONCLUSION
Clinicians must be aware of the rare life-threatening spontaneous pneumothorax and pneumomediastinum complications of the Influenza A virus, which have started to be seen in literature.

CONFLICTS OF INTEREST
None declared.

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Aripiprazole-Induced Pulmonary Toxicity in a Patient with Obsessive-Compulsive Disorder

Obesif-Kompulsif Bozukluk Tanılı Hastada Aripiprazol İlişkili Akciğer Toksitesi

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Abstract

A 33-year-old male patient with a diagnosis of obsessive-compulsive disorder applied to the emergency department with fever, cough, sputum and increasing shortness of breath. A physical examination revealed the patient to be dyspneic and orthopneic. Bilateral rales were present in middle and basal lung areas. Oxygen saturation in room air was 84%. Diffuse parenchymal infiltration and consolidation areas were noted in a posteroanterior chest X-ray and a thorax computerized tomography. The patient’s history revealed that the patient used a CPAP machine due to obstructive sleep apnea syndrome and aripiprazole, related to his obsessive-compulsive disorder. The patient was hospitalized in the intensive care unit with a preliminary diagnosis of pneumonia and treated with ceftriaxone 2 gr/day, clarithromycin 2x500 mg and oseltamivir 2x75 mg. Blood and sputum cultures, viral markers and procalcitonin were negative, and so methylprednisolone 40mg/day was started. The patient’s clinical condition improved rapidly after treatment with steroids, and he was discharged on the 8th day after admission, with recommendations for ambulatory care. It was learnt that aripiprazole had been added to his treatment for obsessive-compulsive disorder 1 month earlier, and that his complaints had started and gradually intensified 20 days after this change in medication. The patient’s clinical picture was assessed as lung toxicity caused by aripiprazole.

Key words: Lung toxicity, aripiprazole, drug lung.

Özet


Anahtar Sözcükler: Akciğer toksitesi, aripiprazol, İlaç akığı.

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Lung diseases associated with drugs are common iatrogenic diseases. Drug-induced lung damage leads to acute and chronic lung parenchymal damage. Recognizing drug-related lung diseases can be difficult, as histopathological findings are not specific and have similar features to diffuse lung diseases that develop due to other reasons. For a diagnosis of drug-induced diffuse lung disease, exposure to the drug, and histological evidence of lung damage and other causes must be excluded.

**CASE**

A 33-year-old male patient with a diagnosis of obsessive-compulsive disorder applied to the emergency unit with fever, cough, sputum and increasing shortness of breath that were learnt to have started approximately 10 days earlier, and to have increased gradually. When the complaints had first started, he applied to his family doctor and was treated with paracetamol and cephuroxime – the patient had followed the treatment, but had not benefitted. Upon examination at the emergency unit, the general condition of the patient was moderate–bad, tachypneic and orthopneic. A physical examination revealed blood pressure of 130/80 mmHg; pulse, 118/min; respiration, 22/min; and body temperature, 36.8°C. The mucosa was observed to be slightly cyanotic, and diffuse rales were heard in the bilateral basal lung fields. Without oxygen treatment, oxygen saturation was determined to be 84% (FiO₂ 21%) upon pulse oxymetry. A postero-anterior chest X-ray revealed diffuse parenchymal infiltration and consolidation areas, which were more significant in mid and lower zones of both lungs (Figure 1). A thoracic computed tomography without contrast (CT) revealed diffuse alveolar consolidation areas that were more dominant in the peripheral regions of both lungs (Figure 2). The laboratory values upon emergency unit admission were as follows: hemoglobin, 13.4 gr/dL; white blood cell count, 7600 uL; eosinophil count, 510 /uL (%6.8); thrombocyte, 357,000 /uL; arterial blood gases, pH: 7.44; pO₂, 50 mmHg; pCO₂, 41 mmHg; and HCO₃⁻, 26 mmol/L. All parameters other than high creatinine in blood biochemistry were normal (creatinine, 1.61 mg/dL). Due to the need for advanced respiratory support, the patient was admitted to the ICU with a preliminary diagnosis of pneumonia. Treatment was started with oxygen 4-5 L/min, CPAP 10 cmH₂O, ceftriaxone 2 gr/day and oseltamivir 2x75 mg.

Sputum and blood cultures were negative; the procalcitonin value was 0.349 ug/l, which was within normal limits. In the serologic tests requested due to vasculitis suspicion, antinuclear antibody (ANA), antimitochondrial antibody (AMA), Anti jo-1, Anti ssA and ssB, cytoplasmic anti-neutrophilic antibody (c-ANCA) and peri-nuclear anti-neutrophilic antibody (p-ANCA) were negative. No pathologic findings were noted in an echocardiography. When the patient history was inquired, it was learnt that he was using a CPAP device at home due to obstructive sleep apnea, and that he had been followed up for more than one year due to obsessive compulsive disorder, being on medication that had been changed within the last 2 months. There was no other medication, allergen exposure, asthma history, animal contact, travel history or smoking history. The patient’s shortness of breath had started approximately 20 days after starting aripiprazole treatment (Abilify® 5mg/day) and had then gradually intensified, with a significant increase seen in the last 5 days. Accordingly, the Aripiprazole treatment was stopped, and thereafter, 1 mg/kg/day methyl prednisolone was started. On the second day of methyl prednisolone treatment, symptoms and oxygen saturation started to recover. After three days in the ICU, the patient was transferred to the service, and eight days after presenting to the emergency unit, the patient was discharged with a 24 mg/day methyl prednisolone oral and dose reduction plan. The patient’s medication was replaced with citalopram and haloperidol treatment after obtaining the opinion of the psychiatry department. The lesions saw almost complete remission on lung imaging and thorax CT performed in the first month (Figure 3 and 4). Due to the observation of radiologic improvement, the methyl prednisolone treatment dose was reduced and then stopped.

**Figure 1**: Postero-anterior (PA) chest radiography: Diffuse parenchymal infiltration and consolidation areas in both lungs that are more significant in the middle and lower zones.
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Figure 2: Thorax computerized tomography (CT) without contrast: alveolar consolidation areas in both lungs that are more dominant in peripheral areas

DISCUSSION
Due to their large contact area, the lungs are a potential target for toxic materials through both inhalation and hemathogenic paths. Medications can be included among such toxic materials, as they may cause specific respiratory tract reactions. It is well known that there are more than 380 pharmaceutical agents that can cause medication-induced respiratory system diseases (1).

Figure 3: PA chest radiograph of the patient taken in the first month: full remission in consolidated areas

Figure 4: Thorax CT of the patient taken in the first month: Normal lung parenchyma
The most common form of drug-induced lung toxicity is drug-related interstitial lung disease (DRILD). DRILD can be observed in almost all histopathologic types, such as interstitial pneumonia, hypersensitivity pneumonia (HP), diffuse alveolar damage (DAD), non-specific interstitial pneumonia (NSIP), eosinophilic pneumonia, organizing pneumonia, alveolar hemorrhage and granulomatous pneumonia (1). The use of oral and parenteral medication can cause interstitial lung disease more frequently than inhaler, intrathecal or local use. That said, it is difficult to diagnose drug-induced lung diseases, as the clinical, radiological and histological findings are not specific. The acute lung damage caused by pneumotoxic agents takes the form of alveolitis and lung edema, as they act as antigens or haptons and create immune cascades, resulting in immune-mediated alveolitis. Secondly, the accumulation of medication-specific antibodies with medication-specific T cells in the form of antigen/antibody complexes result in lung edema. Acute damage may advance to chronic inflammation in a short period, and may cause fibrotic changes that hinder gas transportation (2).

Acute, sub-acute and chronic phases of drug-induced lung toxicity may be observed. In the acute form, fever, chills, nausea, cough, shortness of breath can be observed; in the sub-acute form, gradually increasing cough, shortness of breath, loss of appetite and weakness can be seen; while in the chronic form, insidious coughing, shortness of breath, loss of weight and fatigue are observed (3-5).

