Case Report

Hereditary Hemorrhagic Telangiectasia

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Abstract

Background: Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disorder, which affects various internal organs and has a tendency for bleeding. It has a classic triad of mucocutaneous telangiectasias, recurrent hemorrhages and positive familial history of first-degree relative. Epistaxis or gastrointestinal telangiectasia can be fatal in a small number of cases. **Case Report:** A 44-year-old woman came with complaints of recurrent episodes of hematemesis and epistaxis. Patient had a family history of similar complaints. Patient underwent esophagogastroduodenoscopy (EGD), which revealed telangiectasia in the stomach. Imaging of the abdomen showed features suggestive of arteriovenous shunting. **Conclusion:** HHT can remain undiagnosed for a long time, and is rarely being reported in the literature with management needing a multidisciplinary approach with early inputs from a gastroenterologist.

Keywords: Anemia, Arteriovenous malformation, Epistaxis, Hereditary hemorrhagic telangiectasia, Osler-Weber-Rendu

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Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is a rare disorder marked by telangiectasias on the oral mucosa, skin, and various internal organs.[1] Lesions begin as tiny, flat telangiectasias, with a few vessels radiating from a single point. Clinical features of HHT include epistaxis in more than 90% cases, Skin, lips and mouth telangiectasias in 80% cases, Pulmonary Arteriovenous Malformations (AVMs) in about 40% of cases, Hepatic AVMs in at least 30% cases, GI bleeds in about 15% cases, Cerebral AVMs in 10% and Spinal AVMs in 1% cases of HHT.[2] HHT has an incidence of about one in 5000-8000.[3] Its prevalence is about 1 in 10,000. The disease may cause significant morbidity but mortality rate is less than 10%.[4] We report a typical case of HHT, who had recurrent episodes of upper gastrointestinal (UGI) bleeding and several skin and visceral manifestations who recovered promptly on proper symptomatic treatment.

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Case Presentation

A 44-year-old woman was referred to us with history of recurrent episodes of hematemesis and melena. On taking a detailed history, we found that the patient had 2-3 episodes of nasal bleeding and bleeding gums of unknown cause over the past 1 year. Patient complained of generalized weakness, easy fatigability, with 4 episodes of hematemesis over past 8 months, family history (brother) of similar episodes of epistaxis. Patient denied of having cough, nausea, vomiting, abdominal pain, fever, sweats or chills, and dysphagia. Patient had good appetite, moderate sleep and no weight loss. There was no history of liver disease or any abdominal trauma. Echocardiographic stress test and Tread mill test done 1 year back was negative. Hysterectomy was done 3 years back in view of menorrhagia. Patient was not on any anticoagulation therapy, Nonsteroidal anti-inflammatory drugs or other herbal supplements. Patient was non-diabetic, normotensive, non-smoker, and non-alcoholic. Physical examination was remarkable for severe pallor; liver was firm 2 cm below the right costal margin and non-tender; few petechiae were seen over the fingertips of both hands and telangiectasias

over dorsum of tongue. Patient's vital signs were BP: 130/80 mmHg, PR: 74 bpm, RR: 16 cpm, BT: 37.1°C. Cardiac and respiratory examination was normal. The laboratory work-up at admission revealed: Hemoglobin of 6.4g/dL, hematocrit of 24.4%, serum ferritin of 3.4 ng/mL, serum iron of 13.0 µg/dL, serum total iron binding capacity of 472.0 µg/dL, white blood cells of 5.2×10^3/µL and platelet count of 183×10^3/µL. Coagulation profile was normal. Patient's glycosylated hemoglobin, vitamin B_{12}, folate levels and serum electrolytes were normal. Viral markers were negative for hepatitis C virus, hepatitis B surface antigen, and blood antibodies for HIV1 and HIV2. The renal parameters and liver function tests were normal. Urine microscopy was unremarkable and hemoglobin was absent in urine. There was no laboratory evidence of sepsis and blood cultures were sterile at admission.

