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Case Report

Ear,Nose and Throat Section

Hereditary Haemorrhagic Telangiectasia of Nasal Mucosa- A Case Report

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ABSTRACT

Hereditary Haemorrhagic Telangiectasia (HHT) is also known as Osler-Weber-Rendu syndrome is a developmental disorder of blood vessels. It is characterised by multiple telangiectases and Arteriovenous Malformations (AVMS) that cause direct connections between arteries and veins bypassing intermediate capillaries. The most prominent sites for telangiectasia are the lips, tongue, face, mucosa of the nose, oral cavity, and gastrointestinal tract. Telangiectases can rupture and bleed easily due to their thin walls, narrow tortuous courses, and proximity to the skin's surface or a mucous membrane. Depending on the organ affected, these symptoms include repeated persistent epistaxis, skin lesions, haemoptysis, gastrointestinal haemorrhage, and stroke. Complications of HHT include bleeding, anaemia, followed by stroke, pulmonary AVM, Transient Ischaemic Attack (TIA), hypovolaemic shock due to severe intractable bleed, eventually leading to high output failure. Present case is of a 45-year-old female who presented with complaints of recurrent epistaxis. Diagnostic nasal endoscopy showed multiple telengiectasic spots which were cauterised with trichloroacetic acid. However, recurrent episodes of bleed were encountered.

Keywords: Blood vessels, Epistaxis, Endothelium

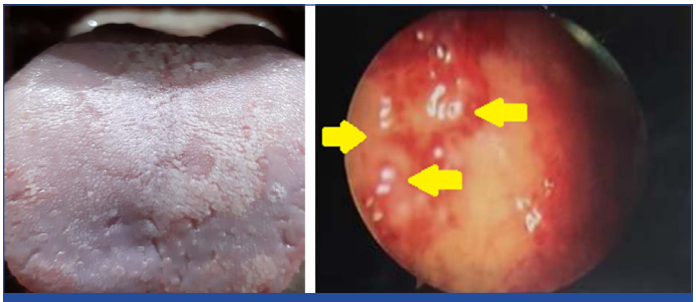
CASE REPORT

A 45-year-old female presented to the Outpatient Department (OPD) of Otorhinolaryngology with complaints of recurrent episodes of nasal bleed since childhood. She gave a history of minimum of three episodes per day, history of frequent bouts of nasal bleed that stops spontaneously on its own. There was no history of headache or facial heaviness, trauma to face and nose, upper respiratory tract infections, heart disease. Patient was not on any other medication. There were similar complaints in the family, patient's mother had similar history of frequent nasal bleed. There were multiple telengiactesias, history of frequent epistaxis and a positive family history which all point to the diagnosis. Patient was not on any treatment for these complaints since childhood. Patient gives history of each episode of nasal bleed being managed conservatively.

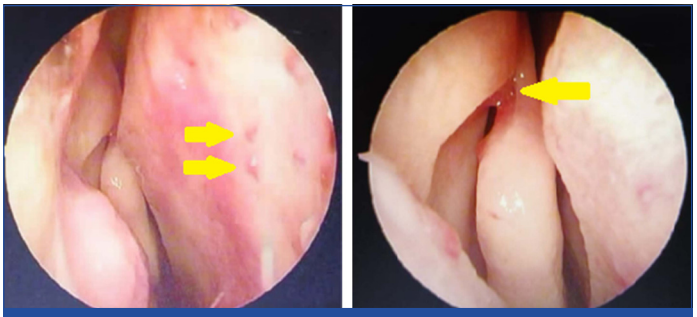
General examination of the patient showed pallor on tongue [Table/Fig-1], lower palpebral conjunctiva and nail bed. Patient was conscious, oriented to time and space and was afebrile. Pulse rate was 76 beats/min regular rhythm, volume and character, Blood pressure was 120/70 mmHg, saturation was 100% at room air.

Anterior rhinoscopy was done to assess the nasal cavity and to look for any sites of active bleed and clots. Examination of the nose on anterior rhinoscopy showed blood clots in the left nasal cavity, there was no active bleeding at the time of examination. Nasal mucosa was pink. There was no obvious septal deformity or mass in the nasal cavity.

