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Original Research Article

Focal Nodular Hyperplasia in a Man Revealing Rendu-Osler's Disease

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Abstract

Liver disease during Osler-Rendu-Weber disease (ROD) is frequent. Its screening must be systematic. Focal nodular hyperplasia is a vascular hepatic disease of osler rendu disease, which is very rare in males. Through an observation of a patient with an ROD revealed by hepatic injury (FNH), we will discuss the epidemiological, diagnostic, and evolutionary aspects of hepatic manifestations during MRO.
Keywords: Rendu-Osler's disease, Man, liver.

INTRODUCTION

Rendu-Osler's disease (MRO) or hereditary hemorrhagic telangiectasia is a rare condition. Its prevalence is estimated to be between 1 per 10,000 and 1 per 100,000 population in the general population [1, 2].

It is an inherited autosomal dominant disease with variable expressivity and penetrance. Three genes coding for TGFβ interacting proteins have been identified [3]: the ENG gene located on chromosome 9 coding for endoglin [3,4]; the ACVRL1 gene located on chromosome 12 encoding a serine-threonine kinase-active membrane receptor (ALK-1, ALK-4) [4] and the MADH4 gene located on chromosome 18 encoding the SMAD4 protein [5]. This last mutation is responsible for a rarer phenotype associating ROD and juvenile polyposis (<4% of cases).

Pathophysiologically, ROD is a systemic dysplastic vascular disease characterized by hyperangiogenesis that is caused by abnormalities in the intracellular signaling of TGFβ, having a role in remodeling and vascular angiogenesis [6].

The diagnosis of ROD is clinical and is based on the combination of Curaçao criteria [7]:

- Spontaneous and repeated epistaxis;
- Cutaneomucous telangiectasia;
- The existence of visceral arteriovenous malformations (pulmonary, hepatic, cerebral and / or spinal, digestive ...);
- The existence of at least one first-degree relative, with a diagnosis of ROD, the diagnosis being made using the same criteria.

The diagnosis of ROD is certain if at least three criteria coexist, suspected or possible if two criteria are found and unlikely if only one criteria is present.

Through an observation of a patient with MRO revealed by liver injury in the form of focal nodular hyperplasia, we will discuss the aspects epidemiological, diagnostic, evolutionary manifestations of liver during the ROD.

OBSERVATIONS

A 61-year-old male patient, smoking and chronic alcoholic weaned 13 years ago, with a personal history of repeated epistaxis, sent to us for atypical abdominal pain, the clinical examination did not find any cutaneous signs of hepatic insufficiency and / or portal hypertension or dullness to abdominal percussion. Cutaneous-muqueus examination showed telangiectasia in both hands, lower lip and tongue.

Abdominal Doppler ultrasound allowed the diagnosis of a homogeneous liver with multiple hyperechogenous images surrounded by a hypoechogenous halo, the largest of which measured 8 cm at segment VII without signs of compression, the abdominal CT scan showed a Non specific hepatopathy type focal nodular hyperplasia or peliosis hence the indication of a liver MRI, that confirmed the diagnosis of liver, multi nodular consistent with focal nodular hyperplasia. A biopsy on liver lesions shows a

morphological aspect in favor of focal nodular hyperplasia. Biological assessment including blood count (NFS), prothrombin time (PT), electrophoresis of serum proteins, ferritinemia was normal. B and C viral serology and immunoassay (anti-smooth muscle, anti-LKM1, antimitochondria antibodies) were negative.

The detailed interogatory revealed a family history (brother and mother) of repeated epistaxis, and lesions of telangiectasia in a family setting, a nasal endoscopy showed lesions of telangiectasia.

Given this highly suggestive picture of MRO, an extension assessment including thoracic and cerebral CT and echocardiography was performed and was normal. The endoscopic exploration made of total colonoscopy objectified 2 rectal polypoid formations, resected corresponding to cloacogenic polyps.

The diagnosis of rendering disease on criteria of curacao, with vascular liver injury of focal nodular hyperplasia was retained, and therapeutic abstention with surveillance was recommended in this patient. On a retreat of 2 years the patient is asymptomatic.