The dose and period of potential drug exposure should be queried in detail. In suspected cases, lung imaging and high-resolution tomography (HRCT) must be performed. The most frequently observed change indicating the stage of the disease is ground-glass or patched opacities (6). Bronchoalveolar lavage (BAL) is the most sensitive method for the detection of alveolitis, and especially in patients with an exposure history and typical findings in HRCT, BAL is not necessary. The role of open lung biopsy in diagnosis is also controversial (7).

Aripiprazole is an atypical anti-psychotic drug that binds to dopaminergic and serotonergic receptors with high affinity. It has fewer side effects (dystonia, Parkinsonism, akathisia, dyskinesia, etc.) than typical anti-psychotics (8). Aripiprazole-related pulmonary complications are few in number, however one such case presented with hypersensitivity pneumonia. It was shown that the same case recovered clinically and radiologically as the result of getting away from the factor and following treatment with steroids (9).

In patients presenting with shortness of breath, cough, high fever and diffuse parenchymal involvement in lung imaging, it is important to consider drug toxicity in a differential diagnosis, and to take a detailed history of drug exposure. In our case, considering the sub-acute interstitial pneumonia diagnosis after aripiprazole use, the medication was discontinued and steroid treatment was applied, and clinical and radiological recovery was observed.

The target of treatment is the prevention of inflammatory response and fibrotic tissue accumulation, which requires the avoidance of the triggering factor and treatment with steroids. The response to acute damage can take 24–48 hours, although the treatment response to chronic attacks can take longer. It is recommended to reduce and then stop the steroid treatment over a period of weeks (7).

As regards to the limitations of our study, we carried out no bronchoalveolar lavage or biopsy for diagnosis. The diagnosis was confirmed through the discontinuation of the medication causing lung toxicity. In general, bronchoscopy with transbronchial biopsy will not aid in the establishment of a diagnosis of drug-induced pulmonary toxicity. Bronchoalveolar lavage (BAL) can contribute to the expected clinicopathological pattern of a given drug-induced lung disease, such as identifying eosinophils in drug-induced eosinophilic pneumonia. BAL also is helpful in differential diagnoses, primarily by excluding an infective etiology to the pulmonary infiltrates.

We present here a case of drug-induced toxicity, which we submit to literature as a rarely encountered condition.

**CONFLICTS OF INTEREST**

None declared.

**AUTHOR CONTRIBUTIONS**


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REFERENCES


Massive acute pulmonary embolism (PE) is a life-threatening medical condition. Occasionally, patients experiencing a massive PE may develop concurrent thrombocytopenia. A 64-year-old female was admitted for left femur osteomyelitis with a sub-periosteal abscess that was causing pain and immobility. There were no indications suggesting underlying thrombophilia or malignancy. On day 5 of admission, the patient developed acute onset respiratory distress, necessitating intubation and vasopressor support. A computed tomography pulmonary angiogram revealed a massive PE involving the left main trunk and left ascending pulmonary artery. The patient had experienced an unexplained worsening thrombocytopenia that despite without heparin use previously.

There was clear indication for thrombolysis, but the treatment was contraindicated. After a multidisciplinary meeting it was decided to optimize platelet counts prior to the performance of a surgical embolectomy, however the patient succumbed 2 days later. The unexplained thrombocytopenia could be the only clue for massive PE. Clinicians should remain vigilant to ensure early diagnosis and improved outcomes.

**Key words:** Pulmonary embolism, thrombocytopenia, thrombosis.

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**Anahtar Sözcüklar:** Pulmoner emboli, trombositopeni, trombozis.
Venous thromboembolic diseases (VTE) such as deep vein thrombosis (DVT) and pulmonary embolism (PE) are commonly encountered in daily clinical practice. Massive acute PE, defined as systolic arterial pressure of less than 90 mmHg, is a life-threatening medical condition (1,2). Occasionally, patients with massive PE can present with concurrent thrombocytopenia of various etiologies, including heparin-induced thrombocytopenia (HIT) and acute thrombosis associated thrombocytopenia, leading to diagnostic and therapeutic dilemmas (3,4). In this case report, we present a patient with massive PE with thrombocytopenia, as first manifestation of the disease without prior heparin use.

**CASE**

A 64-year-old female with no prior medical conditions was admitted to an orthopedic unit complaining of worsening pain and swelling in the left thigh, leading to physical immobility for approximately one month prior to admission. She reported no preceding falls or physical trauma, although she had attended multiple left thigh acupuncture sessions with an unlicensed practitioner in an attempt to relieve the pain in the left thigh. There were no other signs or symptoms suggesting underlying thrombophilia, malignancy or connective tissue disease. A magnetic resonance imaging (MRI) of the left thigh revealed features of osteomyelitis in the distal one-third of the left femur with adjacent collection, consistent with a diagnosis of left femur osteomyelitis with a subperiosteal abscess (Figure 1). With this diagnosis in mind, the patient was scheduled for open drainage and a washout of the abscess. Her baseline blood values upon admission, the results of renal and liver function tests, and her coagulation profile were unremarkable. Her hemoglobin level was 12g/dl, and her platelet count was 409x10⁹/L. She had leukocytosis at 17.4x10⁹/L with a raised C-reactive protein level of 302mg/L.

On day 5 of admission, while waiting for an operation, she developed acute onset respiratory distress, necessitating urgent intubation, mechanical ventilation and vasopressor support. Prior to this, she had experienced unexplained worsening thrombocytopenia for 4 days (from 409x10⁹/L on admission to 22x10⁹ on day 5th of stay) without heparin use. Her hemoglobin and total white cell counts and coagulation profile remained stable (Figure 2). An urgent peripheral blood film revealed no evidence of acute hemolysis, abnormal platelet clumping or presence of blast cells to suggest an underlying hematological malignancy. Other blood parameters, including renal and liver function test results, were all within normal ranges. An urgent computed tomography pulmonary angiogram revealed massive PE involving the left main trunk and the left ascending branch of the pulmonary artery (Figure 3). There was a clear indication for thrombolysis, but the treatment was contraindicated. After a multidisciplinary consultation involving internal medicine physicians, nurses, orthopedic surgeons, intensive care doctors, cardiothoracic surgeons and cardiologists, it was decided to optimize the platelet counts prior to consideration for surgical embolectomy. Unfortunately, she succumbed after 2 days, despite maximal supportive therapy.

**DISCUSSION**

The basis of PE treatment is anticoagulation, with systemic thrombolysis being the treatment of choice in patients with massive PE (5). PE treatment, however, needs to take into consideration various factors, including, but not limited to, the severity of PE, bleeding risk, and patient factors such as history of allergies to heparin or HIT. Our case report highlighted a clinical dilemma with strong indications for systemic thrombolysis and anticoagulation that unfortunately were accompanied by high bleeding risks due to concurrent severe thrombocytopenia.

![Figure 1: MRI images of left thigh demonstrating features of femur osteomyelitis with huge periosteal collection (red arrows). Femur marked with yellow arrows](image-url)
Figure 2: Serial platelet count, white blood cell count and haemoglobin levels since admission

Data on the role and safety of anticoagulation in patients with thrombocytopenia are scarce (6). Clinical workup and management should thus be tailored toward identifying and managing the potential causes of concurrent thrombocytopenia and thrombosis, such as HIT, disseminated intravascular coagulopathy (DIC), paroxysmal nocturnal hemoglobinuria (PNH), anti-phospholipid antibody syndrome, sepsis and hematological malignancies, as well as systemic malignancies with marrow infiltration and thrombotic tendencies (3,6). Our patient received no forms of heparin prophylaxis prior to orthopedic surgery throughout admission, rendering a diagnosis of HIT unlikely, consistent with Warkentin’s exclusionary criteria for HIT (7). Furthermore, there were no clinical signs or symptoms to suggest concurrent thrombophilia, malignancy or connective tissue conditions. Furthermore, laboratory results were not suggestive of conditions such as PNH, DIC, hematological malignancies or connective tissue conditions. Her baseline platelet counts and coagulation profile were normal upon admission.

