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Non-neuropathic Niemann-Pick disease with sea blue histolocytic involvement of the lungs: A case report

Sea blue histiositik akciğer tutulumu ile birlikte olan non-nöropatik Niemann-Pick Hastalığı: olgu sunusu

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ÖZET: *10 yaşında erkek hasta hepatosplenomegali ve ön-arka gögüs filminde her iki akciğerde retikülonodüler görüntü nedeniyle değerlendirildi. Köpüksü ve sea-blue histiositler, kemik iliğinde saptandı. Hastada aynı zamanda biopsi ile kanıtlanmış akciğer ve karaciğer tutulumu da vardı. Nörolojik muayene normaldi. Tanı lipid depo hastalığı, çok kuvvetle non-nöropatik sea-blue histiositli Niemann-Pick hastalığı idi.*

Anahtar Kelimeler: **Non-nöropatik Niemann-Pick hastalığı, sea-blue histiosit**

SUMMARY: *A 10-year-old boy patient was evaluated for hepatosplenomegaly and reticulonoduler appeareance of both lungs on the posteroanterior chest x-ray. Foamy and sea-blue histiocytes were noted in the bone marrow. He also had biopsy proven pulmonary and liver involvement with sea-blue and foamy histiocytes. Neurological examination was normal. The diagnosis was lipid storage disease, most likely non-neuropathic Niemann-Pick disease with sea-blue histiocytes.*

Key Words: **Non-neuropathic Niemann-Pick disease, sea-blue histiocyte**

SEA-BLUE histiocytes were first described in a splenic aspirate by Moeshin in 1947 51). Sea-blue histiocytes may also be noted in specimens of bone marrow, liver and lymph nodes (2).

The "sea blue histiocyte syndrome" was first described in 1970 by the Mayo Clinic Group (3). Clinic spectrum of the primary form of the syndrome varies from a relatively benign mild purpura secondary to thrombocytopenia to progressive hepatic cirrhosis, hepatic failure and death. Patients with this syndrome have characteristic sea-blue histiocytes in the bone marrow and liver. Sea-blue histiocytes, however, are more frequently encountered in the bone marrow as secondary to a variety of metabolic and hematological disorders including inborn errors of lipid metabolism (4-7). Several cases initially presumed to be primary sea-blue hisitocyte syndrome have been thereafter diagnosed to be variants of Niemann-Pick disease (5).

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We report a child with Niemann-Pick disease who had foamy and sea-blue histiocytic infiltration in the bone marrow, liver and lung. Of interest, the patient had low serum levels of high density lipoprotein cholesterol (HDL) levels.

CASE REPORT

A 10-year old boy was referred to our hospital for evaluation of hepatosplenomegaly. In his prior history, the patient first consulted a physician for short stature; during that initial visit hepatosplenomegaly had been noted. The patient was 1.21 m in height (<3rd%) and 26 kg in weight (<10%). On physical examination, the liver was palpable 16 cm and spleen 7 cm below the right and left costal margins, respectively. The neurological examination was normal and there was no evidence of intellectual impairment. Ocular examination was normal.

The complete blood count was normal. The serum aspartat aminotransferase and alanine aminot-

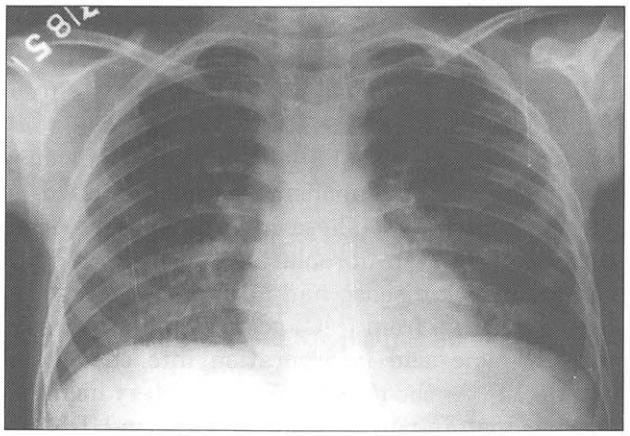

Figure 1. *PA chest radiogram shows diffuse reticulonoduler pattern in both lungs.*

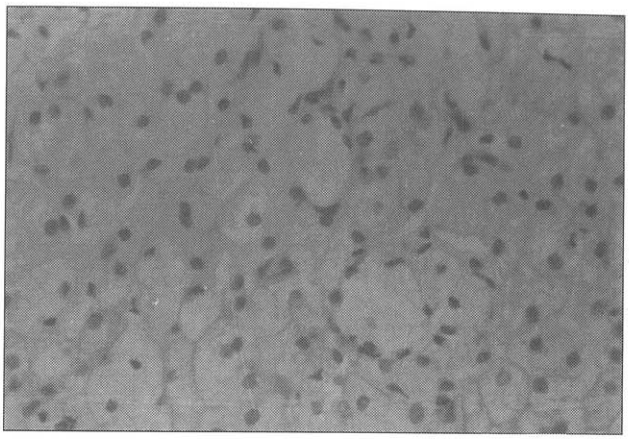

Figure 2. *Bone marrow: Sea blue histocytes and foamy histiocytes typical of Niemann Pick disease (Wright x 400)*

