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CASE REPORT Open Access

Ischemic cholangitis during Osler-Weber-Rendu disease: a case report

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Abstract

Background: Osler-Weber-Rendu disease (OWRD) is a rare autosomal dominant genetic disease that causes skin and mucosal telangiectasias and visceral arteriovenous malformations. These shunts can lead to high-output heart failure, portal hypertension, biliary or mesenteric ischemia. We report the case of a patient with OWRD complicated by ischemic cholangitis and biloma.

Case presentation: A 50-year-old female patient with personal history of spontaneous epistaxis and gingival bleeding, family history of Osler-Weber-Rendu disease (OWRD) in mother, and epistaxis in siblings. She consulted for intermittent and minimal biliary colic. Physical exam found mucocutaneous telangiectasia. Abdominal Doppler ultrasound/CT angiography showed arteriovenous shunts in the liver between hepatic artery and hepatic vein, hepatic artery and portal vein. Other sites of arteriovenous malformations were found in the nostril and jejunum. The diagnosis of OWRD was made. The evolution after 1 year was marked by the appearance of a slight anicteric cholestasis. MRCP found intrahepatic bilomas with associated ischemic cholangitis of segment VII. We decided to continue monitoring only.

Conclusion: The management of OWRD is based on screening for visceral arteriovenous malformations and on symptomatic measures that are often disappointing. Ischemic cholangitis is a rare complication, the diagnosis is based on imaging, liver transplantation is the only therapeutic alternative in this cases.

Keywords: Osler-Weber-Rendu disease, Biliary colic, Hepatic arteriovenous malformations, Ischemic cholangitis, Case report

Background

Osler-Weber-Rendu disease (OWRD), a rare autosomal dominant genetic disease that causes skin and mucosal telangiectasias and visceral arteriovenous malformations (AVM), mainly affects the lungs, liver, digestive tract, and brain [1]. Its frequency is approximately 1/5000 to 1/10,000, without gender difference, the complication mortality rate is reaching about 10% [2]. Here we report the case of a patient with OWRD complicated by ischemic cholangitis and biloma.

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Case presentation

Fifty-year-old female patient with personal history of spontaneous and repeated epistaxis and gingival bleeding since the age of 18, family history of OWRD in the mother (which had epistaxis, mucocutaneous telangiectasias, and cerebral arteriovenous malformations that caused her death), uninvestigated epistaxis in the brother and sister (whom refused to consult for). She consulted for intermittent and minimal biliary colic for 6 months. Physical exam found a hemodynamically stable patient, telangiectasia on the lips, tongue (Fig. 1), gums and hands, painless soft abdomen, absence of splenomegaly or abdominal collateral venous circulation, normal cardiovascular, pulmonary, and neurological examination. Abdominal Doppler Ultrasound showed normal liver, vascular