Thrombocytopenia in sepsis can occur due to various mechanisms. In patients with sepsis, activated platelets bind to the endothelium, leading to platelet sequestration and destruction (8,9). Immune mediated mechanisms and the cytokine-driven hemophagocytosis of platelets can all contribute to low platelet counts in a patient with sepsis (10,11). Patients with severe sepsis are often in a net procoagulant state with a secondary consumption of platelets, such as those observed in cases of DIC (12). While we acknowledge that sepsis may have contributed to thrombocytopenia in our case, it is unlikely to be the main driving or causative factor, for two reasons. Firstly, prior to development of sudden onset respiratory distress, the patient was stable and demonstrate no other clinical signs or symptoms of severe sepsis, such as bleeding, shock or organ dysfunction. Furthermore, her blood parameters, including coagulation profile, liver function tests and renal function, were all normal throughout admission, despite the concurrent worsening thrombocytopenia.

Figure 3: Computed tomography pulmonary angiography demonstrating filling defects along left main pulmonary artery trunk (red arrow) and left ascending pulmonary artery (yellow arrows) due to pulmonary embolism
As mentioned previously, there is only limited data on the use of thrombolysis in patients with thrombocytopenia. Alternative treatments including endovascular embolectomy and surgical embolectomy after the correction of platelet counts have been proposed and reported in various case reports, with mixed results (3,13-16). Our patient was initially considered for a surgical embolectomy after the optimization of platelet counts, but she succumbed to her illness before we were able to carry out the procedure.

We postulated that large fresh clots in her pulmonary circulation had led to platelet adherence on the clot surfaces due to the exudation of thromboplastic substances. This phenomenon has been termed ‘acute thrombosis-associated thrombocytopenia’ (4). In 1887, Welch, a prominent founding professor of John Hopkins Hospital, demonstrated that platelets rapidly adhere to fresh thrombi, with the youngest thrombi attracting the largest number of platelets (17). This phenomenon is observed histologically as the Lines of Zahn, and is characteristic of thrombi formation with laminations formed by successive depositions of platelets and fibrinous materials seen as pale lines alternating with trapped red blood cells seen as dark lines (18). Subsequent studies, including the Urokinase Pulmonary Embolism Trial in 1971, showed that 10% of all patients with PE had platelet counts below 150 x109/L (19). A more recent study by Monreal et al. (20) revealed PE to be associated with a significant reduction in platelet counts, a phenomenon not seen among patients with DVT without PE.

To our best knowledge, however, there have been no prior studies or reports specifically addressing thrombocytopenia as the first manifestation of acute massive PE. It remains unknown whether the rate of platelet decline is correlated with the severity of PE. Nevertheless, in light of our clinical encounter, we recommend that clinicians remain vigilant when dealing with patients with unexplained thrombocytopenia, and consider acute thrombosis associated thrombocytopenia in high risk patients. Earlier diagnosis during a ‘safer’ platelet count window may change the patient’s clinical course and outcome by allowing more time for the consideration of medical and surgical therapy in the presence of massive PE.

CONCLUSION

We present here a patient with massive PE associated with severe thrombocytopenia necessitating systemic thrombolysis and anticoagulation, which unfortunately were contraindicated. Clinicians need to be vigilant when dealing with patients with unexplained thrombocytopenia, and to consider acute thrombosis associated thrombocytopenia, especially among high risk patients. Early detection and prompt intervention are vital to ensure a better clinical outcome.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS


YAZAR KATKILARI


REFERENCES


Evaluation of fitness for work in a Case with COPD

KOAH Tanılı Bir Olguda İşe Uygunluk Değerlendirmesi

Merve Demirci Atik, Ayse Coskun Beyan, Arif Hikmet Çımrın

Abstract

Today, approximately 25% of the working populations have at least one chronic disease, and so the delineation “fitness for work” is quite important. The process for the evaluation of fitness for work is evaluated in this paper, alongside a detailed work analysis and a further functional evaluation of an employee who presented to our work and occupational illnesses clinic with a diagnosis of chronic obstructive pulmonary disease (COPD). A 39-year-old male with the diagnosis of COPD, who was employed at a rim factory, was subjected to a cardiopulmonary exercise test, and a work analysis revealed that the energy requirement of the work was above the acceptable limits for the case. The smoke, dust and metal identified in the environment were thought to contribute to the exacerbation and progression of COPD. Modifications to the patient’s work to suit his cardiopulmonary capacity, and reducing the defined risks was suggested. Evaluating work compatibility is an important area of study requiring the collaboration of many disciplines, and occupational disease specialists in particular, with the aim being to protect the health of the workforce and the continuity of works.

Key words: COPD, functional evaluation, fitness for work.

Özet


Anahtar Sözcükler: KOAH, İşe uygunluk, fonksiyonel değerlendirime.
Factors such as the relative increase in the elderly population and the increase in retirement age have increased the incidence of chronic diseases in the working population (1). In addition, many people need to work after retirement due to financial concerns, or to continue to be a part of social life. It is important, therefore, to provide workers with working conditions that will not be detrimental to their health, and that will safeguard their productivity. Evaluations of work compatibility are the basic method used to ensure these conditions (2).

COPD is the third leading cause of death worldwide (3). Only half of all patients are thought to be diagnosed, although only one in five individuals over the age of 40 years is known to have COPD (4). The prevalence of COPD has been increasing in both developed and developing countries as a result of environmental and occupational exposure; including tobacco use, air pollution, and the increasing elderly population and biomass smoke (5). While the disease is generally associated with advanced age, according to estimations, 50% of patients with COPD are under the age of 65, and most are in paid employment (6). Quality of life is impaired secondary to decreased effort capacity in the advanced stages of the disease, leading to a decreased participation in daily activities. This in turn can limit substantially the participation of individuals in occupational life. It is a known fact that approximately 20% of patients with COPD leave their working life early due to the effects of their disease (7). If diagnosed early and managed well, disease progression can be slowed, which can prolong the duration of active employment (5). Occupational health professionals can play a significant role in this process. This study presents the evaluation of work compatibility of a patient with COPD, with the aim being to highlight the importance of cooperation between in-house physicians and occupational disease clinics when evaluating the compatibility of cases with chronic diseases.

CASE
A 39-year-old male patient was referred to our occupational disease clinic by the in-house physician of his employer with a complaint of dyspnea during work, and for an evaluation of compatibility for occupation. According to his work history, the patient had worked in recycling for approximately 5 years in an aluminum rim factory, where he was employed to transfer scrap rims to melting pots in a foundry. Approximately one month prior to his visit to our clinic, he had requested to change his position, and was transferred to the production department. His new line of work required him to take 300–500 pieces of rim, each weighing 20–25 kilograms, from a 1-meter-high pallet and to place them on a 1-meter-high band, and was engaged in the task for approximately 6.5 hours a day (Figure 1). The location in which he worked was right next to the melting furnaces. According to a workplace measurement report, the respirable dust concentrations in the recycling and production departments was 0.086 mg/m3, which was within the limit values approved in Turkey (<5 mg/m3) (8). The patient had worked as a mechanical assembly worker in a sewing machine production factory for approximately 10 years. His medical history revealed that he had been diagnosed with COPD 2 years earlier. His family history was unremarkable. His past medical history included a smoking habit of 10 packs/year, but he had quit smoking 4 months earlier. During the physical examination, pulmonary auscultation revealed bilateral severely decreased respiratory sounds, while the other system examinations were unremarkable. Hyperlucency was observed in the right lower and middle zone on a postero-anterior (PA) chest X-ray. Bilateral parenchymal emphysematous changes, and a bulla measuring 14 cm in diameter causing compression on the right middle lobe, were observed in thoracic computed tomography imaging (Figure 2).
A severe obstructive functional impairment was identified during a post-bronchodilator spirometric evaluation, performed in the stable period (FEV1 42% expected (FVC) 84% expected, FEV1/FVC: 40% and Body plethysmograph: total lung capacity (TLC): 115%, residual volume (RV): 207%). The case, who had experienced no exacerbations over the past one year and who was evaluated with an mMRC (Modified Medical Research Council) group 2 dyspnea score, was found to be compatible with GOLD B according to the GOLD (Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease) staging system (Figure 3) (4). The case was investigated for alpha-1-antitrypsin deficiency, having been diagnosed with COPD at the age of <40 years. Alpha-1 genotyping was reported to be normal (PiMM allele).