ransferase levels were 124 IU/L and 245 IU/L, respectively. The serum cholesterol level was high (518 mg/dl). The serum high-density liopprotein (HDL) level was low (106 mg/dl) whereas the low-density lipoprotein (LDL) level was high (1410 mg/dl). Viral, autoimmune and metabolic causes of liver function abnormalities were excluded by appropriate laboratory investigations. Chest posteroanterior X-ray displayed a diffuse reticulo-nodular pattern in both lungs (Figure 1). Bone marrow examination revealed abundant sea-blue histiocytes as well as foamy histiocytes typical of Niemann-Pick disease (Figure 2). Liver and transbronchial lung biopsies were performed. On the lung biopsy specimen, foamy and sea-blue histiocytes were noted. Foamy histiocytes was also present in portal areas and vacuolated hepatocytes were seen in the liver specimen (Figure 3).

DISCUSSION

Histiocytes containing lipopigment material stained with Wright or Giemsa stain exhibits cytoplasmic blue-green homogenous granules. These cells were named "sea-blue histiocytes" and the syndrome "the sea-blue histiocyte syndrome" (3). The primary syndrome is quite rare (8). The staining characteristics of sea-blue histiocytes are consistent with the view that they are ceroid-containing macrophages. It has been suggested that accumulation of these cells in bone marrow is a secondary phenomenon associated with excessive turnover of haemopoetic cells (9). Sea-blue histiocytes may also be present in a variety of diseases. These include porphyria, familial lechitin cholesterol acyl transferase deficiency, iron deficiency anemia, leukemia, cholesterol ester storage disease, and many forms of Niemann-Pick disease (5-10).

Niemann-Pick disease is characterized by massive accumulation of lipids, especially in the cells of the reticuloendothelial system. These cells contain lipid droplets and lipopigment (ceroid) which give them a foamy appearance. Lipopigment predominates in the subacute and chronic forms of the disease (10). Patients with Niemann-Pick disease type A and B are clearly sphingomyelinase deficient; whereas patients with types C and D have almost normal sphingomyelinase activity (11).

Niemann-Pick disease type B is manifested by hepatosplenomegaly with a subacute or chronic course. Hepatosplenomegaly is generally slight in the chronic form. The diagnosis is unsuspected in the majority of such cases due to the absence of neurologic manifestations (11).

Although the final confirmatory enzyme studies were lacking, we believe that our patient had non-neuropathic Niemann-Pick disease type B, based on histopathological examinations of liver, lung and bone marrow. There has been only one report of a patient with Niemann-Pick disease in whom involvement of the lungs with sea blue histiocytes were demonstrated via an open lung biopsy (6). To our knowledge, the demonstration of sea blue histiocytes and Niemann-Pick cells in the lung biopsy specimen obtained via transbronchial biopsy have not been previously reported.

The serum lipoprotein profile is usually in patients with Niemann-Pick disease. Of interest, our patient had high serum cholesterol and low-density lipoproteins (LDL), whereas the HDL level was low. There have been rare case reports of pa-

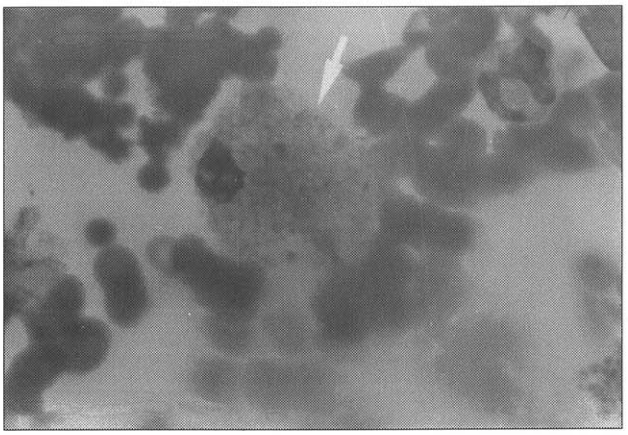

Figure 3. *Liver: Foamy histiocytes in portal areas and vacuolated hepatocytes (HEx400).*

tients with Niemann-Pick disease reported to have low HDL levels (13). The low levels of HDL are believed to be secondary to the deficiency of lysosomal sphingomyelinase activity (12,13). The relationshep between sphingomyelinase deficiency and lipoprotein metabolism has been studied by Maziere et al (13). These investigators reported that cultured skin fibroblasts from patients with Niemann-Pick disease had an increase in cholesterol synthesis from (^{14}C)-acetate and a decrease in (^{44}C)-oleic acid incorporation into cholesterol esters (14). As the risk of coronary artery heart disease is high in patients with low serum HDL levels, we are following up our patient regarding this risk also.

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