A case report on osler-weber-rendu disease

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ABSTRACT

Osler-Weber-Rendu disease, also known as hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant genetic disorder that leads to abnormal blood vessel formation in the skin, mucous membrane and in organs such as lungs, liver, and brain. Here, we report the case of a 68-year-old postmenopausal woman who was admitted to our hospital following multiple episodes of hematemesis and melena during the past 5 days. Upper GI endoscopy revealed multiple telangiectasia with active spurting and gastric polyp. The patient was treated with 1 unit of packed red blood cells transfusion for anemia, Inj. Tranexamic acid 500 mg IV tid and Inj. Ondansetron 4 mg IV for hematemesis. Tab. Thalidomide 100 mg has been given for treating hereditary hemorrhagic telangiectasia. The treatment of HHT is only palliative, with no consensus on the best treatment option. It is essential to promote control of the disease as long as possible.

Keywords: *Arteriovenous malformation, Familial, Hereditary, Telangiectasia.*

Osler-Weber-Rendu disease, also known as hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant genetic disorder that leads to abnormal blood vessel formation in the skin, mucous membrane and in organs such as lungs, liver, and brain. In small blood vessels, these abnormalities are called telangiectasias and when they occur in larger vessels, they are called arteriovenous malformations (AVM). Both are a potential source of serious morbidity and mortality.

Recent epidemiological studies revealed a prevalence of 1:5000-8000 persons worldwide. HHT has a higher prevalence in the certain population such as in Afro-Carribean residents [1]. Incidence of HHT is difficult to determine because the severity of symptoms vary widely and HHT is widely distributed, affects about 1 in 5000 (0.02%). This condition is inherited in an autosomal dominant pattern. It can result in serious life-threatening conditions, and still often undiagnosed by doctors since its manifestations are difficult to rule out the disease.

CASE REPORT

A 68-year-old postmenopausal woman was admitted to our hospital following multiple episodes of hematemesis and melena for the past 5 days. The patient has comorbidities such as mild pulmonary arterial hypertension and asthma and was under medications. She had multiple episodes of epistaxis, palpitations and abdominal pain. There was no history of bleeding gums and rectum, headache, seizure, visual disturbance

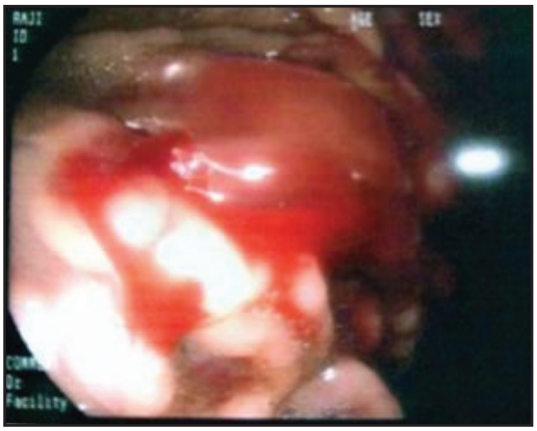

Figure 1: Tiny polyps were evident at the fundus region and active spurting telangiectasia seen at the proximal body.

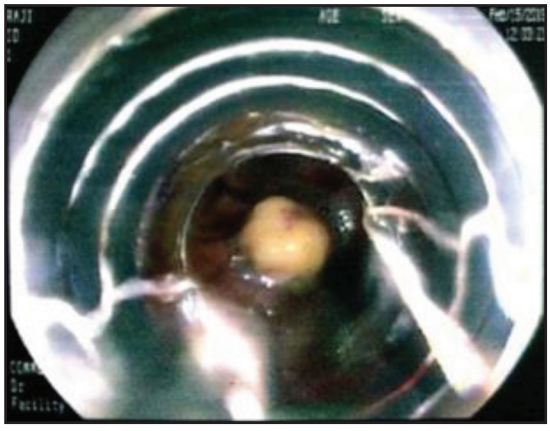

Figure 2: Multiple telangiectasia and small polyps were found at antrum and duodenum.

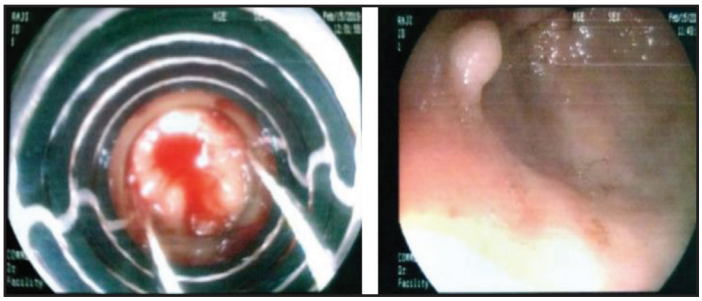

Figure 3: Active ooze noted at the proximal body along the lesser curve.

or bluish discoloration of fingertips or nose. A family history of telangiectasia was present in her brother. On general examination, the patient was conscious, oriented, and anemic with pallor and had stable vitals. The abdominal tenderness was present and there was an absence of organomegaly.

No abnormalities were detected on a chest X-ray. The laboratory workup at admission revealed the following: white blood cells - 2,200cells/mm^3; platelet count - 250,000/mm^3; hemoglobin - 6.9 g/dl and serum iron - 34 ug/dl. Investigations including bleeding time, coagulation time, prothrombin time (PT), activated partial thromboplastin time (aPTT), and stool occult blood reported to be normal. Endoscopy of the upper digestive tract was performed. Serum for antinuclear antibody (ANA), urine for hemoglobinuria and sickling test were found to be negative.