A cardiopulmonary exercise test (CPET) was performed using a bicycle ergometer and the ramp protocol in order to identify aerobic capacity and to evaluate compatibility for the job. The maximum oxygen consumption (VO2max) 

### Table 1: Calculation of the energy requirement of the subject’s job

<table>
<thead>
<tr>
<th>Activity</th>
<th>VO2job (ml/kg/min)</th>
<th>Time of Job (min)</th>
<th>VO2job x Time (ml/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standing, Intermittent weight lifting (mean: 22.5 kg)</td>
<td>12.25</td>
<td>390</td>
<td>4777.5</td>
</tr>
<tr>
<td>Standing, Talking</td>
<td>10.5</td>
<td>45</td>
<td>472.5</td>
</tr>
<tr>
<td>Eating during sitting</td>
<td>5.25</td>
<td>15</td>
<td>78.75</td>
</tr>
<tr>
<td>Talking during sitting</td>
<td>5.25</td>
<td>15</td>
<td>78.75</td>
</tr>
<tr>
<td>Combination of Standing/walking</td>
<td>10.5</td>
<td>15</td>
<td>157.5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>480</td>
<td>5565</td>
</tr>
</tbody>
</table>

Mean aerobik demand for job activities: 11.6 ml/kg/min (5565/480)

* VO2job, aerobic demand of the job

**Note:** The working time of the case was calculated as 8 hours / day. (it includes one meal break of 1 hour / day and also two need breaks of 15 minutes)

#### Symptom assessment using modified Medical Research Council dyspnea scale (mMRC)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying or walking up a slight hill</td>
</tr>
<tr>
<td>2 (red circle)</td>
<td>I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on the level</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing</td>
</tr>
</tbody>
</table>

#### Disease severity assessment according to the GOLD stages

- **C:**CAT <10, mMRC 0-2
- **D:**CAT ≥10, mMRC ≥3
- **A:**CAT <10, mMRC 0-2
- **B:**CAT ≥10, mMRC ≥3

**Figure 3:** Determination of COPD severity based on symptoms and exacerbation risk. The symptom level of the present case was mMRC stage 2, and he was evaluated to be in the GOLD B group given the absence of exacerbation
was calculated as 19.5 ml/min/kg; with the mean oxygen consumption acceptable for 8 hours of work accepted as 34% of the VO2max value (9,10). This value in the present case was calculated at 7.8 ml/min/kg (34% of 19.5 ml/min/kg). The patient’s job was analyzed in collaboration with the in-house physician. The required mean oxygen consumption was calculated as 11.6 ml/min/kg, based on the 2011 Compendium physical activities reference list (11) (Table 1).

The clinical and functional condition of the patient was evaluated alongside the work analysis. The required energy level for the performance of the determined job was suggested to be above the accepted limit value of the case. In addition, the dust, metal smoke and thermal risks in the environment were considered to carry risks for the exacerbation of COPD and disease progression. Furthermore, the properties of the determined task and the working environment were suggested to increase the risk of progression of the bulla found in the lung and for the development of complications. The in-house physician was informed of the importance of regulating the defined job in order to prevent the defined risks. The case was referred to a pulmonary diseases clinic for optimal medical treatment, pulmonary rehabilitation and evaluation for bullectomy, and a reevaluation of the functional condition of the patient was planned after optimal treatment.

**DISCUSSION**

The basic steps in a job compatibility evaluation include confirmation of the COPD diagnosis, clinical staging, advanced functional evaluation performed during the stable phase of the disease and a detailed job analysis. The diagnosis was confirmed according to GOLD criteria in this case, and the disease burden on the case was determined. The case was moved away from anything that may exacerbate his COPD, including occupational exposure, and supportive treatment was initiated in which the aim was to increase quality of life case through appropriate pharmacotherapy, and he was evaluated for job compatibility after the optimal conditions were met.

The pathophysiological processes that cause COPD affect exercise capacity. Traditionally, although COPD is defined and graded based on the degree of limitation of FEV1, static and dynamic air trapped (hyperinflation) in the lung has demonstrated to be more important in defining functional dyspnea (12). CPET is a dynamic method, in addition to such static measurements as TLC and RV, and is based on exercise performed under controlled metabolic conditions, and evaluations of the responses of the respiratory system, cardiovascular system and cellular level reveal the holistic response to exercise. The approach allows an objective, quantitative evaluation of the demonstrated aerobic capacity (13). In literature, limit values have been defined based on the concept of aerobic threshold in the studies evaluating job compatibility (14). The aerobic metabolism allows for the long-term maintenance of effort at the complete submaximal level, at which an adequate amount of oxygen is carried to the muscle cells, and most of the ATP required during exercise is provided. The aerobic threshold is defined as the point at which the anaerobic metabolism starts to be used and the blood lactate level starts to increase. The difference from the anaerobic threshold (lactate threshold) is that the blood lactate level is yet <2mMol. The anaerobic threshold, on the other hand, is the point at which no ventilatory response can be created in response to the developing metabolic acidosis. The blood lactate level is defined generally as >4 mmol, and exercise above this point cannot be tolerated for long. The anaerobic threshold is reached at approximately 50-60% of VO2max in sedentary people (15).

For all these reasons, acceptable workload is suggested to be 30–50% of VO2max in some studies in literature (16,17). Wu et al. (9) suggested that the defined limit values for workload may vary according to the working hours, and thus suggested 28.5%, 31%, 34% and 43.6% of VO2max% values for 12, 10, 8 and 4 hours of work, respectively. In the present study, we calculated the oxygen requirement of the case for 8 hours of work, and found it to be below the oxygen requirement for the task to which the case was assigned, indicating his incompatibility with the task.

The most important risk factor in the etiology of COPD has been defined as exposure to tobacco smoke, although occupational exposures to such materials as coal, silica, cement, cadmium, asphalt, coke and welding fumes are also suggested to increase the possibility of development of COPD (18,19). The patient in the present study was employed in the production of aluminum alloy rims, where the substances used in production included aluminum (90%) and silicon (9%), and titanium, magnesium and other metals in smaller quantities (<1%) (20). Working in the vicinity of melting metal involves a risk of exposure to metal smoke. The case stated that he had been exposed to metal smoke for 3 years and welding smoke for 10 years (30 min/day) prior to his COPD diagnosis, although it is difficult to establish a cause/effect relationship in the development of occupational COPD.
due to the mixed effects of cigarette smoking. It should be further kept in mind that the defined respiratory exposure might lead to the progression of COPD and an increased risk of exacerbation if exposure is not prevented. Today, the established treatment strategies for COPD are based on the reduction of symptoms and the slowing of rapid progression. These strategies can be summarized as early diagnosis, the prevention of such risk factors as cigarette smoke, etc., the prevention of exacerbations, the control of comorbidities and the preservation of current functional capacity (4). An indispensable proportion of the management of these patients is provided by in-house physicians, since one-third of the lives of individuals are spent at the working environment in a work order of 8 hours. In-house physicians should be aware of the burden of the disease in COPD, as with all other chronic diseases, and they should develop skills in primary and secondary preservation strategies. Early diagnosis and the appropriate management of the disease will allow such patients to remain productive and to stay in active employment for longer (5).

