Novel nodules: A previously unreported manifestation of Aicardi-Goutières syndrome

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Introduction

- Aicardi-Goutières syndrome (AGS) is a rare autosomal recessive genetic disorder resulting from mutations of genes encoding multiple proteins, including DNA 3' repair exonuclease 1 (TREX1).
- This form of leukodystrophy is characterized by increased interferon-alpha in the cerebrospinal fluid and serum leading to immune dysfunction primarily targeting white matter myelin in the brain.
- Late onset AGS can affect other organs, including liver, kidneys, heart, and lungs.
- Hepatic inflammation is associated with the neonatal form of AGS, but the incidence of hepatitis across other ages remains unknown.
- There have been no reported cases of nodular regenerative hyperplasia in adults with Aicardi-Goutières syndrome.

Case Description

- A 63-year-old man was evaluated for proteinuria and microscopic hematuria.
- Laboratory workup was unrevealing and renal ultrasound was normal.
- Family history was significant for father with kidney transplant for unknown renal disease and brother with recurrent bilateral vitreous hemorrhage. Subsequently, the patient and brother had kidney biopsies that showed findings consistent with thrombotic microangiopathy (TMA).
- Familial TMA prompted whole genome sequencing that revealed a mutation in TREX1 in all three family members.
- Following nephrology workup, the patient was incidentally found to have a nodular hepatic contour suggestive of cirrhosis.

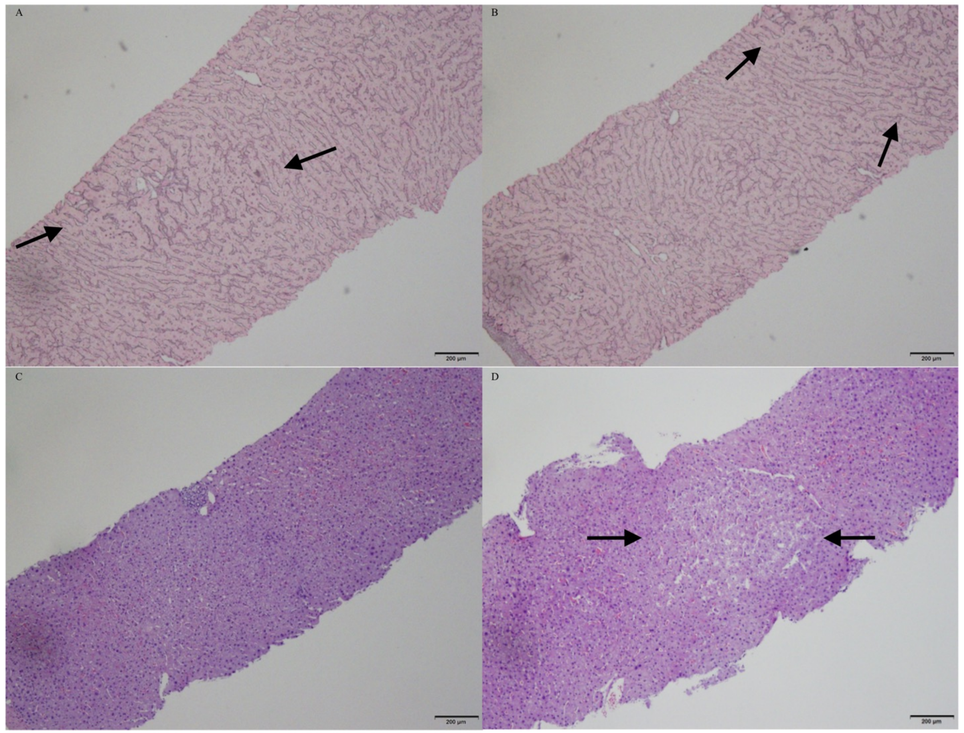

Figure (No 1). Percutaneous liver biopsy with nodular regenerative hyperplasia

AST/ALT	Total bilirubin	Alkaline phosphatase	Viral hepatitis serologies (A,B,C)	Serum total protein	Serum albumin	Ceruloplasmin	Anti-smooth muscle antibody	Alpha-fetoprotein	Alpha-1-antitrypsin
14/21 units/L	0.4 mg/dL	92 units/L	Non-reactive	7.4 g/dL	3.4 g/dL	24.6 mg/dL	11 units	1.0 ng/mL	126 mg/dL

Table (No 1). Serum laboratory results

- Patient denied any risk factors for liver disease and physical exam was absent of stigmata of liver disease.
- A focused laboratory workup was unrevealing (Table).
- MRCP revealed a nodular liver consistent with fibrosis and no intrahepatic or extrahepatic biliary dilation. MR elastography was consistent with F2-F3 fibrosis without evidence of hepatic steatosis or iron overload.
- A liver biopsy demonstrated nodular regenerative hyperplasia (NRH).

Discussion

- NRH has been associated with autoimmune conditions such as systemic lupus erythematosus (SLE) and is thought to be caused by blood vessel inflammation within the liver leading to an overcompensated replication of hepatocytes.
- The finding of NRH in this patient is representative of the phenotypic overlap between AGS and SLE related to the common underlying feature of IFN-α upregulation.
- As seen in this patient, NRH typically does not cause any overt signs or symptoms of liver disease.
- However, given it can eventually lead to the development of non-cirrhotic portal hypertension, further monitoring of this patient is warranted.

References

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