Upper gastrointestinal endoscopy revealed multiple small, sessile, numerous telangiectasia in the pharynx and esophagus (Fig. 1). Tiny polyps were evident at the fundus region, active spurting telangiectasia was seen at the proximal body (Fig. 2), multiple telangiectasia and small polyps were found at the antrum and duodenum (Fig. 3) and active ooze was noted at the proximal body along the lesser curve.

The patient was treated with 1 unit of packed red blood cells (PRBC) transfusion for anemia, Inj. Tranexamic acid 500 mg IV tid and Inj. Ondansetron 4 mg IV for hematemesis. Tab. Thalidomide 100 mg HS has been given for treating HHT. Hence, the severity of nasal bleed and hematemesis were significantly reduced, hemoglobin level improved and there were no side effects reported by the patient at subsequent follow-up.

DISCUSSION

The diagnosis of Osler-Weber-Rendu disease is based on the Curaçao criteria which consist of (a) epistaxis: spontaneous, recurrent nosebleeds, (b) telangiectasias: multiple, at characteristic sites (lips, oral cavity, fingers, nose), (c) visceral lesions such as gastrointestinal telangiectasias (with or without bleeding), pulmonary AVM, hepatic AVM, cerebral AVM, spinal AVM and (d) family history: a first-degree relative with HHT. The presence of 3 criteria indicate a definite diagnosis of the disorder; 2 criteria depicts a possible or suspected case and less than 2 means that unlikely the disease is present [1]. Also, the detection of the causative mutation through a molecular study is acceptable. Three genes are implicated in this disease. The first, ENG, is located on chromosome 9 (9q33-q34) and it encodes for endoglin. A mutation in this gene causes type 1HHT.A mutation in the ACVRL1 gene causes type 2HHT. This gene is located in the 12q11-q14 region of chromosome 12 and encodes for ALK1 (activin receptor-like kinase) [1]. A small percentage of patients have juvenile polyposis/ hereditary HHT syndrome (JPHT) due to mutations in the MADH4 gene located on chromosome 18.

The primary and most common manifestation of HHT is usually epistaxis that begins during childhood or adolescence at a mean age of 12 years [2]. They typically occur on the face, lips, tongue, palms, and fingers including the periungual area and the nail bed. Telangiectasia are the dilated blood vessels that appear as thin spider web-like red and dark purple lesions that blanch with pressure. AVMs are abnormal connections between arteries and veins that bypass the capillary system. Patients with HHT have multiple AVMs throughout the body. However, the most important AVMs for which clinicians should screen are in the brain, lungs, GI tract, and liver. AVMs in the lung and brain can be asymptomatic [3].

The overall treatment of HHT is oriented towards the predominant clinical manifestation and its severity. The first step in epistaxis management should always be necessary for patient counseling and use of preventive measures within the home to prevent the nasal mucosa from becoming dry. These include nasal humidification, use of over-the-counter saline sprays or ointments to keep the nasal mucosa moist and avoidance of nasal trauma [4]. In a double-blind randomized controlled trial, 50 µg ethinyloestradiol and 1 mg norethisterone resulted in a significant reduction in transfusion requirements in 10 patients with a mean transfusion requirement of 19.4 packed cells units per year. These data have been extrapolated in clinical practice to patients with lesser degrees of hemorrhage not necessarily associated with regular transfusion requirements.

The use of higher dose conjugated estrogens in the "hormone replacement" range of over 625 µg ethinyloestradiol equivalent or prothrombotic agents such as tranexamic acid and aminocaproic acid are also widespread in management of HHT related bleeding [5]**.** Hormonal or antifibrinolytic therapy may be used as an adjunct therapy to prevent ongoing bleeding. In patients that have liver AVMs, embolization is not recommended given the risk post-embolization necrosis and death. Surgical intervention should only be considered if they become symptomatic or develop complications.

For those with significant hepatic AVM involvement, partial liver resection is a safe treatment option. If a patient's hemoglobin and hematocrit are low, an upper endoscopy should be completed if the anemia is disproportionate to epistaxis. Iron supplementation should be initiated, either oral or intravenous (IV) and endoscopic cauterization can be considered. It is recommended that acute epistaxis be managed with low-pressure, less-traumatic packing techniques. In some studies, a mild benefit was shown for the use of humidifiers to prevent chronic epistaxis [5].

Anti-angiogenic factors can be useful in treating vascular malformations such as thalidomide that inhibits tumor necrosis

factor-alpha, thereby acting as a potent anti-angiogenic drug in case of this patient as well. Newer treatment modalities available are (a) hormone-related drugs containing estrogen. Anti-estrogen medications such as tamoxifen, raloxifene have been used to control HHT; (b) drugs that block blood vessel growth such as bevacizumab IV, pomalidomide, pazopanib; (c) drugs that slow disintegration of clots includes tranexamic acid [6].

Procedures to reduce frequency and severity of nosebleeds include are ablation that uses energy from lasers or a high-frequency electrical current to seal the abnormal vessels that are causing nose bleed; skin graft which is done from another part of your body, usually thigh and surgical closing of nostrils in which connecting flaps of skin are used within the nose to permanently close the nostrils but this procedure is only done when other approaches failed [7,8].

CONCLUSION

Hereditary Hemorrhagic Telangiectasia is a fibrovascular dysplasia for which complete cure cannot be established. Repeated endoscopic hemostasis for all dilated capillary vessels could be effective in preventing relapse of hemorrhage. In short, management includes blood transfusion, antifibrinolytics, and surgical hemostasis.

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