Neonatal GALD Progressing to Autoimmune Hepatitis in the Setting of Anti-RNP Antibodies

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BACKGROUND

Neonatal lupus erythematosus (NLE) is an uncommon disease that occurs in the neonate from transplacental passage of maternal autoantibodies in utero. The most common autoantibodies passed from the mother are anti-Ro/SSA and anti-La/SSB, though other autoantibodies have been implicated. It commonly manifests as skin lesions or congenital heart block but can involve the liver. Rarely, hepatobiliary disease is the sole clinical manifestation of the disease and can present similarly to gestational alloimmune liver disease (GALD). We present a case of severe liver disease in an infant born to a mother with systemic lupus erythematosus (SLE) with histopathological features of perinatal autoimmune hepatitis.

CASE SUMMARY

An infant was delivered at 37 weeks gestational age for growth restriction. The mother was a 34-year-old G1P1 who was diagnosed at age 16 years with SLE with pericarditis, severe joint pain, fever, alopecia, and malar rash, without liver involvement. The mother's SLE had been stable for the past nine years, including during pregnancy during which she was treated with azathioprine and hydroxychloroquine. At age one month, the infant presented with jaundice and thrombocytopenia. Liver biopsy showed cirrhosis with a micronesting pattern, increased iron deposition, and minimal inflammation **(Figure 1)**.

Rapid progression to liver failure at age five months required liver transplant. Grossly, the explant was diffusely nodular with fibrotic septa and areas of dense fibrosis **(Figure 2)**. Microscopically, there was mixed coarse and micronodular cirrhosis with a prominent active chronic inflammatory infiltrate along the margins of most residual nodules. Hepatocytes in smallest nests showed variable differentiation into cholangiocyte-like cells with florid proliferation and occasional inspissated bile without iron deposition **(Figure 3).**

FIGURES

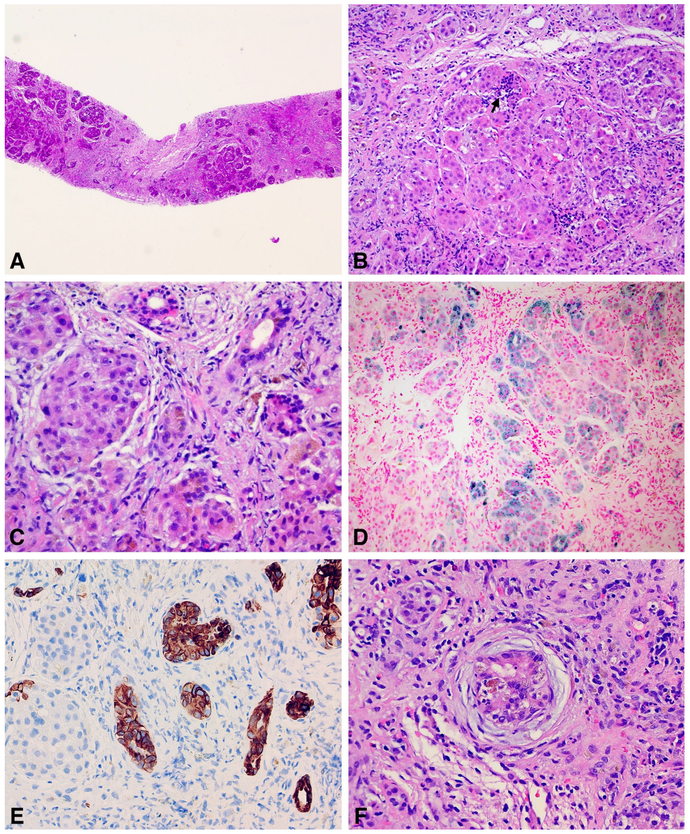

Figure 1. Perinatal alloimmune liver disease: pattern in biopsy at 1 month.

(A) Liver lobules are replaced by nests of residual regenerating micronodules. Inflammation is absent. (H&E, x25)

(B) Lobular architecture has been replaced by small nodules of hepatocytes with subdivision into nests. Portal area at center-top lacks inflammation. Sinusoidal erythropoiesis composed of normoblasts (arrow) is sparse. (H&E, x100)

(C) Nesting hepatocytes contain pigment (bile and hemosiderin). Two residual bile ducts at center-top are lined by injured cholangiocytes. (H&E, x200)

(D) Nesting hepatocytes exhibit focal tubularization with variable amounts of hemosiderin. (Iron stain, x100)

(E) Nesting hepatocytes exhibit variable ductular phenotype. Some hepatocyte clusters are negative and others strongly positive. (CK7 immunostain, x200)

(F) Nesting hepatocytes contain granular hemosiderin and many showed focal circumferential sclerosis. (H&E, x200)

