

# *Liver disease and gastrointestinal bleeding in hereditary haemorrhagic telangiectasia – case report*

## **Doença hepática e hemorragia digestiva na telangiectasia hemorrágica hereditária**

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**RESUMO** | Telangiectasia hemorrágica hereditária (THH) ou síndrome de *Rendu-Osler-Weber* caracteriza-se por displasia fibromuscular dos vasos terminais que propiciam o desenvolvimento de ectasias vasculares e malformações arteriovenosas. Do ponto de vista clínico, os órgãos preferencialmente envolvidos são as mucosas, pele, pulmão e cérebro. Este artigo descreve o caso de uma doente adulta com THH, que apresentava múltiplas lesões angiodisplásicas na pele, mucosa nasal e oral, trato gastrointestinal, fígado e tireóide, e que, em decorrência do grave comprometimento gástrico, apresenta perda sanguínea contínua, exigindo a reposição de concentrado eritrocitário a intervalos de tempo muito curtos.

**PALAVRAS-CHAVE:** Telangiectasia hemorrágica hereditária, Síndrome de *Rendu-Osler-Weber*, Malformação arteriovenosa, Hemorragia gastrointestinal, Doença Hepática. *GE - J Port Gastroenterol 2010;17:212-216.*

**ABSTRACT** | *Hereditary hemorrhagic telangiectasia (HHT) or Rendu-Osler-Weber syndrome is characterized for fibromuscular dysplasia of the terminals vessels that propitiate the development of vascular ectasias and arteriovenous malformations. The mucosae, skin, lung and brain are the most commonly affected organs. This article describes a case of HHT an adult patient associated with multiple angiodysplastic injuries in the skin, nasal and oral mucosa, gastrointestinal tract, liver and thyroid, and who presents continuous blood loss in result of the severe gastric mucosal damage, demanding the replacement of erythrocytes concentrated in very short time intervals.*

**KEYWORDS:** *Hereditary haemorrhagic telangiectasia, Rendu-Osler-Weber syndrome, Arteriovenous malformation, Gastrointestinal bleeding, Liver disease. J Port Gastroenterol 2010;17:212-216.*

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## INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT) or Rendu-Osler-Weber syndrome is a rare autosomal dominant disorder. It affects both sexes in the same way and without any race predilection.<sup>1</sup> This illness is characterized by a fibromuscular dysplasia of the mucocutaneous and visceral terminal vessels that determines the appearance of vascular ectasias and arteriovenous malformations (AVMs).<sup>1</sup> The genetic alterations in the THH has been established for some families linked to chromosome 9q33-q34, associated with pulmonary and neurological manifestations, and in others with the chromosome 12q, related to telangiectasias and recurrent epistaxis.<sup>2</sup>

The angiodyplastic abnormalities are responsible for the clinical manifestations of the illness. The classic clinical pattern is represented by the triad: mucocutaneous telangiectasias, recurrent epistaxis and familiar history of hemorrhagic pictures involving nasal mucous, skin, lung, brain and gastrointestinal tract (GIT).<sup>1,3</sup> Severe digestive hemorrhage occurs in up to 35% of the individuals with HHT, causing significant morbidity, such as severe anemia and repeated blood transfusions during the hospitalization period.<sup>3,4</sup> Liver damage occurs rarely. It is a consequence of secondary hemochromatosis associated with multiple blood transfusions or iron supplement and arteriovenous fistulas formation that propitiates the development of portal hypertension.<sup>5</sup>

The present study describes the case of a patient with hereditary hemorrhagic telangiectasia presenting with recurrent upper digestive hemorrhage and hepatic involvement.

