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Involvement of Hereditary Hemorrhagic Telangiectasia (HHT) in kidneys

Habibullah Fitrat; Yuxin Chen*; Abdul Qahar Saleh; Shanglei Ning; Sayed Ismail; Mu Wentao

Hepatobiliary Department of General Surgery, Qilu Hospital, Shandong University, 107 Wenhua West Road Jinan, China

***Corresponding Author(s): Yuxin Chen**

Hepatobiliary Department of General Surgery, Qilu Hospital, Shandong University, 107 Wenhua West Road Jinan, China

Tel: 0086-1856-008-2080;

Email: yxchen@sdu.edu.cn

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Abstract

Hereditary Hemorrhagic Telangiectasia (HHT) is a rare autosomal dominant vascular condition. The pathophysiology of this condition constitutes lack of capillary beds between arterioles and venules, resulting in direct contact between these vessels. This leads to telangiectases on specific locations such as the face, fingers, mouth, and nasal mucosa. Visceral Arteriovenous Malformations (AVMs) are also observed in many patients, and these are most commonly seen in the brain, gastrointestinal tract, lungs and in this special case in kidneys as well. CT and CT Angiography (CTA) demonstrated arteriovenous shunting in this case. Liver AVMs are also present in many patients with HHT, though these individuals are usually asymptomatic; however, liver AVMs may lead to serious complications, such as high output cardiac failure, other complications include bleeding, iron deficiency and anemia. Diagnosis of HHT relies on fulfilling three out of four criteria: Family history of the condition, mucocutaneous telangiectases, spontaneous and recurrent episodes of epistaxis, and visceral AVMs. Management is guided by international consensus guidelines, which targets patients' specific AVMs. Newly emergent therapies are being explored in clinical trials; bevacizumab and pazopanib retards angiogenesis, while thalidomide reduces blood vessel maturation. This case reports the HHT with kidney involvement that has never been previously reported in the literature.

Introduction

Osler-Weber-Rendu syndrome or Hereditary Hemorrhagic Telangiectasia (HHT) is a rare autosomal dominant vascular disorder characterized by vascular abnormalities of small size (telangiectasias) and large size Arteriovenous Malformations (AVMs). It can involve other multiple organ systems such as lungs, skin, brain and gastrointestinal tract [1]. Patients with HHT can have some other complications which include bleeding disorders such as, gastrointestinal bleeding, epistaxis, iron deficiency anemia and neurologic sequelae including hemorrhage and stroke. The common symptoms of HHT in patients with liver involvement are high-output cardiac failure, biliary disease and portal hypertension [2]. This case reports the HHT with kidney involvement that has never been previously reported in the literature.

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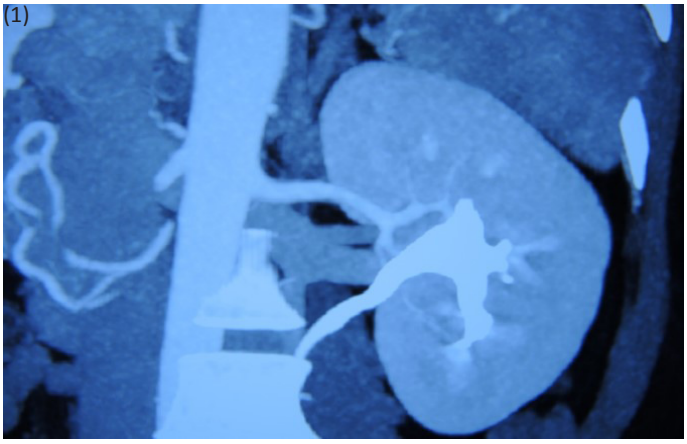
Case Presentation

A 40-year-old female with a history of bilateral nasal cavity and gingival bleeding without obvious cause for 20 years, with bleeding averaging once a day occasionally, lip bleeding spotted as well. The patient was presented with complains of chest tightness, fatigue and dizziness during intense activity. Physical examination revealed a temperature of 36.1oC, pulse 77/minute, respiratory rate 17/minute, B.P: 111/62 mmHg, weight 70 kg with no psychological problems. ALT was 7U/L (ref: 7-40 U/L), AST 15U/L (ref: 13-35U/L), BUN 3.70mmol/L (ref: 2.30-7.80 mmol/L), INR 1.22(ref: 0.80-1.20), creatinine 52 µmol/L (ref: 53-97µmol/L), AKP 31U/L (ref: 35-100U/L).

The patient was free from nasal obstruction and runny nose. Furthermore, there was no requirement for special treatment which could benefit the patient's condition. Family history revealed, the patient's mother died of bleeding and also her sister had a history of epistaxis (nose bleeds) with frequent blood transfusions.

She was admitted to the 3rd people's hospital of Jinan City. CT scan showed that there were multiple low density shadows in the liver and thick blood vessels which required further examinations. For further diagnosis and treatment the patient was admitted in our hospital with suspicion of: Hereditary hemorrhagic telangiectasia.

