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Pulmonary involvement in sea-blue histiocytosis

Ersin GÜNAY[1], Selma FIRAT GÜVEN[1], Zafer AKTAŞ[1], Tuğrul ŞİPİT[1], Yetkin AĞAÇKIRAN[2], Hakan ERTÜRK[3]

[1] Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Kliniği, Ankara,
[2] Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Patoloji Kliniği, Ankara,
[3] Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Radyoloji Kliniği, Ankara.

ÖZET

Sea-blue histiyositoz akciğer tutulumu

Sea-blue histiyositoz Niemann-Pick hastalığının altı tipinden biridir. Çocukluk çağında başlayan hepatosplenomegali olması, nörolojik tutulumun olmaması ve sfingomiyelinaz aktivitesinin azalmasıyla karakterizedir. Akciğer tutulumu sea-blue histiyositozda görülen nadir bir klinik tutulumdur. Bu olgu sunumunda, 15 yaşındayken sea-blue histiyositoz tanısı konulan 39 yaşındaki bir erkek hasta sunulmaktadır. Hasta kliniğimize prodüktif öksürük, hemoptizi, ateş ve kilo kaybıyla başvurdu. Hastanın semptomlarında antibiyotik tedavisine rağmen gerileme olmaması üzerine ileri araştırma sonucunda sea-blue histiyositozun akciğer tutulumu olduğu görüldü. İlginç olarak, hastanın yakınmaları tanısal bronkoalveoler lavaj sonrası düzeldi. Nadir görülmesi nedeniyle hasta literatür eşliğinde tartışıldı.

Anahtar Kelimeler: *Niemann-Pick hastalığı, pnömoni, sea-blue histiyositoz.*

SUMMARY

Pulmonary involvement in sea-blue histiocytosis

Ersin GÜNAY[1], Selma FIRAT GÜVEN[1], Zafer AKTAŞ[1], Tuğrul ŞİPİT[1], Yetkin AĞAÇKIRAN[2], Hakan ERTÜRK[3]

[1] Clinic of Chest Diseases, Ataturk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey,
[2] Clinic of Pathology, Ataturk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey,
[3] Clinic of Radiology, Ataturk Chest Diseases and Chest Surgery Training and Research Hospital, Ankara, Turkey.

Sea-blue histiocytosis is one of the six types of Niemann-Pick disease. It is characterized by childhood onset of hepatosplenomegaly, lack of neurological involvement and diminished sphingomyelinase activity. Pulmonary system is rarely involved sea-blue histiocytosis. In this paper, we present a 39-years-old male who had previously diagnosed as sea-blue histiocytosis at the age of 15. He was admitted to our clinic due to productive cough, hemoptysis, fever and weight loss. His symptoms did not resolve with the antibiotic treatment and further investigations revealed pulmonary involvement of sea-blue histiocytosis. After diagnostic bronchoalveolar lavage, his symptomes were improved, interestingly. This rare entity was discussed with literature survey.

Key Words: *Niemann-Pick disease, pneumonia, sea-blue histiocytosis.*

Yazışma Adresi (Address for Correspondence):

Dr. Ersin GÜNAY, Iğdır Devlet Hastanesi, 2. Göğüs Hastalıkları Polikliniği,
IĞDIR - TURKEY

e-mail: ersingunay@gmail.com

INTRODUCTION

Niemann-Pick disease (NPD) is a lipid storage disease with six subgroups (NPD type A to F). NPD type F, also named as sea-blue histiocytosis (SBH), is seen in adult population (1). Foamy macrophages are called as sea-blue histiocytes that accumulate in visceral organs such as liver, spleen and rarely other organs due to decreased activity of sphingomyelinase. On the contrary, central nervous system is preserved in all cases that is characteristic feature of the disease. Pulmonary involvement in SBH is rare and may be asymptomatic if the disease is only limited within pulmonary system. However, it may also cause mortality and morbidity if respiratory insufficiency develops. Here we report a patient with SBH and pulmonary involvement and review the pertinent literature.

CASE REPORT

A 39-years-old male patient was admitted to our clinic with complaining of cough, purulent sputum, hemoptysis, dyspnea on exertion, fever and weight loss of 4 kg in a month. Previously, at the age of 15 when he was examined for stomach ache, hepatosplenomegaly was discovered and fine-needle aspiration biopsies of liver and bone marrow were performed. The biopsy specimens demonstrated foamy macrophages. Sphingomyelinase defficiency was also detected, hence he received the diagnosis of SBH. Family history was unremarkable. On physical examination, vital signs were within normal limits, rales were present on the lower half of the left hemithorax. Spleen was palpated about 14 cm and liver was palpated about 12 cm under the rib cage. Neurological examination did not reveal any positive findings.