## CASE REPORT

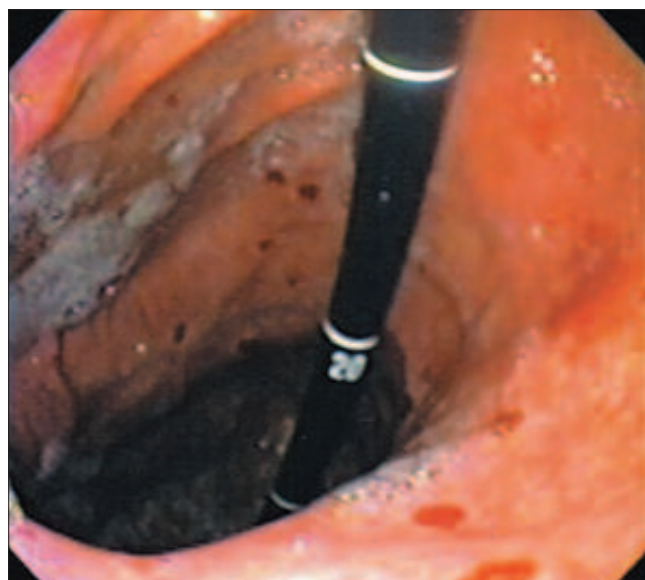
A 48-years-old woman performed an accompaniment in the Gastroenterology Service of the Federal University of Piauí with description of recurrent epistaxis episodes, hematemesis and melena since her childhood. There were multiple angiodyplastic injuries located in the fingers' extremities, nasal and oral mucosae since child. Her mother and two brothers also had history of recurrent spontaneous bleeding of mucosa, mainly epistaxis episodes. Epidemiological antecedents was absent for alcoholism, injectable drugs use, sexual promiscuity or viral hepatitis.

The clinical description of the patient reveals various hospitalizations to receive frequent blood transfusions decurrent of severe anemia owing to occult or manifest of gastrointestinal bleeding. These hospital admissions initially occurred to each six months. However, there was the necessity of hemotransfusion weekly in the last five years with long-term hospital treatment. In these occasions, the patient invariably presenting with hypotension, tachycardia and pale skin, followed by significant reduction of the hematocrit and hemoglobin values, getting hemodynamic stabilization after the treatment replacement with concentrated of erythrocytes.

Physical examination of the patient showed poor health and cutaneous mucosa pallor. Multiple telangiectasias had been perceived in fingers and oral and nasal mucosa (Fig. 1). The thyroid had a visible increase of volume, owing to right lobe, with firm consistency and painless to the manual exam. No local regional lymphonodes were palpable. Cardiac and pulmonary examinations were normal. The abdominal exam evidenced moderate ascites and voluminous hepatomegalia. The liver margin was palpable 16 cm below the right costal margin and



**Fig 1. Ectoscopy: telangiectasias on the (A) lips and (B) finger.**



**Fig. 2. Upper digestive endoscopy: angiodysplastic lesions in the inferior portion of esophagus and cardia.**



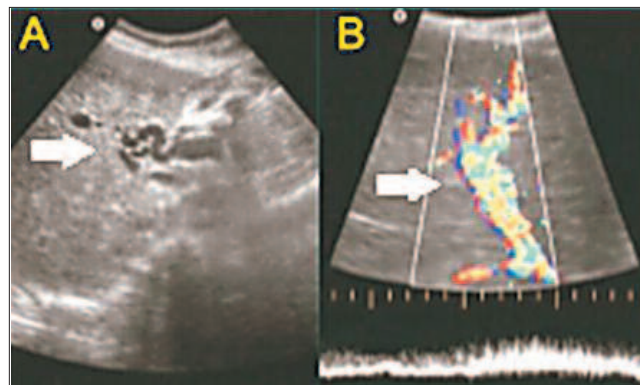
**Fig. 3. Colonoscopy: (A) colonic telangiectasia and (B) lesion with spontaneous bleeding.**

presented lightly painful, with rough surface and without thrill or murmur. Peripheral edema, petequeal hemorrhages or sings of hepatocellular insufficiency were absent.

A digestive endoscopy disclosed discrete angiodysplastic injuries in the superior and medial portions of esophagus and incipient esophageal varices. In the antrum, fundus and body gastric and duodenal bulb had been revealed innumerable angiodysplastic injuries with various sizes and some had central erosion (Fig. 2). The digestive endoscopy also showed a polyp, about to 0.8cm in diameter, located in fundus gastric near the cardia, Yamada IV. Multiple colonic telangiectasias were detected by colonoscopy (Fig. 3).

