Clinical PRACTICE

Osler-Weber-Rendu Syndrome — Dental Implications

Paulo Sérgio da Silva Santos, *DDS, MD;* ***Karin Sá Fernandes,*** *DDS;*
Marina Helena Magalhães, *DDS, PhD*

Contact Author

Dr. Fernandes
Email:
karin.fernandes@usp.br

ABSTRACT

Osler-Weber-Rendu syndrome (OWRS) is a rare hereditary, autosomal dominant disease characterized by a local angiodysplasia. Its clinical characteristics are vascular hamartomas of the skin and oral mucosa, arteriovenous malformations in the lungs, liver, kidney and brain, and episodes of epistaxis. The oral lesions, which become apparent through hemorrhagic telangiectasia, may be the first sign of the disease. This is a case report of a 74-year-old woman whose diagnosis of OWRS was established by her dentist based on the presence of telangiectasia in the skin and oral mucosa, reports of frequent nosebleeds of unknown etiology and a family history of telangiectasia. Amputation of a lower limb and comorbidities, such as cardiopathy, nephropathy and rheumatic disorders, completed the profile. OWRS causes major vascular changes that can be diagnosed initially by a dentist. In this article, we describe the skills and knowledge that dentists need to monitor patients with OWRS properly.

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Hereditary hemorrhagic telangiectasia, or Osler-Weber-Rendu syndrome (OWRS), was first described by Sutton in 1864 and Babington in 1865 as a hereditary epistaxis disease.[1,2] In 1896, Rendu described the disease as a pseudo hemophilia related to hereditary epistaxis. In 1901, Osler described the clinical symptoms of the syndrome and emphasized its hereditary occurrence. Weber (1907) recognized OWRS as a clinical entity distinct from hereditary hemophilia, and Hanes (1909) named the syndrome hereditary hemorrhagic telangiectasia.

OWRS is an uncommon autosomal dominant disorder characterized by an angiodysplasia in the presence of telangiectasias of the skin and oral mucosa and arteriovenous malformations in the brain, lung, liver and gastrointestinal tract.[3] Its incidence is 1 in 5,000–10,000 in the general population.[4] Bleeding episodes may occur due to capillary fragility rather than disturbances in coagulation.[1,5]

OWRS manifests itself in 2 forms: hereditary hemorrhagic telangiectasia type 1 (HHT1) where there is mutation of the endoglin gene on chromosome 9 with pulmonary involvement; and type 2 (HHT2) with a mutation in the activin receptor-like kinase-1 (ALK-1) gene. HHT2 is the milder form and its onset is later. The proteins produced by the involved genes may play an important role in the integrity of the vessel wall.[6]

The clinical characteristics of OWRS are epistaxis, telangiectasias of the skin and oral mucosa, visceral lesions (lungs, gastrointes-

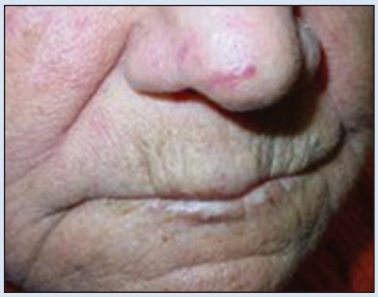

Figure 1: Telangiectasias on the face.

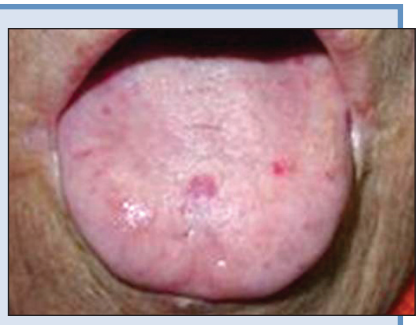

Figure 2: Telangiectasias on the tongue.

Table 1 Results of blood tests

Test	Patient's results	Reference value
INR	1	0.7–1.2
aPTT (s)	33 s	30–45 s
PT (s)	13 s	11–14.6 s
BT (min)	2.17	1–4
Platelet count (no./mm^3)	280,000	165,000–397,000
Erythrocyte count (cells/mm^3)	3.97	4.3–5.9
Hemoglobin (g/dL)	10.9	12–16

aPTT = partial thromboplastin time, BT = bleeding time, INR = international normalized ratio, PT = prothrombin time.

tinal tract, liver and brain) and family history.[7,8] The differential diagnosis of OWRS includes benign liver disease, benign hereditary telangiectasia, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia) syndrome and ataxia-telangiectasia.[8]

Dentists can play an important role in the diagnosis of OWRS, as its first signs often appear in the oral mucosa. Moreover, the management of a patient with OWRS must be suited to his or her systemic profile to ensure safe and efficient dental treatment.

Case Report

A 74-year-old woman was referred to the special care dentistry centre of our dental school for treatment. The patient's medical history included congestive heart failure, chronic renal failure, hypertension, hypothyroidism and rheumatism. Her right lower limb had been surgically amputated because of vascular disorders. She reported frequent nosebleeds and a family history of telangiectasias and epistaxis.

Laboratory tests showed significant changes in her red blood cell count—hypochromic anemia with anisocytosis and a high level of liver enzymes, with no changes in coagulation (**Table 1**).

During the extraoral and intraoral clinical examination, telangiectasias were found on the skin, especially on the face (**Fig. 1**) and upper limbs, and were highly visible on the oral mucosa in the regions of the tongue (**Fig. 2**), hard palate and in the vermilion of the lip. Also present were periodontal disease and caries. Panoramic and periapical radiographs were taken to develop a dental treatment plan.

