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Case Report

Asymptomatic Portal Cavernoma Revealing Activated Protein C Resistance

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Abstract

Introduction: Unlike the child, the portal cavernoma (PC) remains an exceptional and unusual complication of portal thrombosis in adults and the elderly. We report an original observation of asymptomatic PC secondary to chronic portal thrombosis revealing Factor V Leiden mutation in a young adult.

Observation: A 27-year-old female with no significant pathological history was explored for thrombocytopenia found on a routine check-up. Radiological investigation concluded to the diagnosis of post-thrombotic PC with extra-hepatic portal hypertension. Systematic screening for acquired and inherited thrombophilia objectified activated protein C resistance, and genetic test confirmed the specific mutation of the coagulation factor V gene (Factor V Leiden). Under effective anticoagulation, the evolution was favorable.

Conclusion: As rare as it is in adult, PC deserves to be known and his diagnosis imposes a systemic screening for inherited thrombophilic disorders even in the absence of family and/or personal history of thromboembolic disease.

Keywords: Portal Cavernoma; Portal Vein Thrombosis; Factor V Leiden; Activated Protein C Resistance; Inherited Thrombophili

Introduction

Relatively recently known as a clinical entity, portal cavernoma (PC) is poorly known by clinicians; his first description was autopsy in 1903 [1] and clinical in 1944 [2]. It is defined as the replacement of the portal vein by a network of collateral veins and venules, tortuous and hepatopetous, giving the appearance of a vascular bundle in the hepatic hilus [3,4]. The causes are occlusion or often chronic thrombosis of the extrahepatic portal system [3-5]. The PC represents a real diagnostic challenge because it often remains asymptomatic and would be fortuitous discovery on abdominal radiological explorations [3-5]. More rarely, the clinic may be growth retardation in children, upper or lower digestive bleeding, or feeling of abdominal heaviness. These signs are the consequences of extrahepatic portal hypertension secondary to PC [3-5]. Ultrasound, Doppler examination, computed tomography and magnetic resonance imaging (MRI) allow positive diagnosis of PC and detection of its complications [3-5]. PCs following chronic thrombosis of the portal vein are rare in adults [6]. This thrombosis may rarely be due to hereditary thrombophilia type activated protein C resistance (APCR) [7-10]; indeed, only one case of APCR was found as the etiology of this thrombosis in the 36-case series of Denninger MH et al. [7]. The APCR is a hereditary state of blood hypercoagulability, secondary to a point mutation of the coagulation factor V gene [11]. This mutation (R506Q), giving the mutated factor called factor V Leiden, confer resistance to the action of activated protein C and thus increases the risk of thromboembolism [11]. We report an original observation of PC secondary to chronic portal thrombosis revealing APCR/Factor V Leiden in a young adult.

Case Report

A 27-year-old female with no significant pathological history was explored for thrombocytopenia at 104 000/mm^3 then at 108 000/mm3 found on a complete blood cell count requested during a routine check-up. The somatic examination was without abnormalities. Biology confirmed isolated thrombocytopenia (without abnormalities of other blood lines): platelets at 106 000/mm3, hemoglobin at 14g/dl, leukocytes at 8 680/mm^3, neutrophils at 5 550/mm^3 and lymphocytes at 2 520/mm3. In addition, there was a prothrombin level of 65% without other liver test abnormalities: total bilirubin at 14 µmol/l, conjugate bilirubin at 2.2 µmol/l, aspartate aminotransferase at 38 IU/l, alanine transaminase at 35 IU/l, alkaline phosphatase at 184 IU/l, gammaglutamyl transpeptidase at 11 IU/l and vitamin K at 324 ng/l. The rest of the basic biology was within normal limits (glycemia, serum

calcium, ionogram, creatinine, muscle enzymes, total cholesterol, triglycerides, erythrocyte sedimentation rate, C-reactive protein, and electrophoresis of serum proteins). The abdominal ultrasound with Doppler examination showed a moderate and homogeneous splenomegaly, and the absence of visualization of the portal vein which is replaced by a tubular, tortuous, and trans-sound structures evoking a PC (Figure 1).

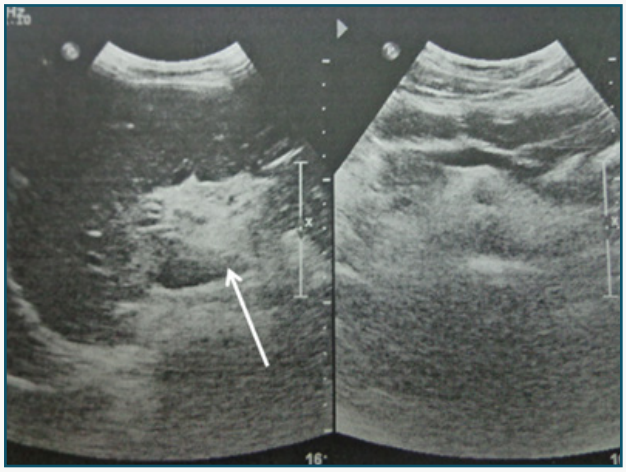

Figure 1: Abdominal ultrasonography with Doppler examination: absence of the portal vein which is replaced by a cluster of small veins and venules in the hepatic hil (arrow).