A past abdominal ultrasonography demonstrated liver with increased dimensions and preserved texture of the hepatic parenchyma and absence of ascites. The complementation with color and pulsed Doppler sonography showed exuberant dilatation of the hepatic artery and left hepatic vein, and characteristic blood flow of arteriovenous fistulas (Fig. 4). Cervical Doppler ultrasonography founded a cystic thyroid nodule containing calcification and thick content, located in the right lobe, and vascularization with moderate impedance suggesting arteriovenous shunts. Computed tomographic (CT) study of skull did not evidence AVMs. The alpha-fetoprotein was 4.6 ng/ml [Reference Value (RV): up to 16 ng/ml]. Echocardiogram, thorax and abdomen X-rays and CT Scan of sinuses had been normal. The hepatic laboratorial evaluation showed: albumn = 26 g/L (RV: 35 g/L), alkaline phosphatase = 4.51 g/L (RV: < 1 g/L) and gama-glutamyltransferase = 374 U/L (RV: < 40 U/L). Aminotransferases and bilirrubines were normal. It still presented levels of seric iron = 132 µg/dl (RV: 50 - 70 µg/dl) and seric ferritin = 77.9 ng/ml (RV: 20-250 ng/ml).

The ascites was solved by the use of furosemida (80 mg) and spironolactone (200 mg) per day. It was instituted therapeutical



**Fig. 4. Abdominal Doppler ultrasonography: (A) dilated tortuous portal vein and (B) characteristic blood flow of arteriovenous fistula between hepatic artery and hepatic vein (arrows).**

support with blood transfusion under demand. The patient had used medroxyprogesterone acetate (5 mg) associated with conjugated estrogens (0.625 mg) for some years, however without observation of a reduction of the gastrointestinal bleeding episodes. Prophylaxis and treatment of the digestive hemorrhage was attempted by cauterization of the telangiectasias in gastric mucosa. However, this therapeutic strategy did not show feasible and was abandoned in result of the great number of angiodysplastic injuries affecting extensive areas of the stomach. The frequency of hospitalization increased in the last two years decurrent of the persistence severe anemia provoked by uninterrupted episodes of hemorrhage digestive and epistaxis frequent.

## DISCUSSION

Hereditary Hemorrhagic Telangiectasia consists of a rare syndrome with dominant autosomic inheritance and incidence of 1 to 2 cases for 100.000 individuals.<sup>1</sup> The fibromuscular structure of the sanguineous vessels is modified, providing a formation of arteriovenous malformation and vascular ectasias. The organs affected are mainly: skin, mucosae, lung, liver, gastrointestinal tract and brain. The classic clinical picture is represented by the triad: telangiectasias, recurrent epistaxis and familiar history of hemorrhagic pictures.<sup>1,6</sup>

Recidivant nosebleed is the most common clinical characteristic of HHT, being more frequent during infancy. It results of telangiectasias in the nasal mucosa, generally is spontaneous and without severe clinical consequences. However, in some cases it may be extremely serious and debilitating.<sup>1,6</sup> The initial pictures are usually light without hemodynamic or hematological alterations.<sup>7</sup> Telangiectasias of the skin and the oral mucosa occur in about 75% of the cases, and normally

they are considered delayed manifestations.<sup>8</sup> In the patient of the present report, telangiectasias appeared after epistaxis manifestations. The visceral involvement occurs in about 25% of the cases with gastrointestinal symptoms predominating such as hematemesis, melena and hepatomegaly.<sup>6,8</sup>

Digestive bleeding is caused by the presence of telangiectasias, angiodysplastic lesions and arteriovenous malformations. Its frequency increases with the age, usually manifesting in the fifth or sixth decade of life.<sup>3-5</sup> Although there are few reports, it becomes an important cause of severe anemia necessitating repeated blood transfusion. Ultrasonography, upper digestive endoscopy, colonoscopy and angiographies are diagnostic methods for detection of the angiodysplasias in the GIT. The therapeutical measures include estrogenic therapy, endoscopic methods of hemostasia (laser and eletrofulguration), and surgical resection, reserved for refractory cases.<sup>1,3</sup>