Laboratory findings were as below; erytrocyte sedimentation rate was 60 mm/hour and serum lipids were elevated [total serum cholesterol: 310 mg/dL (normal range: 140-240 mg/dL), high-density lipoprotein: 9 mg/dL (normal range: 30-85 mg/dL), low-density lipoprotein: 269 mg/dL, Very low-density lipoprotein: 33]. Pulmonary function tests revealed a restrictive pattern with FVC: 2.91 L (75% of predicted), FEV_1: 2.15 L (65% of predicted) and FEV_1/FVC: 74%. Carbon monoxide diffusion capacity was lower than normal; DL_{CO}: 5.6 mmol/kPa.min (61% of predicted) and DL_{CO}/VA: 1.2 mmol/kPa.min (74% of predicted). Arterial blood gas analysis in room air revealed pH: 7.38, PaO_2: 40 mmHg, $PaCO_2$: 42 mmHg. On the postero-anterior chest X-ray, consolidation was present in the lower zone of the left lung (Figure 1). Abdominal ultrasound revealed hepatosplenomegaly with craniocaudal length of liver and spleen 20 cm and 19 cm respectively. There was consolidation with air bronchogram at the lingula in thorax computed tomography (CT) sections (Figure 2). Three sputum samples were negative for acid-fast bacilli and tuberculosis skin test was negative. Lipid-poor diet was given to patient for hypercholesterolemia. Although non-specific antibiotic treatment of amoxicillin-clavulanic acid and clarithromycin was administered, no clinical or radiological improvement was achieved. For this reason, fiberoptic bronchoscopy was performed, which showed no endobronchial lesion. Bronchioloalveolar lavage (BAL) fluid was composed of 61% macrophages, 35% lymphocytes, and 4% neutrophiles without any cells with atypical features. After lavage procedure, an increase in oxygen saturation from 75.4% to 96.3% was detected. Cough and hemopytisis of the patient comp-

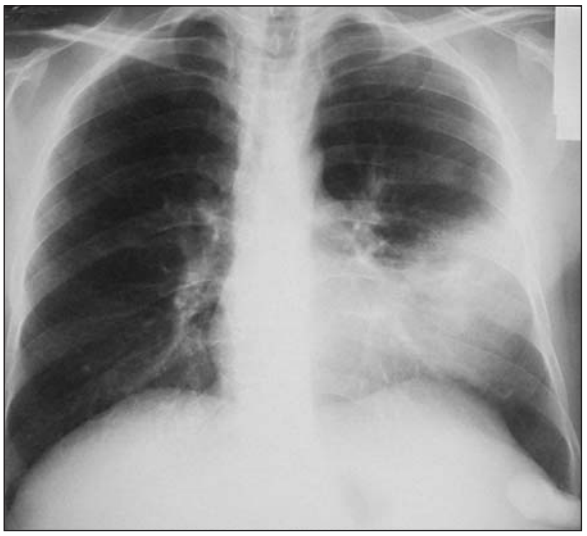

Figure 1. Postero-anterior chest X-ray of patient with infiltration on the left middle lung field.

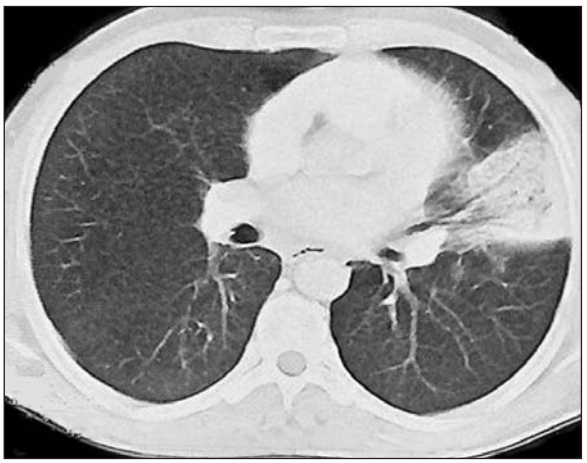

Figure 2. There is consolidation with air bronchogram in lingular segment in thorax computed tomography.

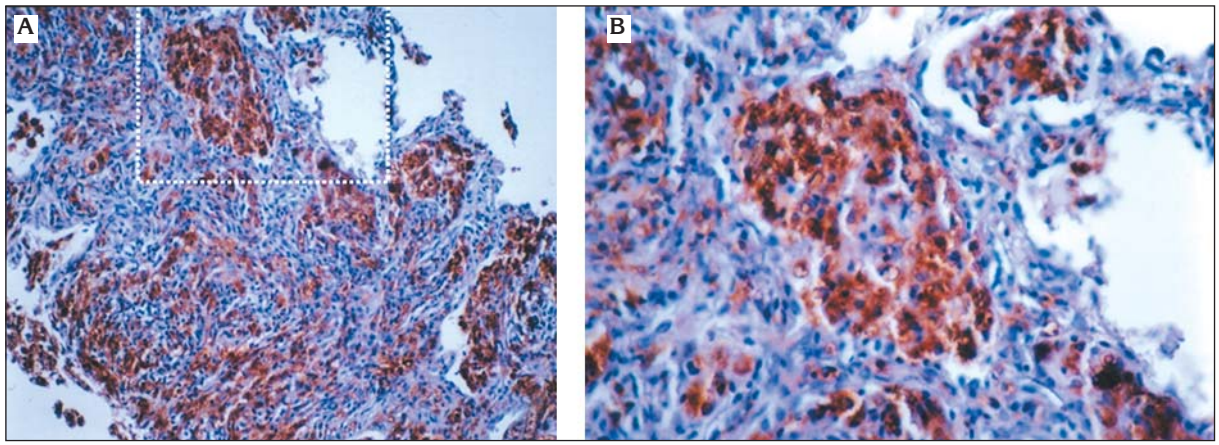

Figure 3. In lung paranchyma, there are intensive accumulation and group formation of CD68 positive foamy histiocytes: immunohistochemistry, x200 (A)/x400 (B).