Patient was given 3 units of packed red blood cells and received intravenous fluids and pantoprazole. EGD performed showed multiple angioectatic spots with bright looking salmon-colored patches [Figures 1 and 2] in the antrum and body of the stomach suggestive of HHT. No active ooze or bleed could be seen endoscopically; thus, no intervention was performed. Ultrasound of abdomen was done, which revealed mild hepatomegaly with multiple intrahepatic collaterals. Hence, Cancer antigen 19-9 and alpha fetoprotein was checked, which were normal. ENT evaluation showed deviated nasal septum to the right side, while posterior pharyngeal wall was normal. There were multiple telangiectatic spots seen over the inferior and mid turbinate. A computed tomography scan of thorax and abdomen revealed hepatomegaly with diffuse heterogeneity of liver parenchyma in arterial phase, dilatation of common hepatic artery [Figure 3], multiple tortuous intrahepatic arteries and arteriovenous shunting [Figure 4] in both lobes of liver. Features were suggestive of multiple hepatic telangiectasia. There was no e/o pulmonary AV malformation. With these findings, a diagnosis of HHT was made. Epistaxis improved and hemoglobin levels increased with tranexamic acid (500 mg 2 times daily). Patient's condition was stable at discharge and was advised to continue pantoprazole, tranexamic acid 500 mg twice daily, and iron supplements. Patient's anemia resolved over the next few weeks, and has been doing well over the past 5 months.

Discussion

HHT, first recognized in 1896,[5] is an inherited disorder and there is no age cut-off. Age and its presentation of symptoms are highly variable. Although HHT can affect any body system, it usually affects the dermatologic and gastrointestinal system; rarely the respiratory and central nervous systems are affected. Curacao criteria are used for the clinical diagnosis of HHT, consisting of recurrent epistaxis, mucocutaneous telangiectasias, visceral AVM and an affected first-degree relative.[6] Diagnosis is definite if three criteria are met; it is suspected or possible with two, and is unlikely if less than two criteria are met. Our case had a certain clinical diagnosis as she met three out of the four criteria for HHT: Recurrent epistaxis, telangiectasias of fingertips, GI and hepatic AVMs, whereas familial history could not be confirmed as relatives were not available for direct medical examination.

Admissions for GI bleeding account for 50% in UGI bleeding, 40% for lower GI bleeding and 10% for obscure bleeding (from the small bowel).[7] The source of GI bleeding is usually confirmed by EGD or colonoscopy. EGD provides enough information on gastrointestinal involvement as well as is cheaper compared to video capsule endoscopy, which may be added in selected cases. Medical management is based on endoscopic interventions to stop and prevent recurrent bleeding.