CONCLUSION

It is important to determine whether an individual is compatible with a defined job to prevent functional capacity being exceeded in cases with limited functionality, and to continue the productivity of the employee. A multidisciplinary approach involving primarily experts in working and occupational diseases is needed in this process.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS


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Hybrid Congenital Lung Malformation with Difficulty in Diagnosis and Treatment: Congenital Cystic Adenoid Malformation and Pulmonary Sequestration Co-existence

Bengisu Arabacı, Kenan Can Ceylan, Nur Yücel, Seyda Ors Kaya

Abstract

Congenital abnormalities of the lung can manifest in any component of the bronchopulmonary system. Congenital lobar emphysema, bronchogenic cyst, congenital cystic adenoid malformation (CCAM) or pulmonary sequestration (PS) are just some of the many kinds of malformations of the lung. The co-existence of CCAM and PS is a very rare condition. Due to such complications as dyspnea or recurrent infection, most malformations are diagnosed antenatally or in the immediate postnatal period. The present case was not diagnosed until late adolescence, and the patient was subsequently referred to our clinic after undergoing a previous operation. After examinations and a preoperative evaluation, a second operation was performed. We present to literature a very rare case of co-existing CCAM and PS (hybrid lung malformation).

Key words: Congenital anomaly, surgery, hybrid malformation.

Özet

Akciğerin konjenital anomalileri bronkopulmoner sistemin tüm bileşenlerinden kaynaklanabilir. Konjenital lobar amfizem, bronkojenik kist, konjenital kistik adenoid malformasyon (KKAM) veya pulmoner sekestrasyon (PS) bronkopulmoner malformasyonlardır. KKAM ve PS birlikte çok nadir görülmektedir. Solunum sıkıntısı, tekrarlayan enfeksiyonlar gibi komplikasyonlar nedeniyleneau antenatal veya postnatal dönemde tanı almakta. Erişkin yaşa kadar tani ve tedavisinde sorunlar yaşanan bir olgu, ileri tani ve tedavi amaçlı klinikimize yönlendirildi. Tetkik ve değerlendirme sonrasını klinikimize ikinci kez operasyon yapıldı. Çok nadir görülen KKAM ve PS birlikteliği (hibrid konjenital malformasyon) saptanan olgunu literatür eşliğinde sunmamızı amaçladık.

Anahtar Sözcükler: Konjenital anomalı, cerrahi, hibrid malformasyon.

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Congenital abnormalities of the lung can manifest in any component of the bronchopulmonary system. Congenital lobar emphysema, bronchogenic cyst, congenital cystic adenoid malformation (CCAM) or pulmonary sequestrations (PS) are just some of the many malformations of the lung. The co-existence of CCAM and PS is a very rare condition. As a result of complications like dyspnea or recurrent infection, most malformations are diagnosed antenatally or in the immediate postnatal period. This case in the present study was not diagnosed until late adolescence, and was subsequently referred to our clinic after undergoing a previous operation. After an examination and a preoperative evaluation, a second operation was performed. We present to literature a very rare case of co-existing CCAM and PS (hybrid lung malformation).

CASE
A 17-year-old patient presented to the Emergency Department with chest pain and dyspnea. The patient was evaluated as primary pneumothorax and a chest tube was inserted. An air leak was observed from day 1, lasting for more than a week. He was diagnosed as prolonged air leak into the chest cavity and underwent an exploratory thoracotomy about a year ago. A preoperative exploration identified a thick-walled hydatid cyst. The cystic fluid was aspirated and the cavity was closed, and was pathologically found to be compatible with benign tissue. A year later, the patient developed the same symptoms and was diagnosed with recurrent pneumothorax, and a tube thoracotomy was carried out. Upon clinical follow-up, the absence of improvement resulted in the case being referred to our clinic for further investigation. A computed tomography (CT) scan revealed branching from the abdominal aorta with vascularization variants in the cystic region in the right lower zone (Figure 1 a,b,c). The patient’s laboratory values were insignificant, and infectious process was excluded in differential diagnosis. A second right thoracotomy was performed, and an exploration of the cystic malformed area revealed an immature bullous image that seemed to be independent of the bronchial and vascular structures of the lower lobe parenchyma. The malformed structure that had been receiving its blood supply from the abdominal aorta was excised from the lower lobe. Histopathologically, the cystic lung tissue showed fibrosis and smooth muscle hyperplasia and contained vascular components, and so was evaluated as a hybrid congenital lung malformation and intralobar sequestration (CCAM and ILS) due to its involvement in the normal lung parenchyma (Figure 2a). The patient is in his 8th month of postoperative follow-up and is recovering well (Figure 2c).

DISCUSSION
CCAM is a hamartoid cystic lung tissue that originates from parenchymal, vascular or bronchial anomalies, and is the most common of the congenital pulmonary airway malformations. While seen previously in 1/25,000–35,000 live births, it has been reported to be more common in recent studies (1/7,200 live births) (1,2). Histopathologically, PS is a combination of the aberrant vascular component and dysfunctional abnormal lung tissue, and can be classified as intra-lobar or extra-lobar. It can be further defined as bronchial atresia with systemic vascularization (3). Congenital lung malformations are generally diagnosed by ultrasonography (USG) or magnetic resonance imaging (MRI) in the intrauterine period. Surgical excision is preferred in diagnosed patients due to the potential for infections or malignancies, even in asymptomatic cases (4). A review of literature reveals the majority of cases operated for congenital cystic lung malformations are below the age of 10 months (5), although patients diagnosed and operated during childhood have also been reported in rare cases (6). In our patient, congenital cystic lung malformation was not considered as a possible cause during the initial stage of the differential diagnosis due to his age. Due to the patient’s increasing shortness of breath, the case was instead evaluated in favor of pneumothorax in the emergency department (Figure 2b).
The number of patients who remain asymptomatic for a long time is small. Asymptomatic cases without antenatal diagnosis are detected incidentally and operated for such reasons as recurrent infections and hemoptysis.

Attention should be paid to understanding the anatomical structures and vascular variants that may accompany. In studies conducted to date, contrast computed tomography (CT) is recommended prior to operation to understand correctly the anatomy of the thorax, the structure of the lung parenchyma and vascularity, and it has been observed that CT largely overlaps with pathology (7). In a contrast CT of the patient in the present study taken before the operation, variants of vascularization in the right lower lobe cystic region were observed, branching from the abdominal aorta (Figure 1b, c).

The surgeon should be aware that the blood supply of the cystic lesion may be systemic and that fissure anomalies may be encountered also in the lung, and the operation approach should be selected with this in mind. The thorascopic method is preferred mostly in asymptomatic neonatal or pediatric cases, and the results are generally satisfying (4,8). A 17-year-old underwent a thoracostomy with a pre-diagnosis of pneumothorax, and after that he was explored with a right thoracotomy due to prolonged air leak into the chest cavity. The patient was referred to our clinic for further examination due to a lack of improvement in his medical condition. A re-operation was made after the examination. Considering the medical history of the patient, we opted to perform a re-thoracotomy during the operation to visualize the aberrant vascular structures accompanying the cystic structure that could be seen in the thorax CT (Figure 1a). Soft pathological tissue with severe adhesion and aberrant vascular structures was excised, and a histopathological examination revealed it to be a hybrid congenital lung malformation (CCAM and ILS) (Figure 2a), which led us to present this very rare case to medical literature. We are pleased to report that at postoperative follow-up, the patient was symptom-free (Figure 2c).

Hybrid congenital lung anomalies are usually excised surgically having become symptomatic in the postnatal period, and have the potential for malignancy. Since our patient was in late adolescence, difficulties were observed during diagnosis and treatment. Rare hybrid congenital lung malformations should be considered in children and young adults with persistent respiratory distress and recurrent signs of infection. It is important to evaluate cases that will benefit from surgical excision in this regard.

CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS

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Langerhans Cell Histiocytosis in the Chest Wall

Göğüs Duvarında Langerhans Hücreli Histiyositoz

Muharrem Çakmak¹, Adile Ferda Dağlı²

Abstract
Langerhans Cell Histiocytosis (LCH) refers to a non-neoplastic proliferation of Langerhans cells with an incidence in the adult population of 1–2 per million. It is considered a pediatric disease, and while rib involvement is very rare, we report here on a 33-year-old patient with LCH located in the rib.

Key words: Chest wall, Mass, Langerhans cell tumor, Eosinophilic granuloma.