In this case, the clinical diagnosis of Rendu-Osler-Weber syndrome was firm by the presence of the picture of epistaxis recurrent since infancy, episodes of upper digestive hemorrhage owing of numerous telangiectasias in gastric mucosa, presence of telangiectasias cutaneous-mucosae and familiar history of spontaneous mucosae bleeding. In a peculiar form, this patient also presented arteriovenous fistulas in the liver and thyroid. An important clinical characteristic was extensive damage of the gastrointestinal mucosa with coalescent and diffuse telangiectasias, some presenting plain erosions on the angiodysplastic injuries. The colonoscopy also showed to focal involvement of the rectum and colon. These alterations explain the gravity of the case, determining occult or manifest bleeding, and therefore demanding repeated transfusions of erythrocytes in very short intervals of time.

In the endoscopic therapeutical of the episodes of the gastrointestinal blood loss, photocoagulation or eletrocoagulation techniques can be used. Nevertheless, this treatment have unsatisfactory results in patients with extensive injuries, as those detected in this case.<sup>9</sup> Diffuse lesions also contraindicate surgical resection of the affected segments. The surgical treatment is more effective when performed focal angiodysplasias.<sup>3-4,9</sup> Although case reports and controlled, randomized and double-blind studies people show the estrogen therapy effectiveness,<sup>10-11</sup> this therapeutic intervention was unsuccessful.

Hepatic involvement is rare, present in 8% - 31% of the patients with HHT.<sup>1-5</sup> According to Martini et al the patients with liver illness in HHT can be divided in three groups: group 1, patients presenting telangiectasias with fibrosis or cirrhosis; group 2, those who develop cirrhosis without telangiectasias; and group 3, patients with telangiectasias without cirrhosis or fibrosis. Generally, the patients of group 2 present a hepatopathy secondary that leads to cirrhosis, such as a chronic

post-transfusion hepatitis. The hemodynamic repercussions in the liver disease illness can become significant as cardiac insufficiency of high debit and portal hypertension.<sup>5,13-14</sup> Initially, it is indicated conservative treatment with beta-blocker and diuretics in hepatic involvement. Some cases must be surgical treatment with hepatic artery embolization or liver transplant in the hepatic end-stage disease.<sup>5,14</sup>

In present case, levels of iron and ferritin seric unsuggested secondary hemocromatosis; although there was necessity of repeated hemotransfusion. The hepatitis markers were negatives with aminotransferases in normal levels, had moved away the hypothesis post-transfusional viral infection. Concomitant chronic hepatic illnesses had been excluded by the absence of risk factors such as alcoholism, negative auto-antibodies and absence of metabolic and cholestatic diseases. The diagnostic confirmation is made with biopsy of the affected tissue. Liver biopsy was not carried out by the presence of MAVs in hepatic parenchyma and possible risk of bleeding. Probably, chronic hepatopathy of this patient occurred as a consequence of vascular malformations determining sinusoidal hypertension with periportal and portal fibrosis.<sup>5,15</sup>

Laboratorial exams are unspecific. Bleeding, coagulation, and prothrombin times and counting of platelet were normal. Recurrent episodes of cutaneous-mucosae blood loss cause ferroprive anemia. However, it can increase the necessity of folic acid consequent to stimulate chronic in the bone marrow.<sup>1,4,7</sup>

In conclusion, gastrointestinal bleeding is a relatively frequent complication, while liver involvement is an unusual manifestation in the Rendu-Osler-Weber syndrome. The digestive hemorrhage can cause severe ferroprive anemia and haemorrhagic shock that demand repeated hemotransfusion. The hepatic illness has periods of spontaneous remission; on the other hand it assumes gradual character, leading to the development of cardiac failure of high debit, portal hypertension and hepatocellular insufficiency.

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