A 4-Week-old Neonate with Jaundice and Hepatosplenomegaly

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CLINICAL HISTORY

This is a 4-week-old girl born prematurely at 35 weeks gestation to a 15-year-old G1P0 mother after an uncomplicated pregnancy. There is a history of consanguinity. She had jaundice at birth and was treated with phototherapy but it did not resolve. Her development was appropriate for age. At follow-up, she was found to have direct

hyperbilirubinemia, hepatomegaly, mild splenomegaly and a suspicious liver lesion on ultrasound. A liver biopsy was performed. **Figure 1** provided shows the hepatic parenchyma stained by H&E (A), Periodic Acid Schiff (PAS) with diastase digestion (B) and CD163 (an activated macrophage marker) (C), and a figure of transmission electron microscopy of the liver (D).

Figure 1 Liver parenchyma showing scattered foamy Kupffer cells stained with H&E (A), PAS with diastase digestion (B) and CD163 (C). An electron microscopy image of the liver biopsy (D) (scale bar = 500 nm).

Keywords: Niemann Pick disease, lysosomal storage disorder, pathology, electron microscopy

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Abbreviations: G1P0: Gravida 1, Para 0; H&E: Hematoxylin and Eosin; NPC: Niemann Pick disease type C; PAS: Periodic Acid Schiff

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What is your diagnosis?**Images in Hepatology—Answer**

Liver biopsy showed neonatal giant cell hepatitis with cholestasis and extramedullary hematopoiesis. There are scattered large Kupffer cells with foamy cytoplasm in the sinusoids (Figure 1A, arrow). These cells contain foamy intracytoplasmic residual material highlighted by Periodic Acid Schiff stain followed by diastase digestion (Figure 1B, arrow). CD163 immunostain demonstrates numerous activated macrophages (Figure 1C). Transmission electron microscopy of the liver showed many concentric membranous myelin bodies (Figure 1D). Metabolic workup revealed Niemann-Pick disease type C (NPC).

NPC is an autosomal recessive neurovisceral lipid storage with a wide spectrum of clinical phenotypes that affects liver, spleen and lungs as well as the central and peripheral nervous systems.¹ Majority of cases present before the age of 10 years. It is characterized by accumulation of large amounts of free and unesterified cholesterol and glycolipids in lysosomes and late endosomes. By electron microscopy, the cytoplasm contains stacked membranes, concentric laminated bodies with central dense cores.² Majority of NPC have mutations of NPC1 gene, which encodes a large membrane glycoprotein, and the remainder have mutations in the NPC2 gene, which encodes a small soluble lysosomal protein with cholesterol-binding properties.^{1,3}

CONFLICTS OF INTEREST

The authors have none to declare.

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