(1)



(2)

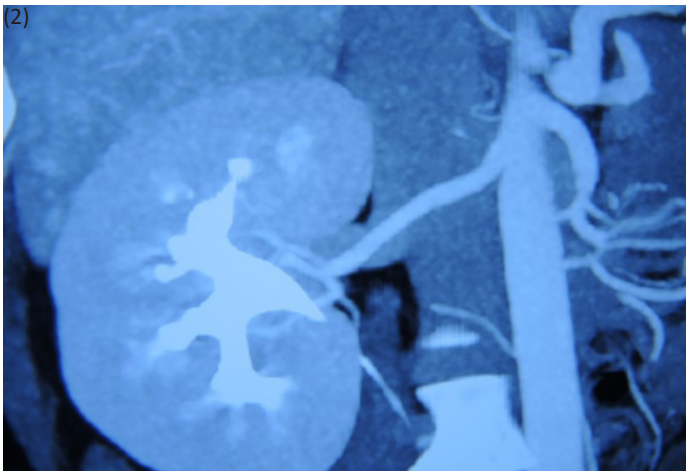


Figure 1 & 2: Computed Tomography of both (1) and (2) arterial phase images showing an increased number of opaque renal arteries with opacification of draining veins, consistent with multiple hepatic AVMs.

Treatment

There were several nosebleeds in our patient over the course of many years, which were treated conservatively by recommending the patient to use humidifiers and lubricants. These remedies can reduce dryness and crusting which in turn reduces the chance of bleeding by preserving nasal mucosa. The patient's gingival bleeding was also dealt with conservatively by suggesting the patient to maintain strict oral hygiene, which was rinsing of the mouth with antiseptics and further advised to increase intake of vitamin K.

Discussion

Hereditary Hemorrhagic Telangiectasia (HHT) is a rare autosomal dominant vascular disorder characterized by vascular abnormalities (telangiectasias) and Arteriovenous Malformations (AVMs) that may present with a variety of clinical manifestations. It can involve multiple organ systems such as lungs, skin, brain and gastrointestinal tract [1].

The process of nephrogenesis (kidney development) originates from intermediate mesoderm, it proceeds through a series of three continuous developmental phases: the pronephros, mesonephros, and metanephros. The metanephros are primordia of the permanent kidney [3].

The inner layer of hepatic cells undergo structural changes from columnar to pseudostratified, which forms liver buds. This leads to a formation of bipotential hepatoblasts [4]. Hepatic stellate cells are originated from mesenchyme [5]. The hepatic configuration is established after the migration of hepatoblasts into the septum transversum mesenchyme, with the appearance of liver sinusoids and bile canaliculi. The bud of the liver divides into lobes: the right vitelline vein becomes the portal vein and the left umbilical vein becomes the ductus venosus. Finally, bipotential hepatoblasts differentiates into biliary epithelial cells and hepatocytes [4].

The scientific advisory board of the HHT Foundation International has formulated the Curacao criteria. The criteria include a family history of HHT and recurrent visceral bleed, epistaxis, mucocutaneous telangiectasia. Patients presenting with two symptoms are considered at risk of developing the disease. A definitive diagnosis of HHT can be made by the presence of three or more of these symptoms [6].

Most of the patients with liver AVMs are asymptomatic, only 5-8% of patients develop symptoms secondary to liver AVMs [7,8]. Symptomatic patients with hepatic involvement usually present with high-output, biliary ischemia, cardiac failure, and portal hypertension [9].

The most common causes of anemia in HHT are GI bleeding and epistaxis. The patient is often born asymptomatic in this disease. While GI bleeding presents in the fifth decade of life epistaxis is more common in younger patients. Frequent blood loss and rupture of angiodysplasias worsens in adults. A study reported that, gastrointestinal bleeding persists in 33% of the patients with HHT. The same study also demonstrated that 25% of HHT patients, greater than 60 years of age suffered from severe gastrointestinal bleeding [10]. Moreover, patients with HHT not only have a higher bleeding risk but they also have an increased tendency of thromboembolism. Livesey et al conducted a study and, reported that the risk of thromboembolism increased by almost two-fold in a patient with HHT compared to the general population. Serum iron levels decreases with recurrent bleeding in HHT. The inverse relationship between low iron and factor VIII contributes a 2.5-fold increased risk of venous thromboembolism in these patients [11].

The significance of this case is that it not only involves the liver but also the kidneys. Most importantly, HHT with kidney involvement has never been previously reported in the literature. Furthermore, the symptoms of HHT involved with the kidneys consists of fragile urinary tract bleeding due to telangiectasis along with possible arteriovenous fistulas [12]. The gold standard for diagnosing AVMs is angiography. Doppler ultrasound, Magnetic Resonance Imaging (MRI), and Computed Tomography (CT) imaging may also be used because these modalities are less invasive. Diagnosis on CT can be identified through dilated hepatic arteries and diffuse liver telangiectasias [12]. Treatment in HHT is patient specific and changes with clinical findings. There are no standard medical therapies for patients with HHT [13]. Candelli and colleagues demonstrated the impact of hepatic AVMs on the liver first-pass effect on drugs in HHT patients and found a statistically significant decrease in metabolism rate compared to controls [14]. Liver transplantation is the only definitive treatment in patients who are unresponsive to medications [15]. Patients with hepatic complications have shown improvement with systemic treatment options such as bevacizumab [16,17]. Perhaps in the near future, with advanced technology and medical treatments we may be able to find a better solution for HHT individuals.

Conclusion

Hereditary hemorrhagic telangiectasia is characterized by vascular abnormalities it can also involve multiple organs such as the lungs, skin, brain and the gastrointestinal tract. In gastrointestinal tract, the most common cases of hereditary hemorrhagic telangiectasia are found with the liver involvement but in our case HHT is also involved with the kidneys which leads to disturbance of kidneys electrolytes.

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