Neonatal McCune-Albright Syndrome with Giant Cell Hepatitis

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Disclosure Statement

We have no conflicts of interest to declare.

Contributions

Y.I. wrote the manuscript. Y.I., Y.Y., N.I., A.K., M.O., and A.Y. took care of the patients. A.Y. was the principal investigator and takes primary responsibility for the paper.

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Text

A female infant was administered to our hospital for evaluation of café-au-lait spots (CAL) and direct hyperbilirubinemia at 4 weeks of age. Hepatobiliary scintigraphy revealed intestinal excretion of tracer, excluding the possibility of biliary atresia. However, the study showed significantly delayed excretion of tracer from the liver. The patient underwent liver biopsy, which showed giant cell transformation with bile thrombus in a bile canaliculus and inflammatory infiltrates in the hepatic parenchyma with a normal bile duct, leading to the diagnosis of idiopathic neonatal giant cell hepatitis (Panel A).

At 6 months of age, the patient presented with several episodes of vaginal bleeding and development of pubic hair. Serum estradiol concentration was elevated (174.1 pg/ml), and gonadotropin responses were suppressed after administration of gonadotropin-releasing hormone. Magnetic resonance imaging (MRI) showed uterine enlargement and right ovarian cysts. Well-defined CAL was observed following Blaschko’s line on the neck and anterior chest (Panel B). Bone scintigraphy revealed an extensive, unusual lesion on the right zygoma, predisposing fibrous dysplasia (FD). The

clinical triad of CAL, precocious puberty and FD suggested a diagnosis of McCune-Albright syndrome (MAS). Direct sequencing of the *GNAS1* gene from a liver specimen revealed a well-known heterozygous mutation (c.601C>T, p. R201C) diagnostic of MAS(1).

The manifestations of MAS, particularly developing in the neonatal period, are more extensive(2). Since ACTH-independent hypercortisolism and myocardial hypertrophy in neonatal MAS is occasionally severe with a high mortality rate, early interventions are warranted. Although hepatobiliary dysfunction appears to represent a rare manifestation of MAS(2), we propose including MAS in the list of differential diagnoses for neonatal cholestasis. Moreover, the existence of bile thrombus and significantly delayed excretion of tracer from the liver suggest that the affected GNAS protein may interfere with the secretion of normal biliary components, leading to development of hepatitis in MAS patients.

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Figure Legend:

Panel A. Microscopic examination confirmed giant cell transformation of hepatocytes (Hematoxyline and Eosin staining)., Panel B. Café-au-lait spots following Blaschko's line on her neck and anterior chest.

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