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CASE REPORT

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A case of Osler-Weber-Rendu syndrome, diagnosed at geriatric age, presenting with gastrointestinal bleeding, telangiectasias, and asymptomatic liver and lung angiodysplasia

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Abstract

Background Osler-Weber-Rendu syndrome (OWRS) is an autosomal dominant disease with recurrent epistaxis, mucocutaneous telangiectasias, and arteriovenous malformations. Its clinical presentation ranges from simple skin lesions to life-threatening complications. When the diagnosis of the disease is delayed, it can be mortal and have high morbidity. This case is presented because OWRS is rare, and although she has all the features of the disease, she was diagnosed in the geriatric age group.

Case presentation A 72-year-old female patient who applied to the emergency department with the complaint of melena was diagnosed with upper gastrointestinal system bleeding. Gastroscopy revealed angiodysplasia in the bulb. Colonoscopy was normal. She had telangiectasias on her face, maxilla, nose, tongue and lips. She also had recurrent epistaxis and a family history. Thorax CT showed aneurysmatic vascular malformations in the lung. Abdominal MRI revealed vascular malformations in the liver. Brain MRI was normal.

The patient was diagnosed with OWRS according to the Curaçao diagnostic criteria because of telangiectasia in the mouth, nose, and face, angiodysplasia in the gastric bulb, aneurysmatic vascular dilatation in the lung, vascular pathologies in the liver, and a history of epistaxis and telangiectasia in the patient's family members.

Conclusion This patient is presented because OWRS is rare, and although she has all the features of the disease, she was diagnosed in the geriatric age group. Clinicians should be aware of this rare disease. Especially in the elderly, when angiodysplasia causing gastrointestinal bleeding is detected, it should be considered in the differential diagnosis that this may be an OWSR case.

Keywords Osler-Weber-Rendu syndrome, Telangiectasia, Arteriovenous malformations

Background

Osler-Weber-Rendu syndrome (OWRS) is an autosomal dominant disease with recurrent epistaxis, mucocutaneous telangiectasias, and arteriovenous malformations in many organs [1]. Arteriovenous malformations can be seen in many organs, especially the lungs, liver, gastrointestinal tract, and brain. OWRS is also known as Babington's disease, Goldstein's hematemesis, Goldstein heredofamilial angiomatosis, Goldstein syndrome, Osler's disease, Osler-Rendu-Weber syndrome, and hereditary hemorrhagic telangiectasia (HHT) [2].

Henry Gawen Sutton first described ORWS in 1864 as epistaxis telangiectasia and internal bleeding. Benjamin Guy Babington reported cases of epistaxis observed in

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a family over five generations in 1865. Later, Henri Jules Louis Marie Rendu described in 1896 that the bleeding in a 52-year-old male patient with recurrent epistaxis was due to telangiectasia, not hemophilia. He also reported that the patient's brother and mother also had a history of epistaxis [3]. In 1901, Sir William Osler noted that the disease may involve internal organs and be hereditary. In 1907, Frederick Parkes Weber added the red, angiomatous appearance of the nails to the symptoms [3]. Today, hereditary HHT is also known as OWRS disease.

Several genetic mutations have been identified as the cause of OWRS. These include endoglin (ENG) on chromosome 9 and activin A receptor type II-like 1 (ACVRL-1) and SMAD4 on chromosome 12. These three genes are involved in the transforming growth factor beta (TGF-β) signaling pathway, which is essential for the development and maintenance of arteriovenous identity. Disrupting the TGFβ pathway leads to abnormal angiogenesis and arteriovenous malformations. This disease is classified into two groups: HHT1 and HHT2, based on ENG and ACVRL-1 mutations. It has been reported that pulmonary arteriovenous malformations are observed at a higher rate in patients diagnosed with HHT1 than in patients diagnosed with HHT2, and accordingly, the prognosis of HHT2 is better [4].

Telangiectatic vessels are red macules and papules that appear in various sizes, ranging from pinhead to a few millimeters. Lesions may appear early in life and increase in number over time. They also have a tendency to ulcerate and bleed [5, 6].

Epistaxis and gastrointestinal bleeding are common findings. It has been reported that the risk of life-threatening bleeding due to telangiectasias increases with age [7]. Recurrent epistaxis affects the patient's daily life. Arteriovenous malformations can cause serious complications in the liver, lung, and brain [8, 9], including high-output heart failure, portal hypertension, liver failure, hemoptysis, polycythemia, cerebral abscess, and stroke. The Curaçao diagnostic criteria are utilized for diagnosing OWRS [10]. Treatment is based on clinical condition and vascular abnormalities.

