

Osler-Weber-Rendu syndrome: A case report with familial clustering

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ABSTRACT

Osler–Weber–Rendu syndrome, also known as hereditary hemorrhagic telangiectasia, is a rare autosomal dominant disorder manifested by telangiectases of the skin and mucous membranes and arteriovenous malformations of various organ systems. We present a case of Osler–Weber–Rendu syndrome with 11 affected members in her family.

Key words: Familial, Hereditary, Telangiectasia

INTRODUCTION

Osler–Weber–Rendu syndrome, or hereditary hemorrhagic telangiectasia (HHT), is a rare genetically determined autosomal dominant disorder identified by the triad of telangiectasia, recurrent epistaxis, and a positive family history for the disorder.^[1] Presenting at any age, the disease has a wide spectrum of presentations, varying from asymptomatic to multiple organ involvement. The major cause of morbidity and mortality lies in the presence of multiorgan arteriovenous malformations (AVMs) and the associated hemorrhage. We present a case of HHT with typical mucocutaneous and gastrointestinal (GI) AVMs and association in 11 other members of the patient's family.

CASE REPORT

A 45-year-old postmenopausal lady born to nonconsanguineous parents presented with multiple red raised lesions on the tongue and both hands of almost 25 years duration. She also had breathlessness on exertion and easy fatig ability since 15 years. She had a history of recurrent spontaneous severe bleeding from the lesions, especially from those on the tongue due to which she had to receive multiple blood transfusions in the past two decades, and multiple

episodes of mild epistaxis, palpitations, and frequent blackouts. There was no history of bleeding gums, abdominal pain, bleeding rectum, headaches, seizures, visual disturbances, hemoptysis, menorrhagia, or bluish discoloration of fingertips or nose. There was history of similar lesions being present in 11 of her immediate family members [Figure 1]. Her three elder sisters died of severe bleeding from such lesions in the mouth and hands; also, her father suffered from hemiplegia.

Clinical examination revealed pallor and absence of organomegaly. Dermatologically, multiple erythematous macular blanchable lesions on both palms, multiple erythematous compressible nonpulsatile papulonodular lesions on the tongue, and multiple petechiae over the palate [Figure 2] were evident.

Investigations revealed microcytic hypochromic anemia, normal reticulocyte count, and normal coagulation profile. Serum for antinuclear antibody (ANA), urine for hemoglobinuria, and Sickling test were negative. Abdominal ultrasonogram, chest skiagram, and fundoscopy were unremarkable. Angiogram of carotids revealed multiple telangiectatic lesions in the tongue fed by bilateral lingual arteries, while those in the palate were fed by sphenopalatine branch of

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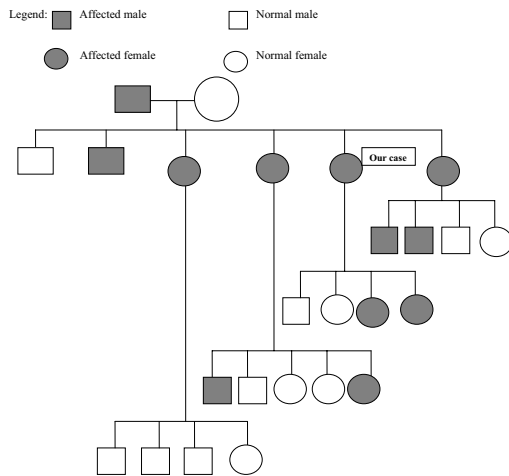