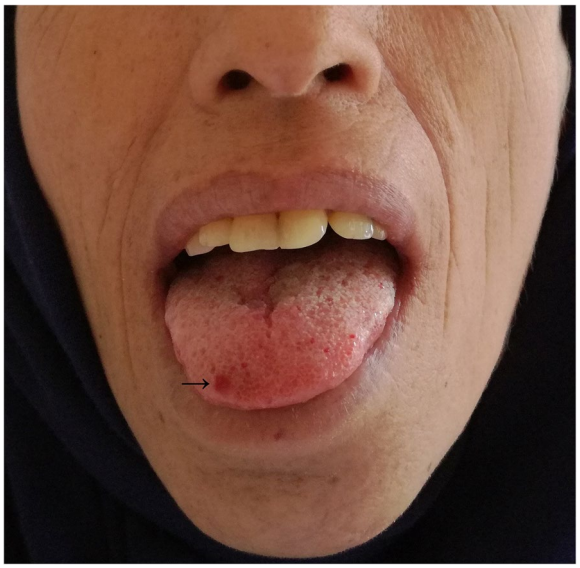

Fig. 1 Tongue telangiectasia

malformations on the portal vein and its branches (Fig. 2), dilated portal vein (18 mm), and hepatic artery (9 mm). CT hepatic angiography revealed hepatic arterialization, multiple arteriovenous shunts, early opacification of the portal vein and hepatic veins in arterial phase (Fig. 3), dilated portal vein and hepatic artery, the hepatic veins were thin and permeable, no splenomegaly or ascites. Nasal endoscopy found telangiectasia in the right nostril. Upper gastrointestinal endoscopy and colonoscopy were normal (no sign of portal hypertension). Video capsule endoscopy had identified two non-bleeding jejunal telangiectasias (Fig. 4). Echocardiogram, pulmonary, and cerebral CT scan were normal. Laboratory tests (Table 1) found iron deficiency anemia at 10.9 g/dl, normal liver function. Diagnosis of OWRD was made in front of (1) spontaneous and repeated epistaxis, (2) telangiectasia in the lips, tongue and fingers, (3) arteriovenous malformations in the liver and jejunum, (4) OWRD in the mother. The patient received oral iron supplementation 160 mg/day for 3 months. The evolution (Table 2) after 1 year was marked by the persistence of minimal biliary colic and the appearance of slight anicteric cholestasis (Gamma-glutamyl transferase = 1.5× upper limit of normal, alkaline phosphatase = 2× upper limit of normal), no anemia. Magnetic resonance cholangio-pancreatography (MRCP) found normal liver, early opacification of the hepatic veins due to hepatic arteriovenous fistulas. Multiple coalescent arteriovenous shunts in the right liver forming vascular lakes. Alteration of short stenoses with dilations of the intrahepatic bile ducts at the level of segment VII in favor of ischemic cholangitis, associated with intrahepatic bilomes measuring 27× 11 mm and 16 × 16 mm (Fig. 5), absence of dilatation of the main bile duct, absence of biliary lithiasis. As the patient could not afford to start treatment with bevacizumab, we decided to continue monitoring only.