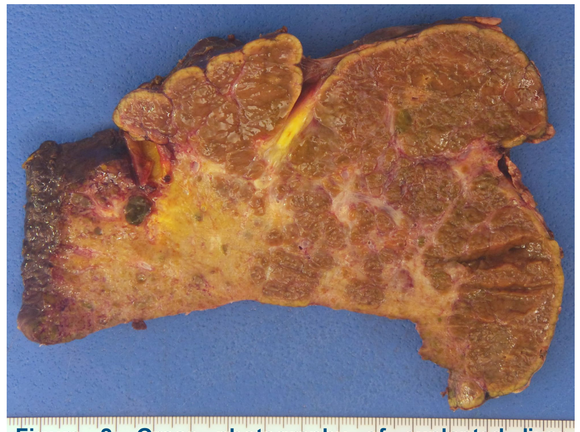

Figure 2. Gross photography of explanted liver parenchyma at 5 months, showing diffuse nodular parenchyma and dense fibrosis.

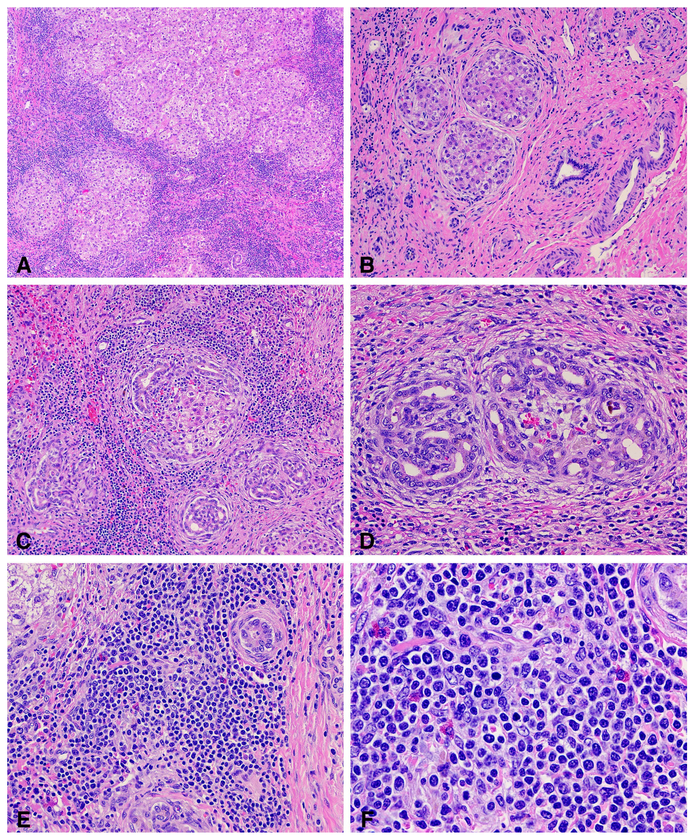

Figure 3. Explanted liver at age 5 months: micronodular cirrhosis accompanied by florid chronic active hepatitis. The iron stain was negative.

(A) Liver parenchyma is universally composed of regenerative nodules of varying size with prominent perinodular sclerosis and heavy mononuclear cell infiltrates at the stromal and portal interfaces. (H&E, x50)

(B) Periportal micronests similar to those in the perinatal liver biopsy often lack an inflammatory component. The bile duct and portal artery at the lower right are normal. (H&E, x100)

(C) Regenerating micronests of hepatocytes often show partial tubularization and are surrounded by a prominent mononuclear cell infiltrate. (H&E, x100)

(D) Regenerating micronests of hepatocytes with florid tubularization are surrounded by sclerosis. (H&E, x200)

(E) Inflammatory infiltrate throughout explant is composed of immature lymphoid cells and plasmacytoid cells concentrated at nodule interface. (H&E, x100)

(F) Cytologic detail of mononuclear inflammatory infiltrates in the explant shows blastoid and plasmacytoid cytological features without lymphoid follicles. (H&E, x200)

DISCUSSION

The overall features suggested GALD progressing to autoimmune hepatitis with cirrhosis, a diagnosis at odds with the young age of the patient. We propose that the liver disease in this infant is related to transfer of maternal antibodies associated with SLE to the fetus. Serologic testing of the infant at the time of presentation revealed positive anti-ANA (1:320) and anti-ribonucleoprotein (anti-RNP) antibodies; post-transplantation testing was negative for both markers. The mother was positive for anti-ANA (>1:1280) and anti-RNP antibodies, along with low-positives for anti-dsDNA and anti-LC1 antibodies. Both mother and infant were negative for anti-SSA and anti-SSB antibodies.

While rare cases of NLE associated with anti-RNP have been reported, liver disease has not been previously described. This case represents a unique hepatobiliary manifestation of presumed neonatal lupus involving anti-RNP antibodies, resulting in a liver disorder that initially with histological features of GALD that rapidly progressed to a phenotype of end-stage autoimmune hepatitis.

DISCLOSURES

The authors have nothing to disclose