yong.xie@outlook.com

From: Sheil, Amy <Amy.Sheil@cchmc.org>
Sent: Monday, March 16, 2015 1:36 PM
To: Yong Xie
Subject: Medical records and liver biopsy

Dr. William F Balistreri, Patient's GI in CCHMC

Dr. Kevin E Bove of CCHMC

Dear Mr. Xie,

Thank you very much for sending these medical records. It will take me a couple days to read through the materials.

Meanwhile, I have shown Jianhua's liver slides to our most experienced liver pathologist, who has nearly 50 years of experience in liver, and also presented his situation to Dr. Balistreri in conference.

Jianhua's pattern of liver disease does appear metabolic, though his histology is not revealing of the etiology. What I can add to the opinions of the other pathologists who have reviewed his slides is that while Jianhua has fibrosis in his liver biopsy, some features may be representative of collapse. This means that his liver may have sustained an insult, which resulted in liver damage and liver cell dropout with scarring, but that his liver may also have had the potential to partially recover from this insult without progressing to end-stage cirrhosis. The best way of assessing the current status of his liver is to perform another biopsy, accompanied by electron microscopy.

Please allow me additional time to review the records you kindly sent. I anticipate signing the case tomorrow or Wednesday.

Sincerely,

Amy Sheil, MD

Patient's pathologist in Cincinnati Children's Hospital Medical Center (CCHMC)

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Cincinnati Children's

Name: Jianhua Draco Xie | DOB: 9/16/2012 | MRN: 11491118 | PCP: UNLISTED UPIR REQUESTED

OC FINAL - Details (Jianhua)

Component Results

Component	Standard Range	Your Value
OC FINAL		Pathology Accession Number: OC-15-00161 Received: 2/19/2015 09:55:00 AM EST Responsible Sheil, Amy T Verified: 3/19/2015 Pathologist: 01:59:21 PM EDT Clinical Dx Cirrhosis Specimen (A) Liver biopsy, (SP13-2373) Gross Description (A) Received from Seattle Children's Hospital, Seattle, WA, are 4 slides labeled SP13-2373 and a copy of the corresponding pathology report dated 06/27/13. Upon request, consultation reports from Massachusetts General Hospital (S13-4433 9, 07/18/13) and Children's Hospital of Pittsburgh (CHS14-5430, 07/02/14) are provided. Microscopic Description (A) 1 slide H&E, 1 PAS, 1 DPAS, 1 Trichrome, : The H&E-stained sections show a core biopsy of liver with several portal

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		triads, the majority of which contain intact bile ducts. The architecture is distorted by portal to portal bridging fibrosis with micronodule formation. Central veins are difficult to discern; there are likely some foci of portal to central fibrosis. Prominent bile ductular reaction occupies the edges of the limiting plates. The portal regions are expanded by mixed inflammatory infiltrates, predominantly composed of lymphocytes with occasional eosinophils and rare neutrophils. The lobules show scattered lymphocytic inflammation. Hepatocytes exhibit moderate nuclear unrest with polyploidy and occasional binucleation accompanied by ballooning degeneration. No viral cytopathic effects are seen. Scattered apoptotic hepatocytes are noted, and occasional cytoplasmic and canalicular cholestasis is appreciated. Focal macrovesicular with scant microvesicular steatosis is seen. Trichrome stain confirms bridging fibrosis with minute nodule formation and illustrates patchy pericellular fibrosis; the blue staining is not intense, but rather lighter, suggestive of a component of collapse. DPAS stain highlights residual bodies in some Kupffer cells, portal macrophages, and hepatocytes, but shows no typical intrahepatocyte globules. PAS stain illustrates apparently normal glycogen stores within hepatocytes. Comment Additional unstained slides were requested, but the liver tissue was reported to be nearly exhausted. The patient's electronic medical records stored in CCHMC's Epic, as well as th ose provided by his father, were reviewed. Dr. Kevin Bove has also reviewed these slides, and the pathology and clinical findings were presented at the Pathology-Hepatology conference on 3/12/15.

Component	Standard Range	Your Value

While the pattern of hepatocyte injury and fibrosis in this liver biopsy appears of metabolic origin, the etiology of this child's liver disease is unfortunately not apparent by light or electron microscopy (as per the ultrastructural examination report included in the medical records).

By H&E histology and PAS and DPAS stain, Jianhua does not have alpha-1-
antitrypsin deficiency. He has no bile duct paucity or excessive cholestasis, and has scant steatosis. He has no evidence of a storage disorder.

The significance of his single allele mutation in the PFIC1 gene ATP8B1 (by
JaundiceChip) is unknown; the histological features of his biopsy do not
conform to PFIC1. Citrin
deficiency may be a consideration, although less
likely as whole genome sequencing did not reveal a mutation in the SLC25A13
gene. A fatty acid oxidation defect may also be a remote possibility, though not clearly evident on review of Jianhua's laboratory studies (elevated CPK may have been due to hemolysis of his blood sample). A post-
inflammatory mechanism may be considered, in light of 1) his acute presentation with liver failure following a presumed viral illness, 2) the potentially reversible parenchymal collapse accompanied by an inflammatory
component in his liver biopsy; and 3) his apparent, at least partial recovery, from the hepatic insult at six months of age.

The possibility of a subtle mitochondriopathy may be investigated via repeat liver biopsy accompanied by ultrastructural examination, at which
time copper quantification might prove useful. Repeat liver biopsy would
also i
llustrate the current condition of his liver.

Anatomical Diagnosis
(A) Liver biopsy, (SP13-2373):
Fibrosis, periportal and bridging, with nodule formation and patchy parenchymal collapse.
Mild, predominantly lymphocytic portal and lobular inflammation.

Component	Standard Range	Your Value
		Scant steatosis. The Attending Pathologist has personally examined the specimen(s) and concurs with the final report. Amy T Sheil (electronic signature) Date verified: 03/19/2015
		Accession Number: OC-15-00161 Received: 2/19/2015 09:55:00 AM EST Responsible Sheil, Amy T Verified: 3/9/2015 Pathologist: 09:36:43 PM EDT Outside Consult There is an image or outside report associated with this report. It may be accessed through EPIC by clicking the appropriate link. The Attending Pathologist has personally examined the specimen(s) and concurs with the final report. Amy T Sheil (electronic signature) Date verified: 03/09/2015

General Information

Collected:

02/19/2015 9:55 AM

Resulted: 03/19/2015 1:59 PM

Ordered By: WILLIAM F. BALISTRERI, MD

Result Status: Final result

This test result has been released by an automatic process.