Özet

Anahtar Sözcükler: Göğüs duvarı, Kitle, Langerhans hücreli tümör, Eozonofilik granuloma.

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Langerhans Cell Histiocytosis (LCH) is a non-neoplastic proliferation of Langerhans cells (1), of which the etiology is unknown. It is characterized by an accumulation of Langerhans cells (LC) in various tissues and organs, with an incidence in the adult population of 1–2 per million. It is considered a pediatric disease (2). The involvement of single or multiple organs can be seen, although rib placement is rare (3). Local pain is the most common symptom, and diagnosis is through biopsy. The optimum treatment depends on the age of the patient, the localization of the lesion, the number of lesions and the size of the lesion (4). In the present study, we report on an adult patient with LCH (Eosinophilic Granuloma) in the rib.

CASE

A 33-year-old male patient was admitted to our clinic with a painful swelling to the chest wall that had gradually increased over the last year. A physical examination of the patient revealed a painful mass measuring 15x35 mm in the inferolateral aspect of the right hemithorax. A chest X-ray revealed an irregularity in the lateral of the 8th rib, along with a thickening of the pleura.

A thorax tomography of the patient revealed a mass lesion invasive to the parietal pleura in the lateral of the 8th rib, as well as multiple millimetric pulmonary nodules in the bilateral lungs (Figure 1). A positron emission tomography of the patient revealed hypermetabolic activity in the mass lesion in the lateral of the 8th rib (SUVmax: 7.9) (Figures 2).

Laboratory tests revealed elevated Glucose (129 mg/dL), Creatine Kinase (CK: 464 U/L), CK-MB (Creatine Kinase-MB: 36U/L), C-Reactive Protein (CRP: 96mg/L) and White Blood Cell (WBC: 12.43 10e3/μL) levels, and low Lymphocyte (1.19 10e3/μL) and Total protein (6 g/dL) levels.

In the planned operation, the mass was observed to have invaded the pleura and the surrounding tissue, and was excised to include intact bone and pleural tissue (Figures 3). The defect in the chest wall was reconstructed with mesh and a titanium plate to prevent flail chest or collapse (Figure 4, 5a, b). The pathology report identified LCH (Eosinophilic Granuloma). Surgical margins were negative (Figures 6a, b, c).

After the pathological diagnosis, a hematology consultation was requested, and brain magnetic resonance imaging (MRI) was requested by the Hematology Department, but came up normal. A bone marrow biopsy was performed by hematology. In the bone marrow cytology, in mature myeloid series, in eosinophils, in megakaryocytes and in dysmegakaryopoiesis were detected increasing. The results of the biopsy reported normocellular bone marrow. The follow-up and treatment of the patient continued with hematology. The patient was followed up for around one year, during which no complications were seen.
DISCUSSION

LCH is a rare disease that causes local or systemic effects with proliferation and infiltration of histiocytes in various organs (2). The etiology offers no definitive evidence of any infective agent, metabolic or genetic factor, or immunodeficiency (5), and there was no etiological cause also in our patient. The disease generally occurs in the 35±14 age group (1). The patient in the present study was a 33-year-old male.

LCH has been classified into two groups by the Histiocyte Society Working Group as a single-system or multisystemic disease. It can be expressed as low-risk or high-risk, depending on the involvement of such organs such as the liver, spleen, lung and hematopoietic system. LCH, Hashimoto-Pritzker disease, Hand-Schüller-Christian disease, eosinophilic granuloma and Letterer-Siwe disease present with four different clinical pictures, although all of these diseases due are referred to as LCH due to their common immunological features (3,6).

Hashimato-Pritzker's disease is characterized by reticulo-histiocytosis; Hand-Schüller-Christian is a chronic disease that is characterized by four findings: bone lesions, diabetes insipitus, exophthalmos and mucocutaneous lesions; Eosinophilic granuloma accounts for less than 1% of all bone tumors, and 90% of patients are under the age of 10 years. It usually involves the head and vertebral bones, and takes the form of a single lytic lesion. The presence of Langerhans cells is pathognomonic. Letterer-Siwe disease is an aggressive, systemic and often fatal histiocytosis that occurs usually in infancy or early childhood (7).
The symptoms in LCH vary depending on the organ involved (1). Local pain is the most common symptom (34%), although other common symptoms include weight loss (11%) and fever (10%). The main complaints of our patient were pain and swelling. Bone lesions are most commonly seen in the skull (51%), although other sites of involvement include the jaw (30%), long tubular bones (17%), vertebral (13%), pelvis (13%) and ribs (6%) (1). Single-zone, single-system LCH in the rib is a rare condition in adults, and can be difficult to predict (2).

The radiological appearances of LCH are not specific, although the most common findings are osteolytic and sclerotic bone structures. Differential diagnoses include metastasis, plasmacytoma, multiple myeloma, aneurysmal bone cysts, fibrous dysplasia, lymphoma, osteomyelitis and chondromyxoid fibroma. The radiological findings of the patient in the present study were nonspecific, in accordance with the literature. A biopsy of suspected osteolytic bone lesions is required to confirm diagnosis (8). The treatment of adult LCH cases depends on organ involvement and clinical course. Options include follow-up, local treatment, immunomodulation, irradiation, chemotherapy and allogeneic stem cell transplantation. The cessation of smoking is vital. Patients should be followed up for recurrence (8). In our patient, the mass was excised, including also intact bone and pleural tissue. The defect in the chest wall was reconstructed with mesh and a titanium plate to prevent flail chest or collapse.

In conclusion, single-site, single-system LCH in the rib is a rare bone tumor in adults that can be successfully treated with surgical interventions such as curettage or partial resection. A differential diagnosis of solitary osteolytic lesions in the rib should be considered.

**CONFLICTS OF INTEREST**

None declared.

**AUTHOR CONTRIBUTIONS**

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**YAZAR KATKILARI**


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A Rare Cause of Pneumomediastinum: Foreign Body Aspiration

Pnömomediastinumun Nadir Bir Nedeni: Yabancı Cisim Aspirasyonu

Tolga Semerkant¹, Hıdır Esme¹, Celebi Kocaoglu²

Abstract

Pneumomediastinum is characterized by the presence of air in the mediastinum. Non-traumatic pneumomediastinum is rarely seen in children, and while the most common cause is asthma, foreign body aspiration should be considered in children younger than 3 years of age. The determinant of the clinical picture in these cases is the severity of dyspnea. Fasciotomy should be performed prior to rigid bronchoscopy, and mediastinal compression should be decreased in the presence of a marked dyspnea. Here, we present the case of a 2-year-old patient with pneumomediastinum secondary to foreign body aspiration, and discuss the alternative approaches to such cases in the light of literature findings.

Key words: Pneumomediastinum, foreign body aspiration, fasciotomy.

Özet


Anahtar Sözcükler: Pnömomediastinum, yabancı cisim aspirasyonu, fasiotomi.

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The presence of air in the mediastinum is referred to as pneumomediastinum, and subcutaneous emphysema develops as a result of the distribution of this air into the neck, upper extremities and thoracic surface. Pneumomediastinum secondary to foreign body aspiration is rare in children (1). This study analyses a case of pneumomediastinum secondary to foreign body aspiration, subcutaneous emphysema and pneumothorax in the light of currently available literature.

CASE
A 2-year-old female patient was brought to the emergency service with dyspnea and cough that had been present for almost a day. Upon physical examination, a pulse of 120/min. was determined, while blood pressure and saturation were 110/50/mmHg and 80%, respectively. Diffuse emphysema was palpated in the skin and the subcutaneous tissue of the neck and anterior chest wall. A detailed anamnesis revealed a complaint of emphysema of the skin and subcutaneous tissue that started suddenly before the patient was brought to the emergency service, with a simultaneous onset of dyspnea. Respiratory sounds were decreased in the upper right zone. A chest X-ray revealed accumulated air in the upper mediastinum around the heart and the soft tissues of the neck (Figure 1). Thoracic computed tomography (CT) revealed emphysema in the soft tissues of the chest wall, pneumomediastinum, pulmonary interstitial emphysema at the right upper and middle lobe levels, pneumopericardium and bilateral slight pneumothorax (Figure 2). Furthermore, a soft tissue appearance was seen to be obstructing the right main bronchus, atelectasis was present in the right upper lobe, and air trapping was present in the right middle and lower lobes. The patient was taken to the operating room, where a fasciotomy was performed following general anesthesia to decrease the mediastinal pressure. The organic foreign body was removed from the right upper lobe using 3.5 no rigid bronchoscope (Figure 3). The patient, still intubated, was transferred to pediatric intensive care and was extubated one day after the procedure. The subcutaneous emphysema was found to have completely resolved upon physical examination and a chest X-ray on postoperative day 4 (Figure 4). The patient was discharged with a good general condition on postoperative day 5.