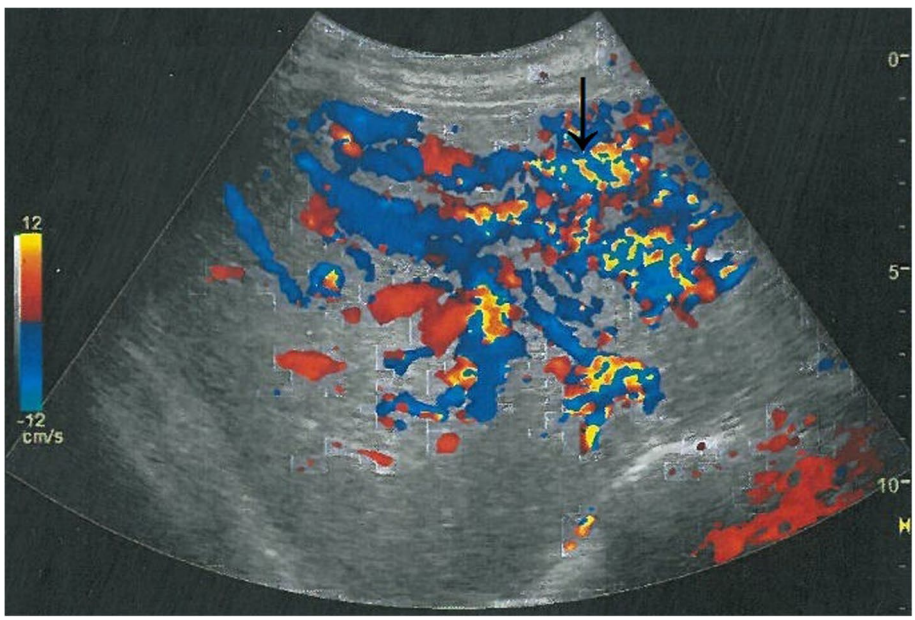

Fig. 2 Abdominal Doppler Ultrasound image of portal vein shunts

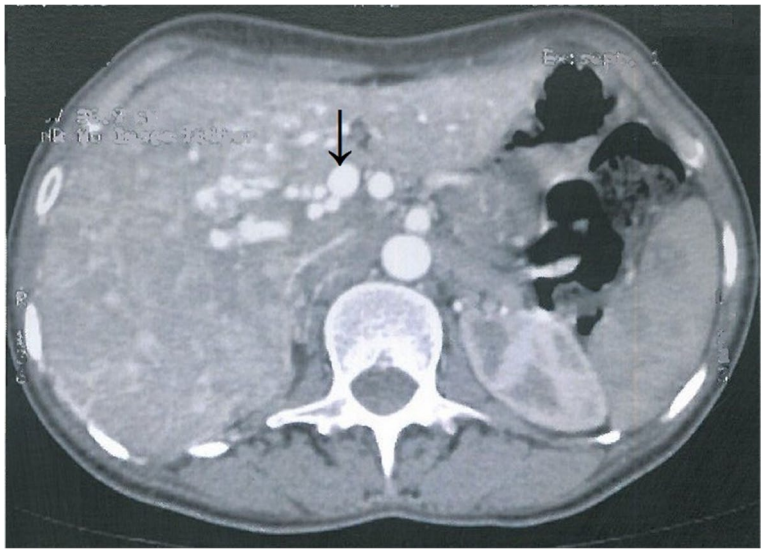

Fig. 3 CT hepatic angiography image of early opacification of the portal vein and hepatic veins in arterial phase

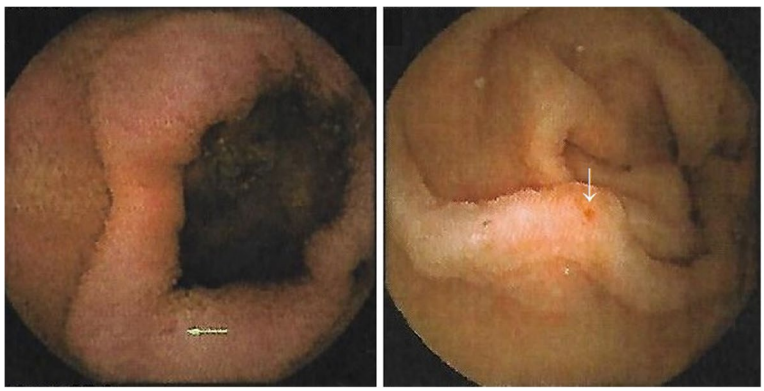

Fig. 4 Video Capsule Endoscopy image of jejunal telangiectasias

Discussion

OWRD was first described by Henri Rendu in 1896 in Paris, then by William Osler in 1902 in Baltimore and finally by Francis P. Weber in 1907 in London, reporting family cases of multiple cutaneous telangiectasias and spontaneous epistaxis [3]. The definite diagnosis is based on the association of at least three of the following four criteria (Curaçao criteria) [2]:

- Spontaneous and recurrent epistaxis
- Cutaneous and mucosal telangiectasias on: tongue, lips, fingers, nose.
- Visceral (pulmonary, hepatic, cerebral, digestive) AVM
- Family history of OWRD in a first-degree relative

Diagnosis is possible in the presence of two criteria, unlikely in the presence of one criterion [2].

Diagnosis can be made by molecular biology, the genetic mutations ENG, ACVRL1, MADH4 are responsible respectively for OWRD type1, OWRD type2, and OWRD associated with juvenile polyposis [2]. The first two genes are responsible for approximately 92% of cases [4]. These genes are located respectively on chromosomes 9q33-34, 12q11-q14, and 18q21 [5], and there are other genes not yet identified.

Epistaxis, 90% of patients, secondary to nasal telangiectasia, can cause severe anemia [6].

Cutaneo-mucosal telangiectasias, 75% of patients, occur on the face, conjunctiva, oral mucosa, ears, and fingers [7].

Table 1 Blood test results of our patient

	UI
Hemoglobin	10.9
MCV	75
MCHC	24
Leukocyte	8750
Neutrophil	5950
Platelets	390000
Ferritin	15
C-reactive protein	1
Aspartate aminotransferase	16
Alanine aminotransferase	12
Alkaline phosphatase	134
Gamma-glutamyl transferase	32
Total bilirubin	3
Conjugated bilirubin	1
Albumin	38
Prothrombin time	100
Urea	0.2
Creatinine	5.9
HAV, HBV, HCV, HIV serology	negative
Lipase	N/A

Table 2 Evolution of the level of liver enzymes of our patient

	Start	After 6 months	After 12 months
Aspartate aminotransferase	16	21	18
Alanine aminotransferase	12	16	13
Alkaline phosphatase	134	510	297
Gamma-glutamyl transferase	32	33	55
Total bilirubin	3	9	6
Conjugated bilirubin	1	3	2

Gastrointestinal AVM, 15–30% of patients [6], identified along the digestive tract but especially the small intestine and stomach, can be complicated by occult anemia, hematemesis or melaena in 33% of patients [2]. Their screening is based on an upper gastrointestinal endoscopy, colonoscopy, and small bowel video capsule endoscopy.