The patient's signs and symptoms pointed toward a working diagnosis of hereditary hemorrhagic telangiectasia or OWRS. The patient was referred to an internal medicine specialist who confirmed our diagnosis and began medical monitoring for possible systemic changes resulting from the syndrome. Before dental treatment, antibiotic prophylaxis (500 mg amoxicillin) was administered every 8 hours, starting 12 hours before the procedure and continuing for 7 days after, to avoid the risk of cerebral abscesses or pulmonary infections due to the arteriovenous malformations found in OWRS patients.[9] Other special measures taken during treatment were use of a vertical dental chair position to reduce the risk of lung and nasal bleeding, measurement of blood pressure before and after the procedure, request for an up-to-date laboratory evaluation and assessment of her clinical condition at the time of treatment, because of the potential for renal failure and liver disease.

Discussion

A final diagnosis of OWRS is based on clinical criteria,[10] usually the Curaçao criteria: telangiectasia on the face, hands and oral cavity; recurrent epistaxis; arteriovenous malformations with visceral involvement; and family history. Diagnosis is confirmed in the presence of at least 3 of these manifestations.[11] In our case, the clinical signs of telangiectasias of the skin, especially in the face, upper limbs and on the oral mucosa, combined with reported nosebleeds and a family history of telangiectasia and epistaxis were important factors leading us to suspect OWRS.

Mucocutaneous telangiectasias occur in about 90% of cases of OWRS.[8,12] Histologically, they appear as a superficial collection of dilated blood vessels with a layer of endothelial cells in the lamina propria. Electron microscope studies show a lack of perivascular elastic fibres and smooth muscle.[1]

Once the diagnosis is established, complementary imaging tests, such as computed tomography ultrasound

and magnetic resonance imaging, are important to detect whether there is any involvement of organs, such as lungs, liver, kidneys and the brain.[10] Pulmonary arteriovenous malformations occur in more than a third of patients with the disease and can cause various complications, such as hypoxia, pulmonary hemorrhage and cerebral embolism.[9] Dental professionals must be aware of these complications, keep the dental chair in a vertical position during dental treatment and be prepared to administer oxygen.

Vascular lesions in the brain predispose patients to cerebral abscesses,[9] a situation that requires special care during invasive dental procedures, such as antibiotic prophylaxis, especially in infected areas. An OWRS patient's risk of developing a brain abscess ranges from 5% to 9%. Few cases of cerebral abscess due to bacteremia of odontogenic origin have been described so far. Most organisms isolated from brain abscess aspirates have been microaerophilic and anaerobic bacteria commonly and often specifically isolated in periodontal infections.[13]

Rivero-Garvia[14] reported the case of a 41-year-old patient with OWRS who had teeth extracted without antibiotic prophylaxis and, after a few days, developed a brain abscess. This finding confirms the importance of careful dental care in this group of patients. Arteriovenous fistulae in the lungs and vascular malformations are important in the pathogenesis of cerebral abscess. A peripheral septic microembolism can reach the brain and cause a brain abscess. Approximately 10% of patients with arteriovenous fistulae in the lungs develop cerebral abscess.[15,16]

There is no evidence in the scientific literature of the need to use antibiotic prophylaxis in invasive dental procedures that may cause bacteremia in patients with arteriovenous malformations, who have a higher likelihood of developing cerebral abscesses.[2] However, the rarity of the disease and lack of prospective studies addressing the risk of brain abscesses through oral manipulation makes the use of antibiotic prophylaxis empirical in this case.

Although for normal patients there is little risk of exacerbation of anemia due to dental treatment, patients with OWRS with severe anemia (hemoglobin level <10 mg/dL) should avoid certain routine procedures, as invasive procedures can exacerbate anemia, depending on the amount of blood that is lost.[17,18]

The medical treatment of OWRS is only palliative and depends on the severity and stage of disease. Symptoms of OWRS increase with age. Some measures, including iron supplements, blood transfusions and laser therapy, have met with varying degrees of success; sclerosing techniques have been used to control epistaxis. In patients with recurrent episodes of epistaxis, surgery of the nasal septum may be indicated.[12]

A study in Italy[19] reported excellent hemostatic results using Nd-Yag laser treatment in 8 patients with OWRS for the control of epistaxis and oral bleeding. This treatment was well accepted by patients and costs were low. However, researchers are divided on the efficiency of the use of lasers with OWRS patients, and there is no specific protocol for their use.

The prognosis associated with OWRS is good, but the morbidity is significant.[20] Moreover, a mortality rate of 1%–2% is reported due to complications related to epistaxis, and it rises to 10% in patients with cerebral abscess.[6]

OWRS causes major vascular changes that may be initially diagnosed by the dentist. Skill and knowledge of the disease are required for proper dental monitoring of patients with OWRS.

THE AUTHORS

***Dr. Silva Santos** is a post-graduate student in the department of oral pathology, School of Dentistry, University of São Paulo, São Paulo, Brazil.*

***Dr. Fernandes** is a post-graduate student in the department of oral pathology, School of Dentistry, University of São Paulo, São Paulo, Brazil.*

***Dr. Magalhães** is professor and chair of the department of oral pathology, School of Dentistry, University of São Paulo, São Paulo, Brazil.*

***Correspondence to:** Dr. Karin Sá Fernandes, Av. Prof. Lineu Prestes, 2227, São Paulo SP, Brazil 05508-000.*

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