Erciyes Med J 2013; 35(3): 174-6 • DOI: 10.5152/etd.2013.29

A Case with Niemann-Pick Disease and Concomitant Kartagener's Syndrome

CASE REPORT
OLGU SUNUMU

Kartagener Sendromu'nun Eşlik Ettiği Bir Niemann-Pick Olgusu

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ABSTRACT
ÖZET

Niemann-Pick disease is a rare lipid storage disorder with autosomal recessive inheritance, which is characterised by the accumulation of sphingomyelin and other sphingolipids in macrophages. Kartagener's Syndrome is a syndrome with autosomal recessive inheritance consisting of chronic paranasal sinusitis, situs inversus, and bronchiectasis. Here we reported a case having Kartagener's Syndrome with concomitant Niemann-Pick disease, as such a case has not been reported in the literature.

Key words: Bone marrow, Kartagener's Syndrome, Niemann-Pick disease

Niemann-Pick Hastalığı, nadir bir lipid depo hastalığı olup otozomal resesif kalıtılır, makrofajlarda sfingomyelin ve diğer sfingolipidlerin birikimi ile karakterizedir. Kartagener Sendromu, otozomal resesif kalıtılan bir sendrom olup kronik paranazal sinüzit, situs inversus ve bronşiektazi triadını içerir.Bu çalışmada, Niemann-Pick Hastalığı ve Kartagener Sendromu birlikteliği olan bir olguyu, literatürde rastlanmamış olması nedeniyle sunduk.

Anahtar kelimeler: Kemik iliği, kartagener sendromu, niemann-pick hastalığı

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Available Online Date/ Çevrimiçi Yayın Tarihi
27.05.2013

Submitted/Geliş Tarihi
04.02.2013

Accepted/Kabul Tarihi
15.03.2013

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Introduction

Niemann-Pick disease is a rarely seen heterogeneous lipid storage disorder. It was first described in an 18-month-old girl with hepatosplenomegaly, progressive mental and motor retardation by Niemann-Pick enabled to differentiate from other entities involved in the disease (1). It is sub-classified according to the age of onset and central nervous system involvement. Sphingomyelinase deficiency has been demonstrated in Type A and Type B disease, while sphingomyelinase values are shown to be normal or near-normal in Type C and Type D (2). Diagnosis is established by observation of lipid-containing macrophages (sea-blue histiocytes) in bone marrow biopsy. Although hepatosplenomegaly is a frequent finding, there are case reports in which Niemann-Pick disease was identified by isolated splenomegaly in the literature.

Kartagener's Syndrome, first identified in 1933, is characterised by primary ciliary dyskinesia and complete situs inversus (3). Mucociliary clearance is impaired due to ciliary dysmotility of the airway; thus, secretions accumulate on the epithelial surface, resulting in bacterial infections (4-6). Bronchiectasis develops at a younger age due to chronic and recurrent infections. Here, we present a case with Kartagener's Syndrome that was referred to a haematologist due to splenomegaly detected during the follow-up period and diagnosed as Niemann-Pick disease by bone marrow biopsy. Such a case has not been reported in the literature.

Case Report

A 21-year-old woman was referred to the Haematology Department due to finding of splenomegaly by another facility where she presented with a cough, abdominal pain, and fatigue. In her history, it was found that she had frequently had upper respiratory tract infections since infancy. It was also found that dextrocardia was detected on a chest radiography performed 4 years previously, when she presented with recurrent sinusitis and cough. We also learned that, on the thorax CT performed after the confirmation of dextrocardia by echocardiography, there was inverse positioning of the liver and spleen and the appearance of bronchial dilatation, peribronchial thickening and consolidation favouring bronchiectasis in the lungs (Figures 1 and 2). She was diagnosed with Kartagener's Syndrome due to the presence of bronchiectasis, situs inversus, and sinusitis. There was intermittent antibiotic use, expectorant therapy, and postural drainage training in her history. She received regular vaccinations against influenza and pneumococcus.

