Case Report

Hepatoportal Sclerosis and Extrahepatic Portal Venous Obstruction Associated with Anti-phospholipid Antibody Syndrome in Child

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Summary

We report a 2-year-old child with extrahepatic portal venous obstruction, hepatoportal sclerosis and pulmonary thromboembolism whose sole hypercoagulability factor was the presence of anti-phospholipid antibodies.

Key words: hepatoportal sclerosis, extrahepatic portal venous obstruction, anti-phospholipid syndrome.

Introduction

Hepatoportal sclerosis (HPS) and extrahepatic portal venous obstruction (EHPVO), also known as portal vein thrombosis, are causes of non-cirrhotic portal hypertension (NCPH), mainly occurring in developing countries [1]. Conflicting studies about the etiopathogeny of NCPH have been reported [2]. One of the theories proposed that individuals genetically predisposed to thrombotic disorders may suffer thrombosis of the portal vein or of its radial branches when exposed to infections or to prothrombotic events [1].

The anti-phospholipid syndrome (APS) is an acquired autoimmune thrombophilia characterized by arterial and/or venous thrombosis or gestational losses associated with the persistent presence of anti-phospholipid antibodies (aPLs). The syndrome is under-recognized and underdiagnosed, and can have devastating consequences if untreated, mainly because of uncontrolled thrombosis [3, 4].

We report here a rare case of a child with EHPVO and HPS associated with APS.

Case Report

A 2-year-old boy with coryza, cough, fever and mouth wounds suffered episodes of melena and a fall in hemoglobin (5.1 g dl⁻¹), requiring replacement with blood derivatives. He had a history of frequent acute gastroenteritis and otitis media. The parents denied umbilical catheterization, omphalitis or abdominal traumas. Physical examination revealed: weight = 11 kg, good general condition, pale +/4, anicteric, liver and spleen not palpable. Laboratory exams: WC = 10 200 cells mm⁻³; Hb = 7.7 g dl⁻¹, platelets = 103 000 cells mm⁻³; albumin = 3.04 g dl⁻¹, γ-globulin = 1.05 g dl⁻¹; GOT = 30 U l⁻¹ (RV < 31 U l⁻¹); GPT = 44 (RV <41 U l⁻¹); γ-GT = 17 (RV <50 U l⁻¹); INR = 1.0; negative serology for hepatitis B–C; α1-antitrypsin = 1.08 g l⁻¹; non-reactive anti-nucleus antibody.

An abdominal ultrasound showed cavernomatous transformation of the portal vein, confirming EHPVO. Liver biopsy data were compatible with hepatoportal sclerosis (Fig. 1). Upper digestive...
endoscopy revealed esophageal varices of medium/large caliber and sclerotherapy sessions were started.

A detailed study of coagulation was normal, except for a positive lupus inhibitor and elevated anticardiolipin IgM antibodies in three measurements performed at 12-week intervals: 21.0, 28.0 and 32.0 MPL ml\(^{-1}\) (NV <12.5 MPL ml\(^{-1}\)), confirming the diagnosis of APS.

At 4½ years, the patient suffered fractures of the right elbow and wrist requiring several surgical interventions. At 5½ years, after removal of an external wrist fixator, he showed signs and symptoms of bilateral pulmonary thromboembolism confirmed by Tc\(^{99m}\) perfusion scintigraphy, fibrin D dimers = 55 μg ml\(^{-1}\) (NV ≤ 0.5 μg ml\(^{-1}\)) and fibrinogen = 551 mg dl\(^{-1}\) (NV = 200–400 mg dl\(^{-1}\)). With clinical treatment, he progressed well without sequelae; with the esophageal varices being eradicated, he started the use of warfarin sodium. Currently, at 8 years of age he is clinically well, with normal liver function and no intercurrences for 2 years.

**Discussion**

This is the first published case of a Brazilian child with EHPVO and HPS consequent to APS. The diagnosis was confirmed by the presence of elevated aPL titers, a positive lupus inhibitor, presence of vascular thrombosis and exclusion of other causes of thrombosis, according to the classification criteria for the APS [3, 4].

The presence of aPL has been described in different types of hepatic diseases ranging from large artery/vein thrombosis to microthrombotic conditions including Budd–Chiari syndrome, EHPVO, hepatic infarction, veno-occlusive disease, occlusion of small hepatic vein branches and thrombosis of a hepatic artery of transplanted liver [5, 6]. About 60–75% of adults with EHPVO have thrombotic disorders: myeloproliferative diseases, polycythemia, natural anti-coagulant deficiency (anti-thrombin III, protein C and S), resistance to protein C activation, mutation of the prothrombin gene and APS [7]. APS is believed to be the cause of 11% of adult EHPVO cases [8].

In children/adolescents, EHPVO is usually associated with intercurrences during the neonatal period (umbilical catheterization, omphalitis, septicemia and congenital anomalies) [7]. Thrombophilic disorders of a hereditary nature do not seem to play an important role in triggering thrombosis [7, 9]. Some isolated cases of children with EHPVO and APS have been published [9–11]. More recently, Avcin et al. [12] found this association in ~4% of children.

Among the factors implicated in the etiopathogenesis of HPS are: exposure to chemical agents, umbilical infection in neonates, bacterial infections and diarrhea episodes in infants, explaining why this disease is more frequent in developing countries [13]. HPS is a rare cause of portal hypertension in children. In a literature survey, we detected two adults with HPS and APS [14] and no child with this association.

Approximately 40–46% of patients with HPS present EHPVO at the time of diagnosis or during evolution [2, 14]. The child reported here showed this concomitance already at diagnosis, with a history of frequent gastroenteritis and otitis episodes.

We have been investigating APS in patients with EHPVO for 7 years and we detected three cases (including the present one). Thus, we believe that this association is underdiagnosed.

We conclude that patients with EHPVO or HPS should be obligatorily investigated for the presence of systemic hypercoagulability. An early diagnosis of APS, an acquired thrombophilia, should not be neglected since treatment with anti-coagulant drugs can prevent a new thrombotic event.

**References**


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**Fig. 1.** Representative photomicrography of hepatoportal sclerosis. We observed mild portal fibrosis without portal inflammation, and irregular intimal thickening of portal vein. There is also a slight dilatation of portal vein. The black arrows point to neo-vascular formations, also termed as ‘herniation of portal vein’. (Masson trichrome stain, 40×).