This case is presented because the disease is rare, presents with gastrointestinal bleeding, has all the features of the disease such as epistaxis, family history, mucocutaneous lesions, and visceral vascular malformations, and was diagnosed in the geriatric age group.

Case report

A 72-year-old female patient presented to the emergency department with complaints of abdominal pain and black stools. She had a history of hypertension and iron deficiency anemia but was not taking any nonsteroidal anti-inflammatory, antiaggregant, or anticoagulant drugs. There was no accompanying nausea or vomiting.

During the physical examination, the patient appeared conscious, cooperative, and oriented. Her blood pressure was measured at 100/70 mmHg and her heart rate at 90 beats per minute. Telangiectasias were present in the maxillary region of the face, nose, and mouth (Fig. 1). The respiratory and cardiovascular systems were normal, and there was no organ enlargement in the abdomen. Upon rectal examination, there was evidence of melena.

The laboratory results were as follows: WBC count is 8900/mm^3, hemoglobin is 9.1 g/dL, hematocrit is 30%, MCV is 81 fL, MCHC is 31 g/dL, RDW is 14%, platelet is 200,000, INR is 1.2, APTT is 26, AST is 21 IU/L, and ALT is 14 IU/L. Upper gastrointestinal endoscopy shows angiodysplasia in the bulb, while colonoscopy is normal (Fig. 2).

Thoracic computed tomography revealed aneurysmal and nodular formations, 1 cm in diameter, in the upper lobe of the left lung, and middle of the right lung, which were continuous with the anterior segment and vascular structures (Fig. 3).

Abdominal MRI shows shunts between the right portal vein and right hepatic vein in the liver, and large collateral venous structures up to 22 mm in its widest part (Fig. 4), and perisplenic and perigastric collaterals are also present. Brain MRI showed no vascular pathology.

During the patient's clinical follow-up, they experienced epistaxis. As this occurs at home from time to time, an examination of the ears, nose, and throat was conducted. No active bleeding was detected in the nasal mucosa, but telangiectatic areas were present. During the patient's clinical follow-up, they experienced

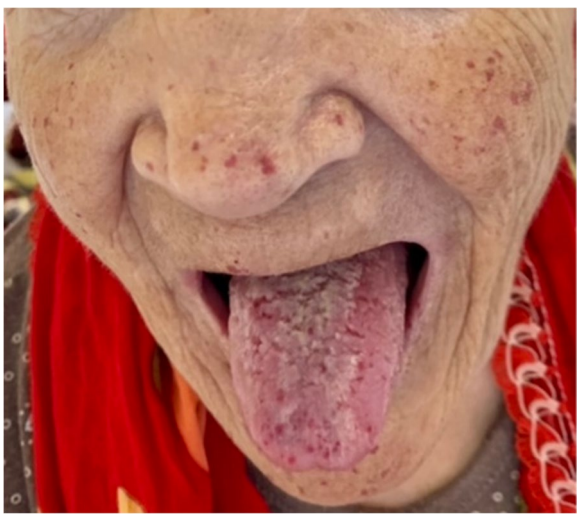

Fig. 1 Photograph showing multiple telangiectasias were present in the maxillary region of the face, nose, tongue, and mouth