Figure 1: Family tree of the case

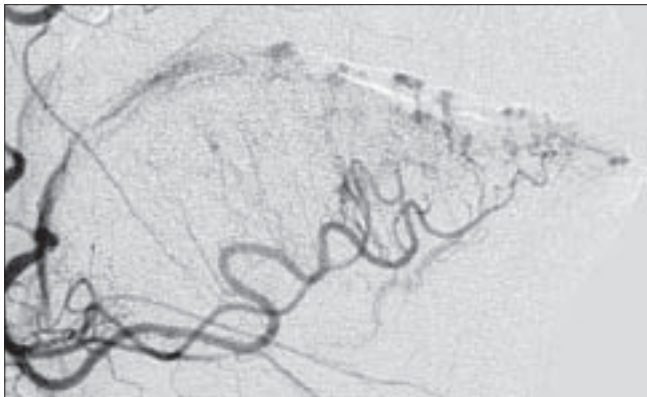


Figure 3: Right external carotid artery angiogram, showing multiple hyper vascular focal areas on the surface of the tongue supplied by the terminal branches of lingual artery

internal maxillary artery (IMA) [Figure 3]. The lesions showed early venous drainage with persistence of stain in the parenchymal phase. Upper GI endoscopy revealed multiple petechiae in the abdominal wall. Neither colonoscopy nor abdominal, pulmonary, and renal angiograms revealed any AVMs in other organ systems.

DISCUSSION

While Henri Rendu (1896), Sir William Osler (1901), and Frederick Parks Weber (1907) emphasized and published detailed observations of the syndrome which bears their names, it was Sutton (1864) who first described Osler–Weber–Rendu disease and Benjamin Guy Babington (1865) was the first to note its familial nature.

A number of variants of HHT have been described in literature. HHT type-1 and type-2 are due to defective



Figure 2: Multiple telangiectasias on both palms and multiple erythematous compressible papulonodular lesions on the tongue

endoglin (*ENG*) and activin like receptor kinase (*ALK1*) genes, respectively. Mutations of *ENG* are located on the long arm of chromosome 9 (9q33-34), whereas *ALK1* mutations are on the long arm of chromosome 12 (12q13).^[2,3] HHT type-3 involves mutations of the long arm of chromosome 5 (5q31.1-32) and type-4 maps to the short arm of chromosome 7 (7p14).^[4,5] A HHT-juvenile polyposis overlap syndrome due to mutations of *SMAD4* has also been described.^[6] Patients with the HHT type-1 genotype have higher prevalence of pulmonary and cerebral AVMs, and more severe GI bleeding than in those with the HHT type-2 genotype. Conversely, the prevalence of hepatic AVMs is higher in patients with HHT type-2 than in those with HHT type-1.^[7] Although the precise mechanism remains poorly understood, bleeding tendency in HHT is attributed to localized vessel wall weakness.

Diagnosis is based on the four components of the Curaçao criteria, established by the Scientific Advisory Board of the HHT Foundation International, Inc., viz. (1) epistaxis: spontaneous and recurrent; (2) telangiectasias: multiple, at characteristic sites, including lips, oral cavity, fingers, and nose; (3) presence of internal lesions: GI telangiectasia, pulmonary, hepatic, cerebral, and spinal AVMs; and (4) family history: first-degree relative with HHT according to these criteria. The diagnosis is considered definite if any three of the above mentioned criteria are present and possible if any two of the criteria are present. The diagnosis is unlikely if less than two criteria are present.^[8] Our case was unique with the presence of all four criteria confirming the diagnosis. In the absence of pulmonary AVMs, her symptomatology is attributed to anemia resulting from frequent bleeding from her

vascular lesions.

The varied treatment modalities include estrogen, ϵ -amino-caproic acid, cryotherapy, cautery, infrared coagulation, radiofrequency, pulse dye laser, Nd-YAG laser, and surgical ablation – all of which may be fraught with risks.^[9-13]

Asymptomatic pulmonary and CNS AVMs and their hemorrhagic or embolic complications, viz. brain abscess and stroke are responsible for most of HHT's 10% mortality rate. It is crucial that a long-term follow-up for identification of potential complications is maintained and patients are counseled regarding the autosomal dominant nature of the condition.

Though cases have been reported with digital and mucocutaneous telangiectasias,^[14] our case is particularly unique as it had all the four criteria for diagnosis and that 12 members of the same family could be identified with this disease.

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