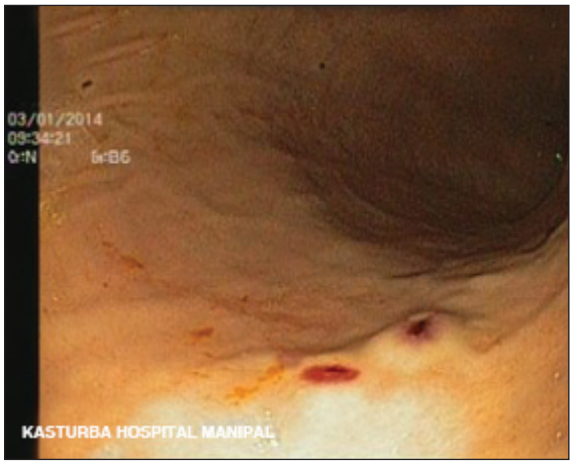

Figure 1: Endoscopic image showing multiple telangiectasias in body

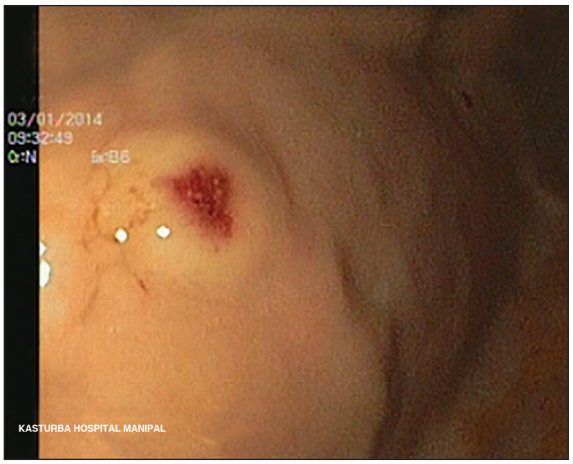

Figure 2: Endoscopic image showing multiple telangiectasias in the antrum

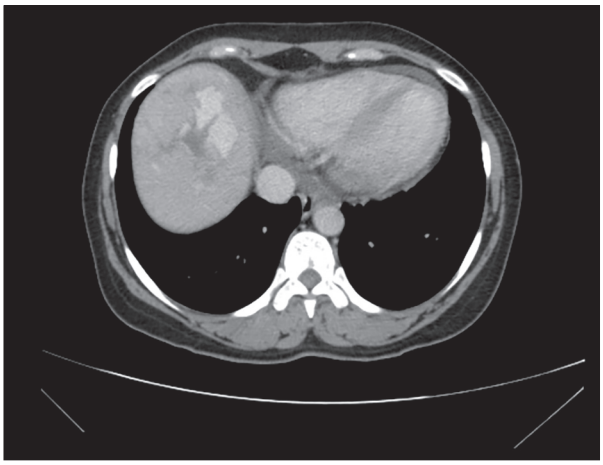

Figure 3: CT image showing hepatic telangiectasia

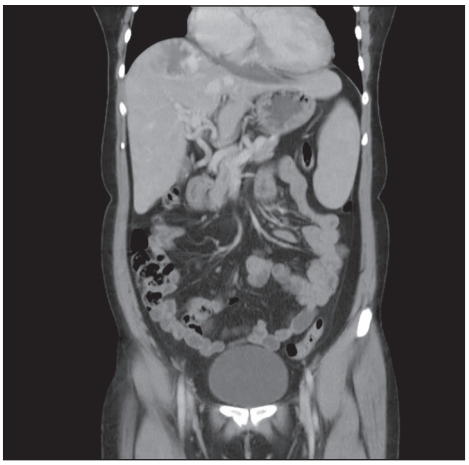

Figure 4: CT image showing arteriovenous shunting

Manifestations of HHT are usually absent at birth, but develop later. Patient may present in childhood with recurrent epistaxis. Plauchu *et al*., found that more than 50% of the affected persons developed epistaxis before the age of 20.[8] GI hemorrhages become apparent between the 4th and the 5th decades of life.[9] Patients who develop cerebral vascular malformations should be screened with MRI of the brain since it is the best procedure available.

Epistaxis is the most common otolaryngologic emergency. It is the commonest manifestation of HHT, affecting about 85-90% of patients.[10] Telangiectasias can involve the gastrointestinal tract, liver, lungs, brain and eyes but hemorrhage can occur at any site.[11] The liver is commonly associated with HHT[12]; its manifestations are seen in about 8-31% of patients. Pulmonary AVMs remain under regular follow-up in pulmonary and chest diseases department, hence referral is often delayed in Pulmonary AVM.[13] HHT can also be confirmed by genetic analysis.[14] Some patients with a clinical diagnosis of probable or unlikely HHT do not show any symptoms. In such cases of absence of typical symptoms of HHT, only genetic analysis provides an accurate diagnosis. Pathogenesis in patients with HHT is yet to be elucidated. However, a germ line mutation in at least two distinct genes, endoglin and ALK1/ACVRL1, are found in the majority of HHT patients. Mutations in endoglin or ALK1/ACVRL1 genes account for HHT type 1 and HHT type 2, respectively. The precise mechanisms underlying HHT-related vascular abnormalities are still uncertain, although recent studies suggest that endoglin or ALK1/ACVRL1 encode for proteins involved in angiogenesis, vascular remodeling and/or endothelial arterio-venous identity.[15]

Treatment is directed towards the presenting clinical manifestations. Anemia from recurrent nasal or GI bleed is treated by oral/parenteral iron, combined estrogen-progesterone preparations[16] and blood transfusion in severe cases. Treatment of HHT is limited to managing complications and giving supportive care. Periodic blood transfusion and iron supplementation may be needed. Argon plasma coagulation may be useful when the telangiectatic lesions in the gastrointestinal tract are localized.

Management for epistaxis needs establishing the bleeding site, stopping the bleeding and treating the underlying cause. Treatment of epistaxis involves the use of ointments (to reduce drying of nasal mucosa), nasal sprays, creams and hemostatic. Telangiectasias have been successfully treated with estrogens,[17] aminocaproic acid,[18] endoscopic thermal ablation,[19] and thalidomide.[20] Bevacizumab has been used for HHT and severe liver involvement.[21] HHT is not that rare but remains underreported. Most patients have a normal life expectancy but about 10% die of complications viz. hemorrhage, or stroke. The first-degree relatives of HHT patients should be screened for the condition. Many patients don't require treatment other than oral iron supplements, whereas some may require transfusions and nasal packing. Surgery has limited use but may be useful in emergency viz. septal dermatoplasty[22] and septal closure[23] in which it has been found to be effective. Despite numerous case reports, understanding of the disease is not fully appreciated by clinicians, who often fail to recognize the disorder until severe manifestations occur. A recent study estimated a diagnostic delay in HHT showing that patients receive a definite diagnosis only after nearly 3 decades from disease onset.[24] A higher degree of suspicion and awareness is needed to identify this disease early, to reduce morbidity, and to improve outcomes and quality of life.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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