Hepatic AVM, 75% of patients (8% will be symptomatic [3]), are detected by angiography, CT scan, MRI, or Doppler ultrasound of the liver [6], showing three types of shunts: between hepatic artery and hepatic vein, hepatic artery and portal vein, portal vein and hepatic vein. These shunts can lead to high-output heart failure, portal hypertension, biliary, or mesenteric ischemia [3]. The biliary complication is presumed to emerge from hepatic arteriovenous shunting resulting in stealing/bypassing of blood from the biliary tree, causing hypoperfusion of the peribiliary plexus, ischemic cholangitis with fibrosis, formation of focal biliary dilatations. In severe ischemic lesion, biliary necrosis occurs with bile extravasating into the adjacent hepatic parenchyma causing bilomes [8]. In imaging, biliary abnormalities related to OWRD resemble Caroli's disease with cystic dilatations of the intrahepatic bile ducts or sclerosing cholangitis with irregular, multifocal biliary strictures, sparing the extrahepatic ducts [8].

Pulmonary AVM, 15–45% of patients, most often asymptomatic, can induce (right-to-left shunt) dyspnea, hemoptysis, hemothorax, cerebrovascular accident. They are sought by helical CT scan and contrast echocardiography [3].

Brain AVM, 10–12% of patients [2], can lead to headaches, hemorrhagic cerebrovascular accident, back pain, paraparesis, or tetraparesis [3]. They are searched for by cerebral MRI, the risk of bleeding is 0.5% per year [9].

The management of OWRD is based on screening for visceral AVM and on symptomatic measures that

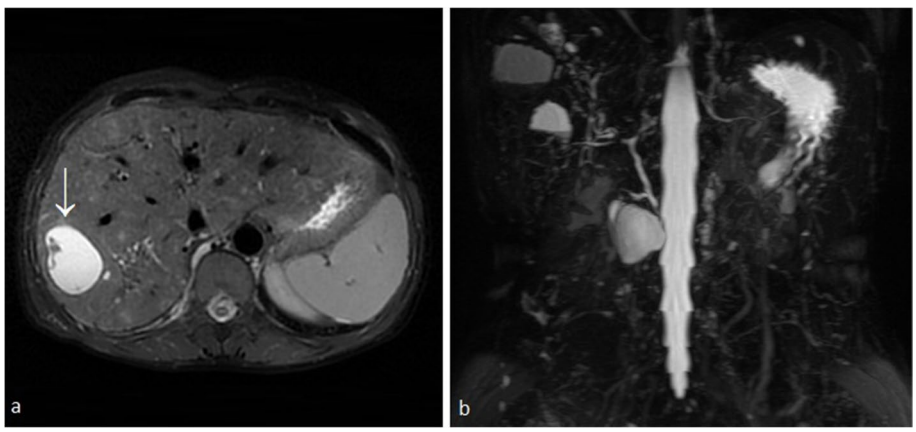

Fig. 5 MRCP image showing **a** biloma (dot sign) and **b** alternation of short stenoses with dilatation of the intrahepatic bile ducts in segment VII (ischemic cholangitis)

Table 3 Osler-Weber-Rendu disease monitoring [6]