In the physical examination, general health status was good in the conscious patient. Mild mental retardation was detected in neurological and psychiatric evaluation. Her body temperature was measured as 36.9°C; blood

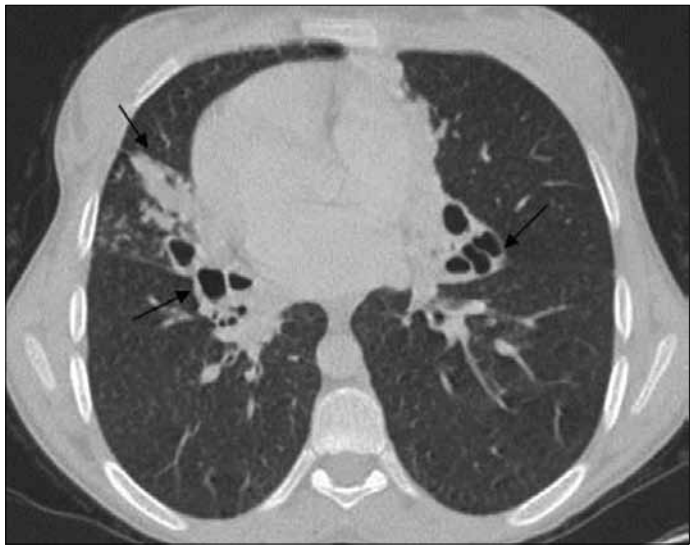

Figure 1. Axial image (lung window) CT demonstrates dextrocardia and bronchiectasis (arrows) consistent with Kartagener's Syndrome, and also shows widespread ground-glass opacity compatible with Niemann-Pick disease

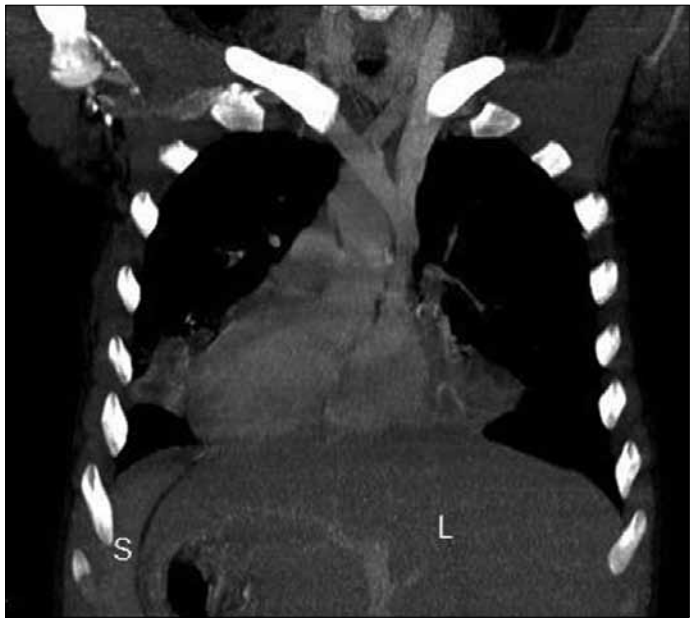

Figure 2. Coronal maximum intensity projection (MIP) CT image (soft tissue window) depicts situs inversus. Spleen (S), liver (L)

pressure was 110/80 mmHg, and heart rate was 78 beats/min. In the auscultation, apex beat was heard on the right side and there were crackles in the bilateral lower zones of the lungs. On the right, the spleen was palpated at 4-5 cm below the last rib. On the chest radiography, the heart and gastric air were localised on the right side. Laboratory results showed that leukocyte counts were $7.12x10^3$/µl (polymorphonuclear leukocyte 57.9%; lymphocyte 33%; eosinophil 3.1%; basophil 0.4%; and monocyte 5.6%), haemoglobin was 13 g/dL, and platelet was $196x10^3$/µL. HBs Ag, anti-HBs, and anti-HCV were found to be negative. On abdominal ultrasound evaluation, it was found that the liver was normal in size with homogenous parenchymal echo, and the spleen was larger than normal (165 x 85 mm in size). On the peripheral blood

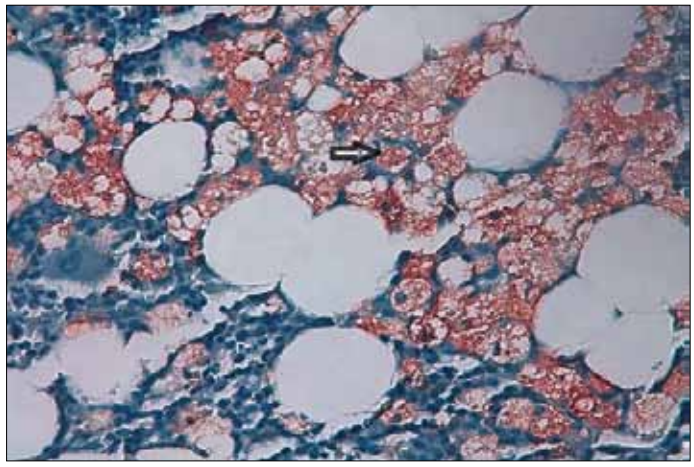

Figure 3. Bone marrow biopsy specimen, with CD68-positive staining of macrophages and bone marrow as detected by immunohistochemistry (magnification X400)

