

Sea-blue histiocytes syndrome: Case report and review of literature

Mounira El Euch, Fatma Ben Fredj Ismail, Amel Rezgui, Monia Karmani, Belgacem Mrad, Hassen Hosi Mhiri, Chedia Laouani Kechrid

Department of Internal Medicine, Sahloul Hospital, Soussa, Tunisia
Email: ach_mounira@hotmail.com, bfi.fatma@yahoo.fr, rezguiamel@yahoo.fr, chedia.kechrid@rns.tn

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ABSTRACT

A 57-year-old female was admitted with pancytopenia, and mild splenomegaly. The multiple myeloma diagnosis was wrongly made since the discovery of monoclonal peak to the protein electrophoresis. Further microscopic examination of bone marrow revealed the accumulation of sea-blue histiocytes. The evolution was stable and the patient did not receive any treatment due to the lack of nervous symptoms.

Keywords: Syndrome of the Sea-Blue Histiocyte; Pancytopenia; Splenomegaly

1. BACKGROUND

The syndrome of the sea-blue histiocyte is a rare disorder first described by Silverstein et al in 1970 [1]. It was given the name due to the histiocyte color upon May-Giemsa staining. The etiology is unknown. This disorder is classified as either primary or secondary; most cases are secondary to lipid metabolic diseases. The clinical course is usually benign but some cases develop fatal liver cirrhosis [2-4]. We report a case of this syndrome with a review of the literature.

2. CASE REPORT

A 57-year-old female was referred to Gastrology department for further examination of anemia. She was the product of consanguineous marriage. It was not similar cases in her family. She had not fever. The hemodynamic parameters were normal. The spleen was slightly palpable. We did not detect any peripheral lymphadenomegaly.

The diagnosis of portal hypertension was referred to the presence of esophageal varicosity grade II to upper gastrointestinal endoscopy with probable liver cirrhosis.

The patient we was addressed for exploration of a spike in serum protein electrophoresis.

The examination was a blood pressure at 14/9 cm Hg; a temperature at 37.3°, a BMI at 25 kg/m² and a pleno-

megaly at 3 cm from the costal margin. Laboratory investigations showed the renal failure with urea at 23.4 mmol/l, creatinine at 186 μmoles/l, Natremia at 136 mg/l, K⁺ at 4.8 mg/l, Na⁺ urine = 42 mmol/d; urinary K⁺ = 34.34 mmol/day; 24 h proteinuria = 0.34 g; Ca⁺⁺ = 2.29 mg/l, CRP < 5, TP = 82%.

The blood count showed pancytopenia with GB = 2910; PNN = 2000; lymphocytes = 5800, monocytes = 3100; eosinophiles = 10, basophiles = 100; Hb = 8.7 g/dl, MCV = 83.6 fl; MCH = 25.1 pg, reticulocytes = 48,235/μl, platelets = 54,000/μl.

Electrophoresis of serum protein showed: albumin = 35.8; α1 globulin = 3.5, α2 = 7; β1 = 4.5, β2 = 2.7 and a globulin spike to 20.1 g/l. The blood immunophenotyping was IgG kappa.

The search for urinary light chains was positive with a rate of 31.5 mg/day. The dosage of β2 microglobulin was 10,830 μg/l. The skull radiograph (**Figure 1**) was without abnormalities. The diagnosis of multiple myeloma was discussed and sternal puncture did not show plasma cells but rather the presence of histiocytes.

Bone marrow biopsy showed a marrow made of wealth between 1 and 2, the seat of histiocytes with abundant cytoplasm vacuolated, the vacuoles are of unequal size, positive PAS staining and Giemsa negative for Perls stain, concluding the diagnosis histiocytosis of “blue sea”. The evolution of our patient was stable by anemic syndrome corrected symptomatically at regular controls.

3. DISCUSSION

The sea-blue histiocyte syndrome, similar to Niemann-Pick disease, is a congenital, hereditary histiolipidosis due to an inborn enzymatic error. Accumulation of non saturated, oxidated, polymerized lipids is observed; ceroids of lipofuscin, glycopospholipids and sphingomyelin, like bulky granules 1 to 3 μ in diameter, turn blue with May Grunewald staining, orange reddish with PAS and black with Sudan III and osmic acid.

