Case study

Rendu-Osler-Weber Syndrome: case report and literature review

Abstract
Rendu-Osler disease is a rare inherited vascular disorder. Through this article, the authors recall the digestive manifestations of this condition, which when associated with other clinical signs, are sufficiently characteristic to allow the gastroenterologist to suggest the diagnosis.
Keywords: Telangiectasia, Rendu-Osler-Weber disease, iron deficiency anemia

Introduction
Rendu-Osler disease is a vascular dysplasia also known as hereditary hemorrhagic telangiectasia (or HHT according to the Anglo-Saxon initials).

Case presentations

A 63 years old *patient* , was hospitalized in our department for exploration of iron deficiency anemia. Her history was marked by iterative episodes of low-abundance epistaxis that began in early childhood. The same symptomatology was reported in the mother. Its clinical history dates back years with the installation of spontaneous recurrent epistaxis complicated by an anemic syndrome without any other site of exteriorized bleeding. The clinical examination on admission found: an eupneic patient at rest without orthopnea weighing 70 kg for a height of 1.80, therefore a BMI of 28.4 kg/m, normocardium carding at 70 B/min, afebrile, with pallor cutaneo-mucous membrane and telangiectasias on the tongue and thorax (Figure 1, 2) . The rest of the clinical examination is unremarkable. . The specialized otolaryngeal examination revealed a bright red nasal mucosa, erosive in places with multiple telangiectasias. (Figure 3)

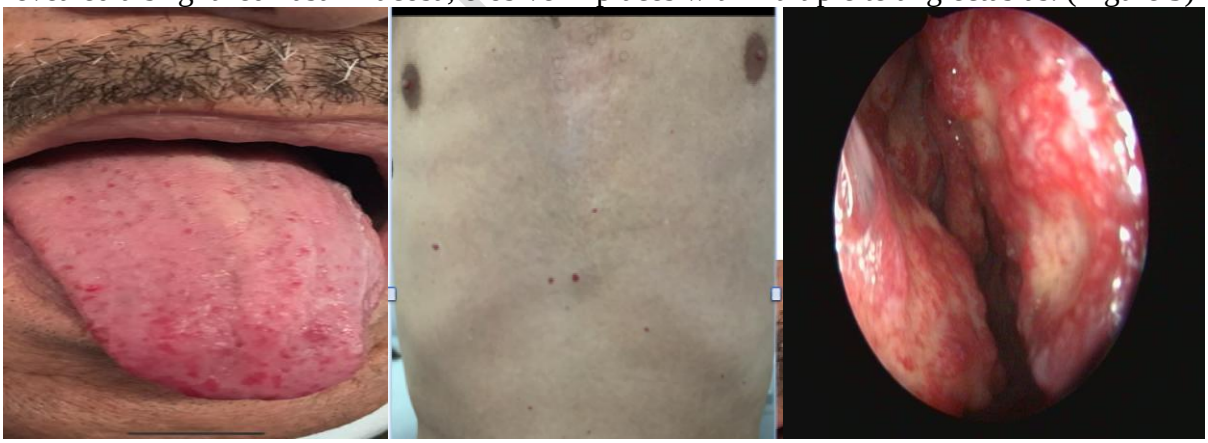

Figure 1-3. Disease morphology

Biologically:

- hypochromic microcytic anemia at 10 g/dl.
- Ferritinemia: 56 ng/ml.
- No inflammatory syndrome
- Normal liver function

- Correct kidney function

Morphologically:

- Chest CT : presence in the subpleural at the level of the left posterobasal segment of a small AVM presenting a double venous and arterial connection measuring 8x5 mm
- duodenal esogastrofibroscopy shows multiple antral, fundic and duodenal angiodysplasias (Figure 4,5)
- total colonoscopy revealed angiodysplaiae in the right colon (Figure 6)

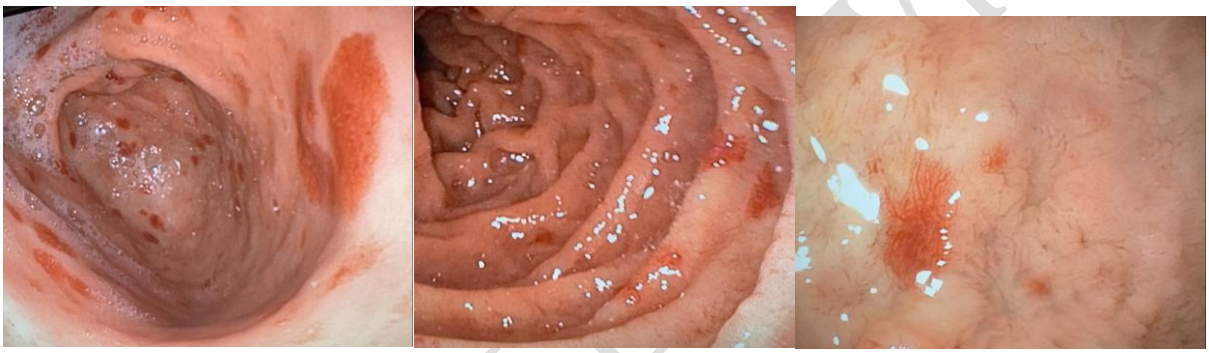

Figure 4-6 : Colonoscopy images

the therapeutic and evolutionary level

The patient was put on iron supplementation, a regular monitoring, both biological and morphological, was decided. At his follow-up, no other complication was noted.

Discussion

The clinical manifestations of hereditary hemorrhagic telangiectasia (HHT) were first described in 1864 by Gawen and then Babington [1] in 1865. It was the Frenchman Henri JLM Rendu [2] who individualized the disease in 1886, differentiating it from hemophilia, noting the association of epistaxis, cutaneous telangiectasias and the familial nature of epistaxis [3] . The Canadian Osler completed this description in 1901 and 1907. He established that it was a hereditary transmission condition and described the possibility of visceral manifestations (telangiectasia of the gastric mucosa). The German Weber contributed to the clinical description of the disease in 1907, as did Hanes in 1909.

