Biological pictures

Ann Biol Clin 2020; 78 (4): 463-4

Sea-blue histiocytes in the bone marrow of a patient with Niemann-Pick disease type C2

Histiocytes en bleu de mer observés dans le myélogramme d'un patient atteint d'une maladie de Niemann-Pick de type C2

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Article received January 17, 2020, accepted May 19, 2020

A 45-year-old woman presented with a one-year history of progressive cognitive impairment, weight loss and walking difficulties. Clinical examination showed hepatomegaly without splenomegaly. Cerebral magnetic resonance imaging revealed frontal and temporal atrophy. Mild anemia led to analyze the bone marrow aspiration which revealed the presence of sea-blue histiocytes (SBH) and several macrophages (*figure 1*). This cytological feature associated with neurological manifestations suggested the search for storage disease. The filipin staining test (fibroblast culture) and the detection of the homozygous mutation of *NPC2* gene (p.Pro120Ser) allowed the diagnosis of Niemann-Pick disease type C2 (NPC2).

SBH are lipid-laden macrophages which stain a deep azure blue with May-Grünwald Giemsa. This common cytological feature is observed in the bone marrow in a variety of metabolic and haematological disorders (chronic myeloid leukaemia, immune thrombocytopenic purpura, sickle cell anaemia, thalassaemia, myelodysplastic syndromes and myeloproliferative disorders).

Niemann-Pick disorders are lysosomal storage diseases. These inherited metabolic disorder result in accumulation of undegraded substrate. Niemann-Pick disease type A and type B are due to acid sphingomyelinase deficiency and differ from Niemann-Pick disease type C (NPC) in their pathogenesis while they share clinical features (*table 1*). NPC is a rare autosomal recessive and multisystemic neurodegenerative disorder. Mutations on either the *NPC1* (95%) or the *NPC2* (5%) genes prevent transport the intracellular of cholesterol and other lipids leading to accumulation of these substances within various tissues of the body, including brain tissue.

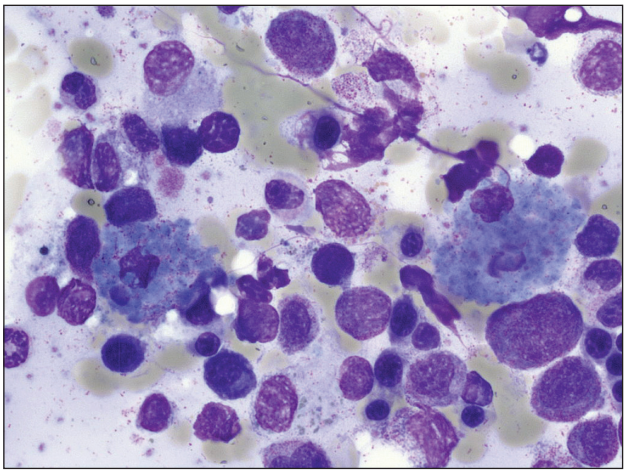

Figure 1. Bone marrow aspirate: typical sea-blue histiocytes among normal haemopoietic cells by May-Grünwald-Giemsa staining.

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doi:10.1684/abc.2020.1569

To cite this article: Fenomanana J, Harzallah I, Martzolff L, Debliquis A. Sea-blue histiocytes in the bone marrow of a patient with Niemann-Pick disease type C2. *Ann Biol Clin* 2020; 78(4): 463-4 doi:10.1684/abc.2020.1569

Table 1. General features of Niemann-Pick disease subtypes.

Niemann-Pick disease subtypes	Type A	Type B	Type C
Gene mutation	*SMPD1*	*SMPD1*	*NPC1* or *NPC2*
Deficiency	Acid sphingomyelinase activity	Acid sphingomyelinase activity	Intracellular trafficking of cholesterol
Incidence	1 in 250 000 individuals	1 in 150 000 individuals	
Onset	Early in infancy	Childhood, adulthood	Infancy, childhood, adulthood
Symptoms	Hepatosplenomegaly Recurrent respiratory Infections Cherry-red macula Failure to thrive Progressive psychomotor regression Dysphagia Intestinal lung disease	Hepatosplenomegaly Recurrent respiratory Infections Cherry-red macula Neurological impairment Hyporeflexia Peripheral neuropathy	Hepatosplenomegaly Recurrent respiratory Infections Vertical supranuclear gaze palsy Cerebellar ataxia Dystonia Severe liver disease Speech delay Dysarthria, dysphagia Saccades

Visceral organs and bone marrow are variably infiltrated with SBH and foamy macrophages. Symptoms can develop at any age and most affected people develop features of the condition during childhood. NPC-C2 may be characterized by ataxia, characteristic vertical supranuclear gaze palsy, poor muscle tone, hepatosplenomegaly, interstitial lung disease, intellectual decline, seizures, dysarthria, and difficulty swallowing, dystonia, frontotemporal dementia and untreatable schizophrenia or psychosis. There is, unfortunately, no specific treatment.

Conflict of interest: A. Debliquis received honoraria from Sanofi Genzyme and L. Martzolff received honoraria from Actelion for their participation in symposia. None of the other authors has any conflict of interest to disclose concerning this article.