letely resolved in a few days. However, the consolidation seen on the radiographies persisted. Therefore, we performed CT guided tru-cut biopsy from consolidation area in lingular segment to exclude any malignancy. On microscopic examination of the biopsy specimen, lipid laden foamy histiocytes were seen with immunohistochemically expression of CD 68 covering the lung parenchyma (Figure 3). These findings were consistent with pulmonary involvement of SBH. Since pulmonary symptoms including hemoptysis were completely disappeared following BAL and declining of serum cholesterol levels was achieved with diet modification. No further treatment modality was planned. In his follow-up, the symptoms did not reoccur but the consolidation in the lingular segment persisted even after three years of diagnosis of pulmonary involvement.

DISCUSSION

NPD consists of a group of congenital lipidoses autosomal recessively inherited in which sphingolipids accumulate in cells, particularly reticuloendothelial cells, throughout the body. Six types of NPD has been described. SBH, known as type F of NPD, is a rare type without neurological involvement. SBH is generally seen in adults (1-3). Sea-blue histiocyte is a macrophage that contains varying numbers of cytoplasmic granules imparting a distinct blue color on Wright's-Giemsa stain (4). In 1970, Silverstein et al. have described the syndrome of sea-blue histiocytes, characterized the presence of large foamy macrophagic cells in the bone marrow, spleen, and sometimes liver and lungs (5,6). SBH can be seen in different diseases of which hematological involvement such as chronic myeloid leukemia, idiopathic thrombocytopenic purpura, and myelodysplastic syndromes and metabolic involvement such as NPD and Gaucher diseases (6-9). SBH is differentiated from these diseases with sphingomyelinase defficiency and clinical appearance (7). Symptoms of Sea-blue histiocytes differ depending on the organs involved. NPD type A and C are seen in childhood and have poor prognosis. In SBH, hepatosplenomegaly is common. Other organ involvements are rare, as well neurological involvement is very rare (1). Our patient was 39-years-old. Although, he was first diagnosed when he was 15-years-old, he did not have any other complaints except for stomach ache for the following two decades. As expected, he had no neurological symptoms either.

Pulmonary pathologies are rarely encountered in NPD (8,10). In literature, there are only few cases about pulmonary involvement of SBH. In NPD, at the beginning, lipid-laden macrophages accumulate in lower lobes of lung fields which can be seen as diffuse linear or nodular infiltration in chest X-ray. Subsequently, upper lung fields may also be involved. In thorax tomography, interlobular septal thickening, multiple pulmonary nodules and ground-glass appearances can be seen secondary to partial accumulation of alveoli with foamy histiocytes. Less commonly, lenfadenopathies, pleural involvement and cavitation may be present (8,10). In our case, CT revealed nodular interstitial thickening, ground-glass infiltration with air bronchogram and bronchiectasis. In NPD type B, although pulmonary involvement can be asymptomatic, it may be the main cause of mortality and morbidity if it leads to respiratory insufficiency (10).

There is no known effective treatment of pulmonary involvement of NPD. A lot of therapeutic modalities have been applied for palliation. If respiratory failure with hypoxia was present, nasal oxygen supplement can be

provided (1). If bilateral lung involvement is present, patient can be succesfully treated with whole lung lavage (10). After application of diagnostic BAL of lingular segment, interestingly, oxygen saturation of our patient increased, but, infiltration on chest X-ray was not be resolved. We did not need to apply whole lung lavage because of limited involvement of lingular segment. Since lipid poor diet may be effective for hiperlipidemia in NPD we also modified the patient' diet and achieved improvement in serum lipid levels (1).

There are some additional treatment alternatives, which are not routinely used. One of them is stem cell transplantation which was claimed effective for NPD (11,12). Also, bone marrow transplantation have shown improvement in lung infiltrations and provided regression of hepatomegaly (13). Additionally, amniotic epithelial cell implantation can be effective for sphingomyelinase deficiency (14,15). Enzyme replacement therapy and gene therapy are promising but further studies are required.

In conclusion, lysosomal storage diseases are rare in the population and pulmonary involvement is not a common feature of this group of diseases. Nevertheless, lipidosis with lung involvement should be considered in differential diagnosis of the patients with persistent pulmonary infiltrates, particularly of those with a pertinent personal or family history.

CONFLICT of INTEREST

None declared.

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