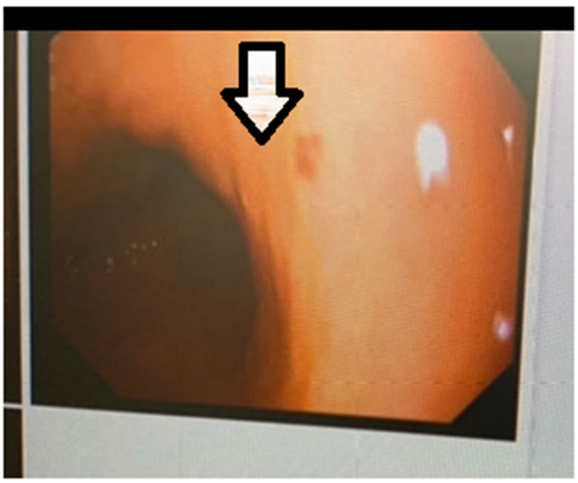

Fig. 2 Gastroscopic image showing area of angiodysplasia in the bulb mucosa

epistaxis. As this occurs at home from time to time, an examination of the ears, nose, and throat was conducted. No active bleeding was detected in the nasal mucosa, but telangiectatic areas were present. The patient was diagnosed with OWRS based on the Curaçao diagnostic criteria (Table 1). The diagnosis was made due to the presence of telangiectasias in the mouth, nose, and face, angiodysplasia in the gastric bulb, aneurysmal vascular dilatation in the lung, and vascular pathologies in the liver. Additionally, the patient's family members had a history of epistaxis and telangiectasia. The patient was treated for gastrointestinal bleeding and discharged with a plan for clinical follow-up. Additionally, here epistaxis resolved spontaneously.

Discussion

OWRS is genetic disorder that causes multiple vascular malformations with a wide range of clinical symptoms. Initially called hemophilia with nevi and epistaxis, it was later redefined as familial telangiectasia and mucosal hemorrhages by Rendu, Osler, and Weber, respectively [11].

The prevalence OWRS is 1/5000–1/8000 and it is rare. It is frequently detected in males in the newborn and childhood period, and in females in 3–4 decades in adulthood [1]. However, our case was rarely diagnosed at the geriatric age (72 years old).

Genetic factors have been implicated in the etiology of OWRS. ENG, ACVRL-1, and SMAD4 gene mutations are related to this. These three genes are involved in the transforming growth factor beta (TGF-β) signaling pathway, which is essential for the development and maintenance of arteriovenous identity. Abnormal angiogenesis occurs as a result of disruption of the TGFβ pathway, leading to arteriovenous malformations [12]. OWRS is an autosomal dominant disease, but 80% of

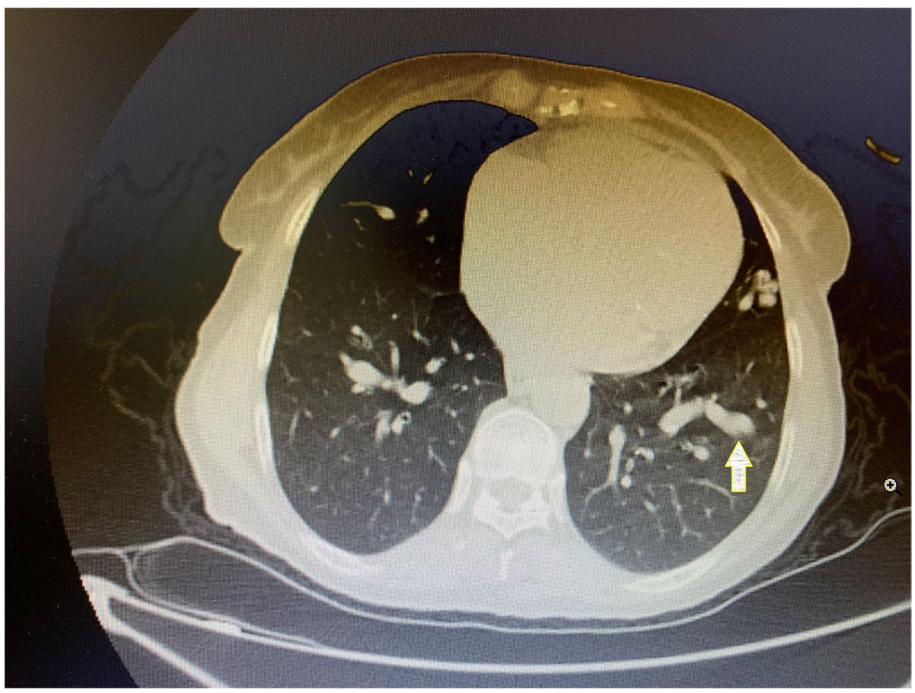

Fig. 3 Computed thoracic tomography showing aneurysmal and nodular arteriovenous malformations

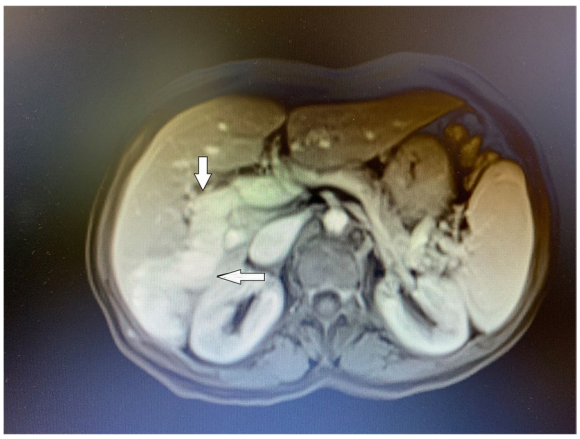

Fig. 4 Abdominal MRI shows shunts between right portal vein and right hepatic vein in liver and large collateral venous structures

