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CASE REPORT

Hepatitis during pregnancy: A case of hemophagocytic lymphohistiocytosis

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KEYWORDS
HIV;
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Summary Hemophagocytic lymphohistiocytosis (HLH) is a rare but severe and potentially fatal syndrome that can occur during pregnancy. A 36 years-old woman, at 29 weeks of gestation, presented with itchiness and jaundice since a week. On clinical examination she was apyrexial and frankly icteric. Laboratory data showed evidence of acute hepatitis. A complete work-up was made excluding viral hepatitis (HAV, HEV, HBV, HCV, HHV6, CMV, EBV) and autoimmune liver disease. Liver diseases related to pregnancy were not completely excluded. A liver biopsy was performed and firstly interpreted as showing features of acute hepatitis. The clinical situation worsened, she developed fever with signs of fetal distress and emergent delivery was done. A second look at the liver biopsy showed features compatible with HLH, which was also confirmed on bone marrow biopsy. Extensive work-up with exclusion of infectious and malignant diseases, lead us to the diagnosis of HLH secondary to pregnancy and short term steroid therapy was started. She then completely recovered and didn't present any relapse after 4 months of follow up. HLH during pregnancy is very rare and this is the first case of HLH presenting as acute hepatitis and diagnosed on a liver biopsy.

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Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a rare and potentially fatal disease due to uncontrolled immune system activation. The diagnosis is based on the HLH-2004 criteria [1]. It can be primary or secondary to infections, malignancies and rheumatologic diseases. Only few cases of pregnancy-related HLH are reported in the literature with various clinical presentations and no systematic liver and bone-marrow histological diagnosis confirmation. We report here a new case of HLH developing during pregnancy and take this opportunity to review the literature and present the main characteristics of these patients.

Case report

A 36 years-old woman presented to the department of gynecology for itchiness and jaundice since a week. She was at 29 weeks of gestation and her medication was based on antiretroviral treatment (darunavir, ritonavir, emtricitabine, tenofovir disoproxil fumarate) for an HIV infection diagnosed in 2014. It was her third pregnancy and she had no other past medical history. She didn't travel abroad and has not taken any drug, alcohol or herbs recently. On clinical examination she was apyrexial and frankly icteric with a blood pressure of 125/72 mmHg without clinical signs of chronic liver disease. Relevant laboratory data were: total bilirubin, 10.2 mg/dL (normal value [NV] < 1.2 mg/dL); conjugated bilirubin, 8.2 mg/dL (NV < 0.3 mg/dL); biliary acids: 232,8 (NV < 10 μmol/L), aspartate aminotransferase 4267 U/L (NV < 40); alanine aminotransferase 1245 U/L (NV < 40); gamma glutamyl transpeptidase 52 U/L (NV < 60); LDH, 1789 IU/L (NV < 250 UI/L); neutrophil count 4380/μL (NV 1600—7000/μL); hemoglobin 7.2 g/dL (NV 13—18 g/dL); platelet count 416,000/mm^3 (NV 150,000—350,000/mm^3); ferritin 853 (NV 13—150 μg/L); renal function and coagulation parameters were normal. Serologic tests for CMV, EBV, herpes virus, toxoplasma, parvovirus B19, hepatitis A, B, C and E were negative. Plasma HIV viral load and CD4 count were below 40 copies/mL and 604/μL respectively, compatible with well-controlled HIV infection. Antinuclear antibodies (ANA), rheumatoid factors, antiphospholipid antibodies were negative. Chest X-ray, liver and obstetric ultrasonography as well as urinalysis were normal. In this situation of hepatitis of unknown origin in the third pregnancy trimester, a liver biopsy was performed at 31 weeks 1/7 of pregnancy to rule out severe conditions imposing premature delivery and to look for a treatable disease. This biopsy was firstly interpreted as showing signs of acute hepatitis without evidence of intrahepatic cholestasis of pregnancy (Fig. 1A). A viral or drug induced hepatitis was suspected and antiretroviral treatments were stopped.

As the biliary acids were higher than 40 μmol/L, we considered a high risk for stillbirth. The delivery was programmed at 32 weeks of pregnancy with fetal pulmonary maturation and until then daily monitoring of the baby. Unfortunately, the patient developed temperature of 39 °C at 31 weeks 5/7 days and the monitoring showed signs of fetal distress. An emergency cesarean section was performed at 31 weeks 6/7 days. After surgery, the temperature remained high. Intravenous empirical antibiotherapy with

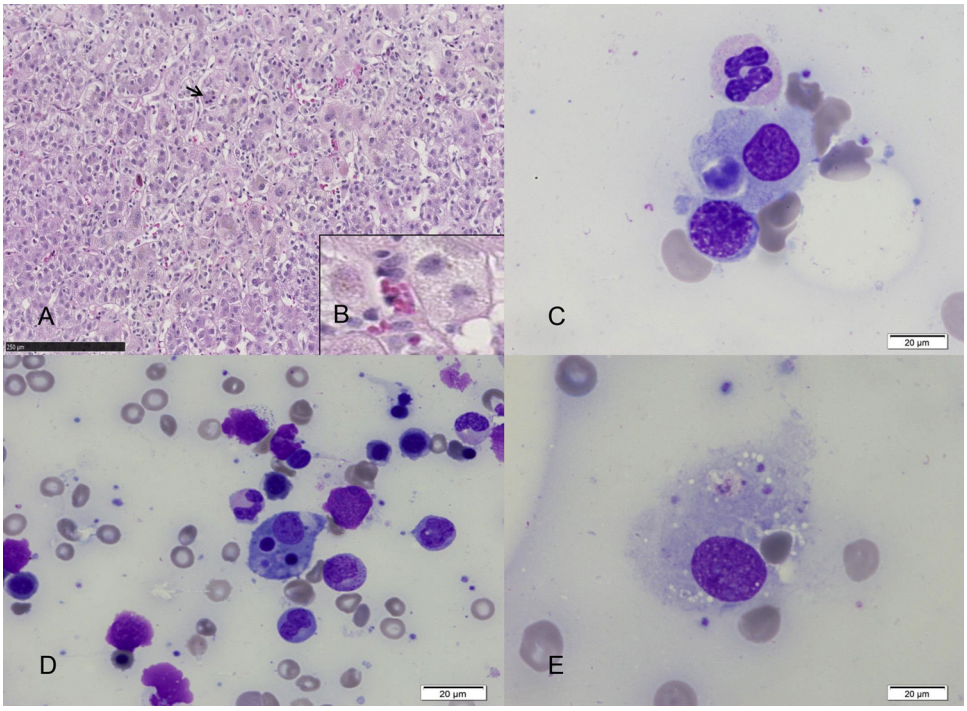

Figure 1 A. Liver biopsy-haematoxylin and eosin stain. The liver parenchyma showed severe lobular inflammation composed of lymphocytes and neutrophils associating with giant cell transformation of the hepatocytes (arrow). B. The liver parenchyma showed hemophagocytosis. C—E. Bone marrow. May—Grunwald Giemsa staining. Bone marrow showing signs of hemophagocytosis. A macrophage engulfing neutrophils, lymphocytes and red cells are shown on C, D and E.

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