DISCUSSION
Foreign body aspiration is a common condition in patients aged 1–3 years due to the high tendency in this age group to place objects in the mouth, inadequate chewing, laughing and tendencies to move while eating (2). Tracheobronchial foreign body aspiration is a life-threatening emergent condition in childhood, characterized by cough, wheezing and dyspnea in varying degrees. Pneumonia, lung abscess and bronchiectasis can develop in undiagnosed cases, and pneumomediastinum may also develop, although rarely (3). Since pneumomediastinum has many causes, a detailed anamnesis should be obtained and a careful physical examination should be carried out in all cases. Asthma is the most common cause of especially non-traumatic pneumomediastinum, which may be encountered even in the first asthma attack (4). Foreign body aspiration should be investigated in all children, especially those under the age of 3 years, and those presenting with pneumomediastinum (5). The most important criterion in the diagnosis of foreign body aspiration is history of aspiration and choking (1). A detailed anamnesis was obtained in the present study. There was no history of foreign body aspiration in the anamnesis of the patient, who presented with a severe dyspnea and subcutaneous emphysema. Air densities were observed around the pericardium on a chest X-ray, and the present clinical picture was thought to be due to an asthma attack, although advanced imaging techniques were used to exclude the diagnosis of foreign body aspiration since the patient was under the age of 3 years, and a thoracic CT revealed a foreign body in the right main bronchus.

Figure 1: A chest X-ray revealed accumulated air in the upper mediastinum around the heart and the soft tissues of the neck.
Pneumomediastinum develops when air diffuses from the tracheobronchial tree into the mediastinum via the interstitial and perivascular space, and subcutaneous emphysema subsequently occurs with the diffusion of air into the subcutaneous tissue (6). The incidence of pneumomediastinum secondary to foreign body aspiration is 1.5%. The clinical picture of pneumomediastinum can vary, ranging from chest pain to subcutaneous emphysema, dyspnea, hemodynamic instability and death. The severity of the clinical picture can be determined from the degree of dyspnea (7). Pneumothorax concurrent with pneumomediastinum may also be seen in foreign body aspirations. The mechanism behind the development of pneumothorax can take two forms. First, a foreign body obstructs the trachea or the bronchus and causes obstructive emphysema, which in turn results in pneumothorax due to the sudden increase in pressure in the lungs. Another mechanism is the direct erosion of the mucosa by a foreign body (4).

In a previous study, the incidence of concomitant pneumomediastinum, subcutaneous emphysema and minimal pneumothorax after foreign body aspiration was reported to be 0.2%, and a severe clinical picture of dyspnea is present in all such cases. An immediate fasciotomy will decrease mediastinal compression, and a subsequent rigid bronchoscopy to remove the foreign body is recommended (8). Diffuse mediastinal and subcutaneous emphysema and slight pneumothorax were present in the present case, together with a severe clinical picture of dyspnea. A fasciotomy was performed to release the mediastinal compression before initiating a rigid bronchoscopy for the removal of the foreign body was removed. At follow-up, the emphysema was found to have completely regressed on postoperative day 4. The postoperative course of the patient was uneventful, and she was discharged in good health.

CONCLUSION
Non-traumatic pneumomediastinum is rare in children, and should be investigated cautiously for foreign body aspiration when seen in patients under 3 years of age. An initial fasciotomy should be carried out to decrease mediastinal pressure in patients with a poor general condition, severe dyspnea and pneumomediastinum, followed by a rigid bronchoscopy.
CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS

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Malignant Peripheral Nerve Sheath Tumor Related to Diffuse Neurofibroma of Chest Wall

Göğüs Duvarının Diffüz Nörofibroma ile İlişkilı Malign Periferal Sinir Kılıfı Tüümörü

Muhtarrem Çakmak¹, İsmail Demirel²

Abstract

Malignant peripheral nerve sheath tumors account for 5–10% of all soft tissue tumors. These tumors are closely related with Neurofibromatosis type 1. Although many such tumors have been reported in different locations, malignant peripheral nerve sheath tumors arising from diffuse neurofibroma located in the chest wall are extremely rare. In the present study we report on a malignant peripheral nerve sheath tumor arising out of a diffuse neurofibroma of the chest wall.

Key words: Chest wall, Mass, Malignant peripheral nerve sheath tumor.

Özet

Malign periferik sinir kılıfı tümörü yumuşak doku tümörlerinin %5-10’unu oluşturur. Bu tümörler Nörofibromatözis tip 1 ile yakından ilişkilidir. Farklı lokalizasyonlarda birçok olgu bildirilmiş olsa da göğüs duvarı yerleşimli diffüz nörofibroma zemininde gelişen malign periferik sinir kılıfı tümörü son derece nadirdir. Bu çalışmada, göğüs duvarı yerleşimli diffüz nörofibroma zemininde gelişen malign periferik sinir kılıfı tümörü sunuyoruz.

Anahtar Sözcükler: Göğüs duvarı, Kitle, Malign periferik sinir kılıfı tümörü.

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Chest wall tumors are classified as either primary or secondary. While primary tumors originate from soft tissue, bone, cartilage, vessels, and nerves, secondary tumors are metastatic. Some 60–70% of primary tumors are malignant (1). Malignant peripheral nerve sheath tumors (MPNST) account for 5–10% of all soft tissue tumors, and are closely associated with neurofibromatosis type 1 (NF-1). Although many such cases have been reported in different locations, MPNST tumors related to diffuse neurofibroma located in the chest wall are extremely rare (2-4).

The symptoms are nonspecific, but the most common complaint is a painless growing mass. In tumors including bone-derived factors, accompanying pain due to periosteal injury is common, and is a predictor of poor prognosis (1).

Diagnoses are made based on anamnesis, physical examination, radiological evaluation, and biopsy. Fine needle aspiration biopsy, incisional biopsy, or excisional biopsy can be performed for a definitive diagnosis. The treatment is surgical, with complete tumor resection with negative margins in tumors smaller than 2cm having been shown to be important for a successful cure (2).

In the present study we report on a rare case with low grade MPNST arising from diffuse neurofibroma of the chest wall. Such tumors, which are extremely rare, should not be ignored in differential diagnosis.

CASE
A 56-year-old female patient was admitted to our clinic with a complaint of a painful, enlarging mass on the chest wall, having been operated three times in the last 6 years due to chest wall masses.

During the subsequent examination, a lesion measuring approximately 8x7cm in size and painful to palpation, as well as incision scars from previous operations, were detected in the left posterolateral hemithorax (Figure 1). There was no significant pathology on chest X-ray.

A thoracic MRI was performed to understand the extent of the lesion on the chest wall. MR imaging of the thorax revealed a mass lesion of 11x7 cm in axial and 11x6 cm in coronal, extending from the infraspinatus and teres minor muscles to the subscapular and lattice dorsi muscles in the left inferior hemithorax (Elastofibroma dorsi ? Rabdomiosarcoma ? Metastatic involvement ?) (Figure 2).

The patient’s medical history was unremarkable, other than three separate operations in the same region. Her family history was unremarkable and laboratory tests were normal. An operation was planned for the patient, whose previous pathology results were evaluated as fibrolipoma. The mass was determined macroscopically before the operation. The excision was made 4 cm distant from the mass, and the mass and the surrounding abnormal tissues were excised up to the ribs (Figure 3). The removed mass area was repaired with a skin graft from the thigh region (Figure 4a and b).