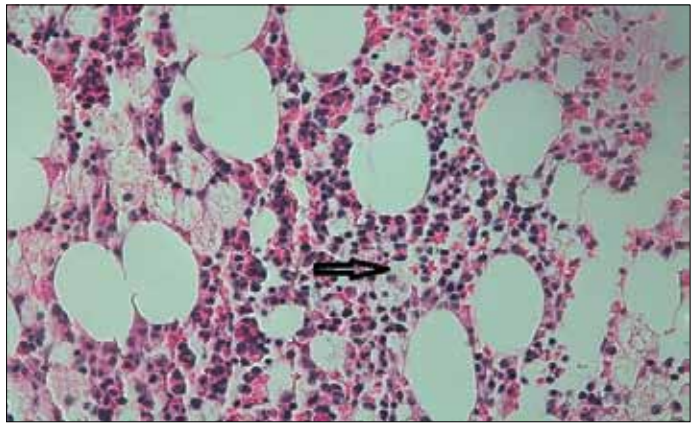

Figure 4. Bone marrow biopsy specimen revealing macrophages with cytoplasm containing vacuoles among bone marrow cells (H&E, magnification X400)

smear, a few atypical monocytes were detected; thus, bone marrow aspiration and biopsy were performed. On the bone marrow smear, elements from three cell lineages and sea-blue histiocyte infiltration were detected (Figure 3). Results of the biopsy were reported as Niemann-Pick disease (Figure 4). Sphingomyelinase activity (7.73±3.08 nmol/17 hours/mg protein) in leukocyte was found to be 1.38 nmol/17 hours/mg protein. Thus, the patient was diagnosed with Type B Niemann-Pick disease. She declined the upper gastrointestinal endoscopy evaluation recommended for the investigation of splenomegaly aetiology.

Discussion

Niemann-Pick disease is a disorder of lipid metabolism in which sphingomyelin and secondary cholesterol accumulate in lysosomes either as a result of acid sphingomyelinase enzyme (sphingomyelin phosphodiesterase-ASM) deficiency or ASM gene mutations (7). Diagnosis is made by the assessment of sphingomyelinase activity and observation of lipid-containing macrophages (sea-blue histiocytes) in bone marrow biopsy. There are data on Niemann-Pick disease with pulmonary involvement in the literature; however, there is no report about Niemann-Pick disease with concomitant

Kartagener's Syndrome (8). Kartagener's Syndrome is characterised by the triad of chronic sinusitis, bronchiectasis, and situs inversus (9). It is classified under the group of disorders known as primary ciliary dyskinesias. It is inherited in an autosomal recessive manner. No evaluation directed to sinusitis was performed in our case, as there was no sinusitis-related symptom at presentation.

In Niemann-Pick disease, there may be increased total cholesterol and LDL cholesterol as well as reduced HDL cholesterol as lipid abnormalities; these values were in the normal range in our case (10). In the follow-up for Kartagener's Syndrome, antibiotic therapy, postural drainage and maintenance of prophylactic vaccination were recommended for bronchiectasis by the Department of Chest Diseases.

Conclusion

We present this case as there is no reported case of Niemann-Pick disease with concomitant Kartagener's Syndrome in the literature. Enzyme replacement, gene therapy, and stem cell transplantation should be recommended in the treatment of appropriate cases. Cases diagnosed as Kartagener's Syndrome should be informed about autosomal recessive inheritance of the disease. Vaccinations against influenza and other frequent causes of pulmonary infection should be performed annually. It should be kept in mind that multiple syndromes may exist together in cases presenting with recurrent respiratory tract infection in the presence of splenomegaly.

Conflict of Interest
No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Authors' contributions: Conceived and designed the experiments or case: MK. Performed the experiments or case: MK, SB, AY, OK, FK, and CP. Analysed the data: MC and AU. Wrote the paper: MK. All authors have read and approved the final manuscript.

Çıkar Çatışması
Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

Hakem değerlendirmesi: Bağımsız hakemlerce değerlendirilmiştir.

Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

Yazar katkıları: Çalışma fikrinin tasarlanması: MK. Deneylerin uygulanması: MK, SB, AY, OK, FK ve CP. Verilerin analizi: MC ve AU. Yazının hazırlanması: MK. Tüm yazarlar yazının son halini okumuş ve onaylamıştır.

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