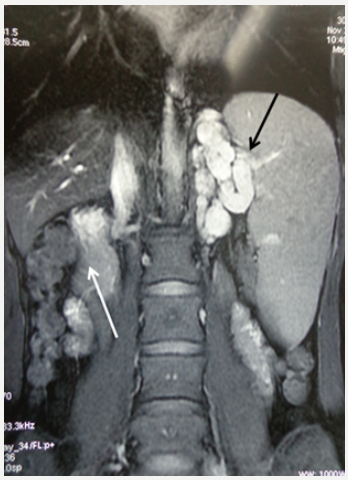

Figure 2: Coronal T1-weighted abdominal MRI with gadolinium: Portal Cavernoma (white arrow) and splenomegaly with very marked splenorenal collateral circulation (black arrow).

MRI of the abdomen confirmed the diagnosis of PC, probably related to chronic thrombosis of the portal vein (Figure 2) with marked splenorenal collateral venous circulation (Figures 2 & 3), and moderate splenomegaly at 18 cm without focal lesions (Figures 2 & 3). Oeso-gastroduodenal fibroscopy noted the presence of grade I oesophageal varices. Thus the diagnosis of a PC with extrahepatic portal hypertension was retained. Given the absence of known local, locoregional or systemic causes that could explain portal thrombosis, a systematic screening for acquired and inherited thrombophilia was requested. Anti-nuclear antibodies, anti-soluble nuclear antigens antibodies, anti-neutrophil cytoplasm antibodies, anti-phospholipids antibodies, lupus anticoagulant, and cryoglobulins were negative. Activated protein C was at 65%, activated protein S at 70%, and antithrombin III at 83%. The search for APCR with coagulometry was positive: Coagulation time without activated protein C at 43 seconds and coagulation time with activated protein C at 300 seconds. The specific factor V mutation (G1691A) was subsequently confirmed by the genetic test. The patient was effectively anticoagulated with a favorable evolution.

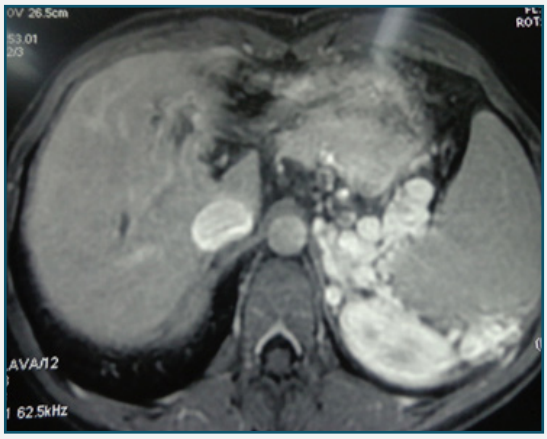

Figure 3: Axial T1-weighted abdominal MRI with gadolinium: splenomegaly with very marked splenorenal collateral circulation.

Discussion

Thrombosis of the portal vein is rare in adults and in the Western world [3]: The large Swedish autopsy series of 23 796 cases concluded with a prevalence of portal thrombosis of 1% in the general population [12]. The pathogenesis of these thromboses is classically multifactorial resulting from the combination of local causes and systemic prothrombotic conditions [3,4]. The main local causes are abdominal trauma, local infections, abdominal surgery, inflammatory bowel diseases, colon diverticulosis, appendicitis, chronic liver diseases with or without cirrhosis, and digestive cancers [3,5,13]. The prothrombotic diseases most frequently responsible for portal thromboses are myeloproliferative syndromes, paroxysmal nocturnal hemoglobinuria, anti-phospholipid syndrome, and hereditary thrombophilias such as deficiency of protein C, S, and antithrombin III, factor V Leiden, and mutation of the factor II gene [3-5]. The portal cavernoma typically complicates chronic portal thrombosis and child's portal thrombosis [3-5]. The coagulation factor V mutation (factor V Leiden) responsible for APCR is rarely reported as etiology of portal thrombosis; its frequency is estimated at 2.8-7.6% in the different series [7-10]. It is likewise exceptionally reported as the cause of portal cavernomas [6]. However, these clinical findings seem to be very underestimated: indeed, the systematic screening noted the factor V Leiden mutation in 30% of cases of child portal

thrombosis in the series of El-Karaksy H et al. [14]. Similarly, in the series of Egesel T et al. [15], of 23 patients with portal cavernoma initially labeled "idiopathic", the systematic complete screening for inherited thrombophilias revealed APCR in 30% of cases [15].

Thus, both APCR and factor V Leiden mutation appear to be significantly associated with portal thrombosis and cavernomatous transformation of this vein [8,15]; this was confirmed by the extensive review of the literature by Qi X et al. [16], where factor V Leiden mutation was significantly associated with portal thrombosis with or without cirrhosis, with an odds ratio of 1.85 and 2.55 respectively [16]. Also note that several inherited thrombophilic disorders may associate to give portal thrombosis and portal cavernoma in the same patient [7].

The treatment of PC secondary to APCR/factor V Leiden mutation is mainly effective anticoagulation for life, which will mainly allow to limit the extension of thrombosis, thrombotic recurrence, and PC-specific ischemic mesenteric complications [3-5]. Surgical treatment such as portal decompression with portosystemic shunt is indicated in PC cases complicated by hepatobiliary involvement ("portal biliopathy" or "Portal cavernoma cholangiopathy") [3,5].

Conclusion

Unlike the child, the portal cavernoma remains an exceptional and unusual complication of portal thrombosis in adults and the elderly. His diagnosis imposes a systemic screening for inherited thrombophilic disorders even in the absence of family and/or personal history of thromboembolic disease. Only early diagnosis and timely and adapted care are the guarantors of a good evolution. The lack of knowledge of this pathology as well as the resulting diagnostic and/or therapeutic delay make the prognosis of the PC very pejorative.

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