The patient experienced no postoperative complications, other than minimal hematoma at the graft site. A patho-
logical examination revealed a low-grade MPNST tumor developing on the basis of diffuse neurofibroma. The surgical margins were negative (Figure 5a and b). After pathological diagnosis, oncology and rheumatology consultations were requested, and the patient was followed up and treated by these departments. The patient was followed up for around five months, during which no complications developed.

DISCUSSION

MPNSTs develop from the peripheral nerve sheath or branches of the peripheral nerve fibers. Although they may develop spontaneously, they are associated with neurofibromatosis type 1 in most cases. NF-1 gene inactivation is thought to play a role in its pathogenesis (5), although there was nothing remarkable in our patient's family history, and an NF-1 gene analysis was negative. MPNSTs are common in the third and fourth decades, but are rare in childhood and adolescence. They are more common in women than in men (6). The case in the present study was a 56-year-old female.

Malignant schwannoma, neurogenic sarcoma, neurofibrosarcoma and anaplastic neurofibroma are the main types of MPNST; approximately two-thirds of them originate from neurofibromas; and 5-year survival is reported to be 15–21% (7).

Diagnosis is primarily by biopsy. For treatment, the tumor should be resected with surrounding tissues up to the intact border. Following resection, it should be performed local radiotherapy, which has been shown to reduce local recurrence. Accordingly, radiotherapy should be started as early as possible in the postoperative period. In recent publications, it has been reported that neoadjuvant/adjuvant chemotherapy after en bloc resection yields similar results to the more radical approaches (3). In the patient in the present study, the mass was completely resected with the surrounding intact tissue, and positive results were obtained with grafting. The patient was then sent to the relevant department for radiotherapy.

Figure 3a and b: Intraoperative views of the mass
In conclusion, MPNSTs are uncommon, and chest wall placements are very rare. MPNSTs should be considered in a differential diagnosis of chest wall malignant masses in elderly patients. For the treatment of such aggressive and progressive tumors, excision, chemotherapy and radiotherapy should be used to prevent local recurrences.

CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
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Thoracic Splenosis

Torasik Splenosis

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Abstract

The spread of spleen tissue through different parts of the body is referred to as autotransplantation splenosis, and is an acquired and rare condition. The focal spread of splenic tissue into the thorax due to diaphragm laceration is referred to as thoracic splenosis, and may present as more than one pleural nodule in the left hemithorax. It usually occurs after a blunt trauma causing a combination of spleen injury and left diaphragmatic rupture. In the present study, we present a case of intrathoracic splenosis in an 18-year-old male patient who had undergone a splenectomy 14 years earlier after suffering a gunshot wound.

Key words: Thoracic splenosis, splenectomy, trauma.

Özet


Anahtar Sözcükler: Torasik splenosis, splenektomi, travma.

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Splenosis refers to the spread of splenic tissue as a result of lacerations to the spleen and diaphragm, and usually occurs in the peritoneal cavity. Upon passing through a ruptured diaphragmatic defect, splenic cells may implant themselves into the parietal pleura and grow in the pleural cavity (1-5). One important feature of the disease is that patients are generally asymptomatic. Splenosis appears as a peripheral nodule on chest radiography. Computed tomography (CT) imaging may suggest primary or metastatic lung cancer. If the anamnesis of the splenic injury is unknown, diagnosis may be difficult, and may require transthoracic biopsy, video-assisted thoracoscopic surgery (VATS) or thoracotomy.

CASE
An 18-year-old male presented to our clinic with left-sided abdominal pain that had started one week earlier. A thoracic CT performed at another center prior to presentation to our clinic revealed a 2.5 cm diameter nodular lesion in the left lower zone of the pleura and in the subpleural region. The patient had no known chronic disease, but had undergone a splenectomy and a partial excision of the left lobe of the liver 14 years earlier for the treatment of liver and spleen laceration resulting from a gunshot. There was no smoking, and no tuberculosis or pneumonia in the patient’s history. He was working as an electrician in building construction, and had no known exposure to asbestos.

A physical examination revealed fever of 37.8°C; pulse 100/min; blood pressure 120/70 mmHg; and respiratory rate 14/min. No pathological findings were noteworthy aside from the abdominal operation scars. Laboratory tests revealed C-reactive protein 60.94 mg/L; white blood cells 13200 µ/L; hemoglobin 13.7g/dL; platelet count 649.8 µ/L; erythrocyte sedimentation 20 mm/hour; blood urea nitrogen 11 mg/dL; and creatinine 0.69 mg/dL. A chest X-ray revealed a 2 cm diameter opacity on the diaphragm in the left lower zone, as well as left sinus closure (Figure 1). The thoracic CT images were reevaluated by the radiologists of our hospital, who made the following report: “In the lower left lobe in the subpleural-juxta diaphragmatic area, multiple smooth-edged nodules, the largest of which is approximately 2x4 cm in size, can be seen. Considering the patient's trauma history, these images are compatible with thoracic splenosis” (Figure 2). A fiberoptic bronchoscopy was performed and the respiratory tract was normal. A CT-guided tru-cut biopsy was performed on the 15 mm nodule in the left lung lower lobe, the pathology of which was reported as “Chronic inflamed fibroadipose tissue and benign striated muscle tissue, with no evidence in favor of malignancy in the material”. The Positron Emission Tomography (PET-BT) report read: “Nodular areas were observed in the left lung lower lobe that did not show significant metabolism in the subpleural or juxta diaphragmatic areas, but showed a slightly increased metabolism (SUVmax: 2.1). May be compatible with thoracic splenosis, as suggested by diagnostic CT. Selective spleen scintigraphy with labeled denatured erythrocytes is recommended” (Figure 3).

A selective spleen scintigraphy (SPECT) report read: “The patient, who has a history of splenectomy after splenic trauma, has multiple focial activity involvements in the left part of the abdomen and in the lower part of the left hemithorax that are evaluated to be consistent with splenosis” (Figure 4).

The patient’s diagnosis was accepted as thoracic splenosis, based on radiological and nuclear medicine results. No invasive diagnostic methods were required.
Splenosis, defined as the autotransplantation of ectopic splenic tissue into the body after a splenic rupture or splenectomy, was first described in 1937. The main cause of splenic implantation is trauma. Although the incidence of heterotopic spleen is high in the abdominal and pelvic cavities, thoracic splenosis is a rare clinical condition that occurs in less than 0.25% of splenectomies. The splenic tissue reaches the serous surface of the pleural cavity via the damaged diaphragm. Thoracic splenosis nodules may locate in the visceral and parietal pleura, the pericardium or in interlobar fissures (6,7). All cases on the topic reported in the English language in literature describe a history of splenic injury or splenectomy. Patients are generally asymptomatic. The lung parenchyma is a rare region of implantation (5).

Chest X-ray, thoracic CT and radionuclide scans can aid diagnosis. A detailed history is taken, and when splenosis is suspected, it can be diagnosed with a 99m-Tc-99m sulfur colloid and indium-111-labeled platelets are other, less sensitive, methods.

Although Ferumoxide MRI has been used for the diagnosis of splenosis, it is reported that more research is needed for the direct comparison of nuclear studies with Ferumoxide MRI in diagnosis of splenosis (9,10).

For the patient in the present study, we opted for the nuclear medicine approach to diagnosis, since we were unable to achieve a significant histopathological diagnosis via a transthoracic needle biopsy. Invasive procedures such as VATS and thoracotomy can be performed when there is suspicion of malignancy for pleural-based nodules, or where required for the removal of implants in symptomatic patients with hemoptyis, cough or pleuritic chest pain (11,12).

CONCLUSION
Splenosis should be kept in mind in a differential diagnosis of lesions when there is a history of splenic trauma and when masses are detected in the thorax upon radiological imaging. No surgical resection is required in asymptomatic and uncomplicated cases.

CONFLICTS OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS

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