Test	Surveillance
Physical exam	Annual, to detect new symptoms
Testing for occult blood in stool	Annual, to detect occult gastrointestinal bleeding
Complete blood count	Annual, to detect new-onset anemia
Pulse oximetry in the supine and sitting	Every 1–2 years during childhood, to screen for pulmonary AVM
Contrast echocardiogram	For patients aged 10 years and older, to screen for pulmonary shuntting
Chest CT scan (existing pulmonary AVM)	Every 3–5 years, to reassess the growth of vascular lesions and to exclude the presence of new pulmonary
Arterial blood gases or a chest CT, or both	1 year after embolization to exclude reperfusion of previously treated pulmonary AVM
Liver screening for arteriovenous malformation	No need to be routinely performed
Cerebral MRI	Once after the diagnosis to exclude cerebral AVM

are often disappointing. For epistaxis, the following may be used: digital compression, hemostatic buffers, tranexamic acid, in case of failure: laser, sclerotherapy, selective embolization, surgical vascular ligation, or even replacement of the nasal mucous membrane by a skin graft (Saunders' operation) or performing a nasal closure (Young's procedure) [3].

The use of pulsed lasers is effective for telangiectasias of the face and lips in case of aesthetic discomfort [10].

In case of bleeding from gastrointestinal telangiectasias, endoscopic treatment by Argon laser photocoagulation is recommended [2].

Embolization of hepatic AVM carries a high risk of complications and is generally not recommended. Portal hypertension is treated in the same way as cirrhotic patients [3]. Liver transplantation may be necessary for patients with acute liver failure [6], and currently remains the only therapeutic alternative in cases of heart failure or biliary necrosis [3].

The treatment of high-output heart failure relies on beta-blockers, diuretics, and the management of anemia and heart rhythm disorders [3].

Embolization is the treatment of choice for pulmonary AVM when the diameter of the feeder artery $\geq$ 3 mm, surgery is an option for patients who are not candidates for embolization [6].

Cerebral AVM are treated by arterial embolization, microsurgery, or stereotactic radiotherapy are used, the therapeutic choice should be made in specialized center [2].

Bevacizumab, modulators of angiogenesis, is used as a nasal spray in recurrent epistaxis, or by intravenous injection (5 mg/kg/15 days with a total of six injections) in refractory anemia, a hepatic disorder complicated by high-output heart failure, showing a significant improvement in clinical trials in small series of case. Bevacizumab is generally well tolerated. The main adverse events reported were grade 3 hypertension which occurred 30 days after the start of treatment and was treated without difficulty, headache, nausea and vomiting, diarrhea, asthenia, abdominal, muscle, or joint pain. No severe adverse events have been reported, including no thrombotic or hemorrhagic events, or gastrointestinal perforations [4].

The monitoring [6] of OWRD is summarized in Table 3.

Family screening is based on genetic testing, it helps to reassure and avoid unnecessary surveillance in non-bearers of the mutation, and to apply adequate follow-up in affected individuals [2].

Conclusion

Osler-Weber-Rendu disease is a vascular disorder with myriad manifestations. Despite a better understanding of the disease, it is still not fully appreciated by clinicians, who often do not recognize the disorder until severe manifestations occur. Ischemic cholangitis is a rare complication where liver transplantation is the only therapeutic alternative. Angiogenesis modulators, such as Bevacizumab, appear to be a promising treatment option for OWRD. This treatment appears to be effective, free of severe side effects, and has improved the prognosis of the disease. These results need to be confirmed by randomized studies.

Key learning

- Osler-Weber-Rendu disease is underrecognized.
- The diagnosis is based on the association of at least 3 of the 4 Curaçao criteria.
- The management of OWRD is based on screening for visceral arteriovenous malformations and on symptomatic measures.
- Many patients will require regular replenishment of iron stores.

Abbreviations
OWRD: Osler-Weber-Rendu disease; AVM: Arteriovenous malformations; CT: Computerized tomography; MRCP: Magnetic resonance cholangio-pancreatography; MRI: Magnetic resonance imaging.

Supplementary Information

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Additional File 1.

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None.

Authors' contributions
OK contributed to the concepts, design, definition of intellectual content, literature search, manuscript preparation, manuscript editing, guarantor. NL contributed to the manuscript preparation, Manuscript review. IB contributed to the literature search and manuscript review. MB contributed to the definition of intellectual content, manuscript preparation, and manuscript review. FZA contributed to the concepts, definition of intellectual content, manuscript preparation, manuscript editing, and manuscript review. All authors have read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article (Additional file 1).

Declarations

Ethics approval and consent to participate
Written informed consent was obtained from patient.

Consent for publication
Written informed consent was obtained from patient.

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

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