HHT expression is usually complete around the age of 40–50 years. Genetically, there are at least two forms: HHT1 for which the anomaly is located on chromosome 9q33–34, the

mutated gene being that of endoglin (ENG), and HHT2 for which the anomaly is located on chromosome 12 (12q13) the mutated gene being that of activin receptor like kinase 1 (ALK1). Endoglin and ALK1 are both membrane receptors of the TGF-ß (transforming growth factor ß) system expressed on the surface of endothelial cells. TGF-ß participates in the control of angiogenesis and vasculogenesis by intervening in the migration, proliferation and adhesion of endothelial cells and in the organization of the extracellular matrix. More recently, germline mutations of a third MADH4 gene at position 18q21.1 have been described [4].
The diagnosis of Rendu-Osler disease is essentially clinical. It is based on criteria established at the international consensus conference held in Curaçao in 2000 which combine [5,6,7]:

- Four criteria were used to establish the diagnosis.

- Spontaneous and repeated epistaxis.
- Cutaneous or mucous membrane telangiectasia, the preferred sites of which are the lips, tongue, fingers, nose.
- Family history: the existence of at least one first-degree relative with a diagnosis of Rendu-Osler disease using the same criteria.
- The existence of visceral arteriovenous malformations: pulmonary, hepatic, cerebral and/or spinal, digestive

- The clinical diagnosis is:

certain if at least 3 criteria are present,
suspected or possible if 2 criteria are present,
unlikely if only 1 criterion is present.

The severity rendu osler's disease is often associated with complications related to the presence of arteriovenous malformations.
Pulmonary arteriovenous malformations result from abnormal communication between pulmonary arteries and veins [8]. they are often undiagnosed because they are generally asymptomatic.
However, pulmonary arteriovenous malformations can cause hypoxia usually manifesting as dyspnea due to a right-left shunt, hemoptysis (sometimes massive), hemothorax or central neurological complications (transient or established cerebrovascular accident, cerebral abscess) [8]. The screening examination is the chest CT scan (without injection), or contrast echocardiography.

Intestinal angiodysplasias occur very frequently in Rendu Osler's disease, whereas they only affect about 3% of the general population. digestive AVMs are generally asymptomatic but they can become haemorrhagic, especially from the 5th or 6th decade, and due to inefficient local treatment, may require regular transfusion support. We find in the literature a prevalence between 46 and 75% for gastric angiodysplasia and 56 to 86% for intestinal angiodysplasia with an increase in prevalence with waking [9,10,11]. The endoscopic capsule allows a check-up of the main locations (stomach and small intestine) and is therefore valuable as a “check-up” examination. Upper and lower endoscopy may be warranted, being wary of the risk of endoscopy-induced epistaxis and therefore aspiration.

The rare and particular forms linked to mutations of the SMAD4 gene associate a picture of Render-Osler disease and juvenile polyposis and/or predisposition to digestive cancers. In these cases, monitoring of digestive endoscopy is recommended every 2 years.
Because of blood loss associated with recurrent epistaxis and digestive angiodysplasia, patients frequently develop an iron deficiency. When dietary iron intake cannot compensate for iron loss, iron deficiency anemia sets in. Rendu Osler's disease having no inflammatory feature, it appears as a pure model of iron deficiency anemia. Detection and treatment of an iron deficiency are essential follow-up objectives [8].

Liver damage defined by a broad spectrum of vascular malformations affects about 30 to 73% of patients [12], but only 8% of them have symptomatic liver disease [8]. Liver damage results from vascular malformations in the form of fistulas between the arterial and portal venous or hepatic systems. Hepatic manifestations are rarer, even pauci symptomatic, associated with hepatomegaly and slight biological cholestasis [12], but potentially very serious. The least invasive screening test is liver Doppler ultrasound. A check-up after 20 years and every 3 to 5 years if normal seems sufficient. In the event of suggestive clinical symptoms (dyspnea on exertion, oedema, cardiac signs) and/or patent abnormalities, monitoring of echocardiography with measurement of the cardiac index is recommended.

Central neurological involvement affects 10 to 23% of patients [4]. There is no specificity of central neurological damage during Rendu-Osler, any type of congenital vascular malformation can be observed. [8]

The different clinical forms of the disease require multidisciplinary care. Clinical or genetic screening, then assessments, are carried out in multidisciplinary consultations
Anemia is the major concern of a large proportion of patients, especially since it is recurrent, long-term, and requires basic martial treatment. Intravenous products such as Venofer®, to be used in cases of digestive intolerance to iron, should be better managed. The indications are extremely variable from one patient to another.

The teams of otolaryngologists have identified the improvement caused by the most complete possible humidification of the nose: better nasal hygiene results in the elimination of clots and nasal crusts, reducing infection and recurrence of the hemorrhagic phenomenon

Screening and appropriate monitoring of arteriovenous fistulas must be done because these fistulas are not a malformation in the etymological sense of the term but are likely to settle during life and recur. Currently, arteriovenous fistulas can benefit from non-surgical treatment by interventional radiology, vaso-occlusion or embolization of the lesions; this treatment can be renewed for recurrent pulmonary fistulas, but it seems ill-suited for hepatic fistulas with clinical repercussions, and it is more difficult to apply early for neurological manifestations.

Conclusion
Rendu-Osler disease is a genetic, autosomal dominant vascular disease. The diagnosis is primarily clinical. It is a progressive disease, as a general rule, patients have a normal life expectancy but this is highly dependent on visceral complications.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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