The sea-blue histiocytes are preferably located at the bone marrow, liver and spleen and less frequently in



Figure 1. Skull radiograph without abnormalities.

lymph nodes, lungs and some other organs [1]. Our patient had only splenomegaly without these other localizations of the histiocytes.

In patients with myelofibrosis, extramedullary haematopoiesis commonly occurs in the spleen and liver, but rarely in the lymph nodes [2]. In these organs, fibrosis frequently develops in association with megakaryocyte infiltration [3]. On the other hand, macrophages loaded with cytoplasmic granules staining blue with Giemsa, so-called sea-blue histiocytes, are commonly seen in various organs including the lungs in Niemann-Pick disease, and occasionally in the bone marrow and spleen as a secondary phenomenon associated with a variety of acquired hematological disorders, such as chronic myelogenous leukemia, chronic immune thrombocytopenic purpura, myelodysplastic syndrome, and polycythaemia rubra vera [4-6]. Fortunately, our patient hadn't these hematological disorders. Pulmonary involvement is a complication occurring frequently in the inherited disorder [7,8], but rarely in acquired disorders.

Within the spleen, which in myelofibrosis functions as an extramedullary hematopoietic organ, monocytes differentiate from hematopoietic stem cells, proliferate, and are transformed into sea-blue histiocytes. Because sea-blue histiocytes have a large cytoplasm, as do megakaryocytes, it is considered likely that the lungs, and probably the liver, function as a physiological sieve of circulating monocytes, which changed into sea-blue histiocytes in the bone marrow and the spleen, respectively. Moreover, it has been reported that, in a labeling experiment with ³H-thymidine, about 15% and 56% of mice monocytes leaving the circulation become pulmonary macrophages and Kupffer cells, respectively [9-11].

Consequently, a heavy accumulation of sea-blue histiocytes in the spleen of this patient could be explained by these hypotheses. The lysosomal enzyme pathway in macrophages of these disorders results in saturation for re-

moval of the membrane lipid, and the cells are transformed into sea-blue histiocytes [9,10]. The sea-blue histiocytes are usually observed in the bone marrow and spleen, where the majority of the blood cells are destroyed and phagocytosed. On the other hand, Links *et al.* [12] reported a case of pulmonary tuberculosis in which pulmonary interstitial infiltration of pseudo-Gaucher cells was caused by incomplete breakdown of mycobacterial cell wall.

Sea-blue histiocytosis [13] describes splenomegaly in the presence of numerous histiocytes stained a sea-blue color. This finding occurs in several conditions, including cholesterol ester storage disease and other lysosomal disorders, Niemann-Pick variant, Gaucher disease, severe hypertriglyceridemia, lecithin-cholesterol acyltransferase deficiency, and Tangier disease [2]. The primary syndrome of sea-blue histiocytosis has no known etiology, although a biochemical derangement in lipid metabolism has been hypothesized [14]. One of the major apolipoproteins controlling lipoprotein metabolisms is apolipoprotein E (apoE) [15]. Splenomegaly has not been associated with this lipid disorder, except in cases of severe hypertriglyceridemia [16]. We described a primary sea blue histiocytosis which had normal serum triglyceride concentrations, but a spike in protein electrophoresis like in myeloma.

Nguyen *et al.* call attention to a new etiology for sea-blue histiocytosis and point out that the 149 variant of apoE appears to stimulate cholesterol ester accumulation in macrophages and could be associated with targeting of lipoproteins to macrophages. Splenectomy unmasked the lipoprotein defect and allowed expression of the hyperlipidemia and accumulation of remnant lipoproteins [17]. The cytochemical reaction on bone marrow smears in this patient and previous cases [18,19] suggested that the storage material in the cytoplasmic granules was glycolipid and/or phospholipid. The etiology of this lipid storage disease is unknown, but most of the reported cases were predominantly females as is the subject of the present report. Some authors have suggested that it is a hereditary disorder [19,20] but the disorder may be acquired and associated with other diseases [21,22].

The prognosis is variable: fatal in the central nervous system location, relatively mild in cases of spleen and bone marrow location. The possibility of complicating hepatic cirrhosis and/or pulmonary fibrosis is always present [1]. Our patient didn't develop any complication but regular controls are necessary in order to treat at time these further manifestations.

4. CONCLUSION

This case described a primary sea blue histiocytosis which had normal serum triglyceride concentrations. We did

not find a particular entity to our patient and her syndrome stay primary. The histology stays of great diagnostic input in this rare entity which stays without a specific treatment.

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