Table 1 International consensus diagnostic criteria (the Curaçao diagnostic criteria)

Components
1. Spontaneous and recurrent epistaxis
2. Multiple mucocutaneous telangiectasia at characteristic sites
3. Visceral involvement (e.g., gastrointestinal telangiectasia; pulmonary, cerebral, or hepatic AVMs)
4. A first-degree relative with HHT
Interpretation
• 3 or 3 + criteria present → Definite HHT • 2 criteria present → Suspected HHT • 1 criteria present → Unlikely HHT

patients have a family history [13]. The siblings in our case also have epistaxis and telangiectasias.

The most common finding is telangiectasias causing mucocutaneous bleeding. Telangiectasias are usually seen on the face, lips, tongue, oral mucosa, gums, conjunctiva, and hands. In our case, telangiectasias were also present on the cheeks, nose, lips, tongue, gums, oral mucosa, and nasal mucosa. Bleeding due to telangiectasias, especially epistaxis, is usually the first symptom. It is seen in 90% of patients [9]. In our case, there was a history of recurrent epistaxis in recent years, and she also had epistaxis while she was lying in our clinic. Vascular malformations can be seen throughout the body, especially in the gastrointestinal tract, genitourinary system, brain, liver, and lungs.

Telangiectasias and arteriovenous malformations are seen in the gastrointestinal tract in 10–40% of patients. Angiodysplasias can be seen on endoscopy and can lead to iron deficiency anemia and gastrointestinal bleeding. Our patient also applied with the complaint of melena and angiodysplasias were seen in his gastroscopy. Colonoscopy was normal.

Arteriovenous malformations in the lung are seen in 14–30% of patients. This condition may be asymptomatic or may lead to cyanosis, clubbing, paradoxical embolism, and cerebral abscess. The lifetime incidence of stroke in patients with lung involvement is known to be 30%, and the incidence of brain abscess is 5.9%. Arteriovenous malformation was also present in the lung of our case, but it was asymptomatic. In addition, 8–31% of patients have arteriovenous malformations in the liver. This may lead to high-output heart failure and portal hypertension [14]. In our case, there was also arteriovenous malformation in the liver, but it did not lead to any clinical echocardiography, and portal Doppler ultrasound was normal. Arteriovenous malformations can also be seen in the brain of 5–10% of the patients. Our patient did not have arteriovenous malformation in the brain.

Patients usually present with gastrointestinal bleeding and hematuria [11, 15]. Abnormal vascular fragility is thought to be responsible for the bleeding in these patients. Platelet functions and coagulation tests were found to be normal, and these were normal in our patient. Curaçao criteria are used in the diagnosis of the disease (Table 1). Our patient had all the criteria for OSWR.

In the treatment of the disease, prevention of complications and supportive treatment are aimed. We also applied appropriate treatment for upper gastrointestinal bleeding in our patient. No treatment was required for epistaxis; it healed spontaneously. We examined the patient in detail for OWRS complications. When the patient's treatment was completed, we planned clinical follow-up and discharged him.

Conclusion

OWRS is a rare multisystemic genetic disorder with abnormal angiogenesis. Its clinical presentation ranges from simple skin lesions to life-threatening complications. When the diagnosis of the disease is delayed, it can be mortal and have high morbidity. Clinicians should be aware of this rare disease. Especially in the elderly, when angiodysplasia causing gastrointestinal bleeding is detected, it should be considered in the differential diagnosis that this may be an OWSR case.

Abbreviations

ACVRL-1	Activin A receptor type II-like 1
ENG	Endoglin
HHT	Hereditary hemorrhagic telangiectasia
OWRS	Osler-Weber-Rendu syndrome

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Authors' contributions
H. Şerife Aktaş designed the study, collected data, and wrote the article. Sema Basat evaluated the data. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
All procedures performed in accordance with the ethical standards of the institution or practice at which the studies were conducted. Since the picture of the patient's face would be used, ethical approval was obtained from the patient.

Consent for publication
This article has never been published before.

Competing interests
The authors declare that they have no competing interests.

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