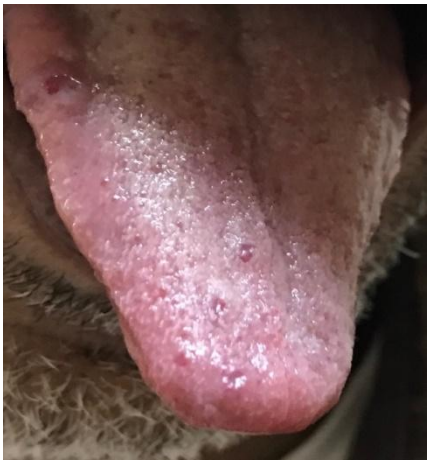

Fig-1: Telangiectsia of the tongue

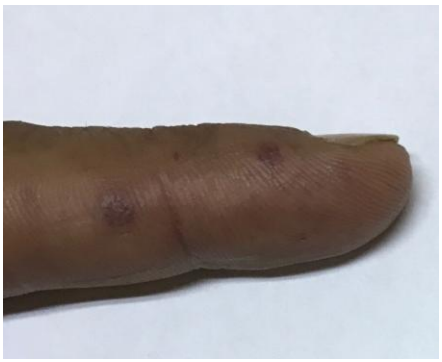

Fig-2: Finger telangiectasia

DISCUSSION

The prevalence of hepatic impairment during ROD is estimated to be between 41 and 74% [8, 9]. This variability is mainly explained by genetic modifications. In fact, genotype-phenotype correlation studies have demonstrated that hepatic vascular malformations of MRO are preferentially associated with mutations in the AVCRL1 gene [10, 11].

The main liver lesions are telangiectasias and arteriovenous anastomoses which lead to the formation of shunts: arteriovenous (between the hepatic artery and the hepatic veins); arterial (between the hepatic artery and the portal trunk); or portovenous (between the portal trunk and the hepatic veins) [10]. These vascular malformations will lead to changes in the hepatic parenchyma and the biliary tree, with essentially hemodynamic consequences determining the clinical symptomatology [8, 10-15].

Clinically, asymptomatic and pauci-symptomatic forms are the most common. They may be latent and discovered by imaging tests performed as part of screening [8, 10]. Clinical examination may reveal hepatomegaly and splenomegaly. Hepatic thrill and vascular murmur with systolic enhancement may also be present.

Severe forms depend on the type and extent of hepatic shunts [9]. Three clinical pictures are described: high rate cardiac failure in arteriovenous and / or venovenous shunts;

- Portal hypertension in case of arterial shunt;

- Ischemic cholangitis that may be the cause of biliary stenosis, intrahepatic lithiasis or abscess necrosis;
- Focal nodular hyperplasia (FNH), as in our patient's case, or nodular regenerative hyperplasia (HNR) secondary to hepatic architecture remodeling have also been described.

The diagnosis of vascular malformations of ROD is based on Doppler ultrasound and high resolution CT [8-10, 13-15].

Doppler ultrasound is the first-line examination for screening and surveillance [8-10]. It shows dilatation, sinuosity and hyperdébit of the hepatic artery, an arteriovenous shunt and veinoportal. The clean hepatic artery is considered dilated if its diameter exceeds that of the splenic artery, and the common hepatic artery is pathological if its diameter exceeds 7 mm. A prognostic classification based on the results of Doppler ultrasound has been proposed. It is currently being evaluated [8].

Treatment is indicated in cases of symptomatic liver injury [10]. It includes fluid restriction with prescription of diuretics in case of high-flow heart failure [10]. B-blockers are prescribed to prevent gastrointestinal bleeding in the presence of oesophageal varices [16]. Some observations have reported the interest of bevacizumab in the reduction of hepatic vascular malformations [17, 18]. Controlled studies are however necessary.

Hepatic embolization is no longer recommended because of its high morbidity and mortality [21].

Hepatic transplantation remains the gold standard in complicated forms, particularly in cases of severe heart failure, portal hypertension and terminal necrotic ischemic cholangitis [19]. Ten-year survival after liver transplantation is approximately 83% [19].

The evolution of vascular malformations during MRO has long been unknown until the recent study by Buscarini *et al*., describing the natural history of liver injury in a large cohort of patients with MRO [20]. This work led to the occurrence of significant morbidity and mortality during MRO with hepatic vascular malformations, with mortality and complication incidence rates respectively of 1.1 and 3.6 per 100 persons per year.

CONCLUSION

Liver injury during ROD is common, but the clinical impact of these abnormalities is more rare. Its screening should be systematic. Doppler ultrasound is the gold standard for screening and surveillance [15].

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