Bilateral nasal cavity was packed with local anaesthetic agent 10 mL of 4% lignocaine mixed with one ampoule of adrenaline, soaked in sterile nasal packs and a diagnostic nasal endoscopy was done which revealed a pink nasal mucosa with multiple telangiectasia spots on the septum over Little's area [Table/Fig-2,3], axilla of right middle turbinate [Table/Fig-4], over right inferior turbinate. Bilateral inferior, middle meatus and spheno ethmoidal recess were free, nasopharynx was also free.



[Table/Fig-1]: Shows pallor on tongue. **[Table/Fig-2]:** Shows telangiectasic spots over left Little's area. (Images from left to right).



[Table/Fig-3]: Shows telangiectasic spots over septum. **[Table/Fig-4]:** Shows telangiectasic spots over right middle turbinate. (Images from left to right).

Laboratory reports showed a Haemoglobin (Hb) of 4 mg/dL. The Hb further improved to 9 mg/dL after four units of blood transfusion. Iron profile showed serum ferritin was 1.2 ng/mL, Total Iron binding capacity (TIBC) was 391 µg/dL and serum iron was 12 µg/dL Laboratory investigations were seen in [Table/Fig-5]. Other cell counts like Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC) and coagulation profile were done and found to be within the normal range. Stool occult blood was negative.

Systemic evaluation of ophthalmological, neurological, gastrointestinal, pulmonary and renal functions were done and found to be normal. There was no evidence of other bleeding sites elsewhere in the body. Urinalysis, ultrasound abdomen was also normal. These investigations were done to rule out other causes for anaemia.

This patient was treated with two sittings of chemical cautery with trichloroacetic acid application over the telangiectasiac spots with a time interval of two weeks between the sittings. A course of antibiotics and nasal drops were given. Post-treatment with trichloroacetic acid cautery application, the episodes of epistaxis occured occasionally and had considerably reduced in duration, quantity and frequency and

stopped spontaneously on its own. She was treated with saline nasal spray postoperatively, and a course of oral antibiotic cefpodoxime proxetil and topical mupirocin ointment for five days. Patient was advised to come for follow-up once a month and was symptomatically better.

Investigation	Result	Reference range
Pretransfusion Haemoglobin (g/dL)	4	12-15
Post-transfusion Haemoglobin (g/dL)	9	12-15
RBC count (million/µL)	3.88	3.8-4.8
MCV (fl)	72.4	83-101
MCH (pg)	23.3	27-32
MCHC (g/dL)	32.2	31.5-34.5
RDW (%)	23.7	11.6-14
Platelet (lacs/µL)	2.64	1.5-4
Bleeding time (min)	2	2-4
Clotting time (min)	4 min 30 sec	4-8
TIBC (µg/mL)	391	240 to 450
Serum Iron (µg/mL)	12	60 to 170
Serum Ferritin (ng/mL)	1.2	12 to 150
Hematocrit (%)	32	35-45
ESR (mm/hr)	17	0-29
Reticulocyte count (%)	0.4	0.5-2.5

[Table/Fig-5]: Laboratory investigations.
RBC: Red blood cells; MCV: Mean corpuscular volume; MCH: Mean corpuscular haemoglobin; MCHC: Mean corpuscular haemoglobin concentration; TIBC: Total iron binding capacity: ESR: Erythrocyte sedimentation rate; RDW: Red cell distribution width

DISCUSSION

The Hereditary Haemorrhagic Telangiectasia (HHT) is also known as Osler-Weber-Rendu syndrome is a developmental disorder of blood vessels. It is characterised by multiple telangiectases and AVMS that cause direct connections between arteries and veins bypassing intermediate capillaries [1]. Endoglin (ENG) is a gene on chromosome 9q3 that is responsible for the expression of an integral membrane glycoprotein which binds to Transforming Growth Factor-β (TGF-β) in endothelial cells. ENG gene mutations result in the loss of normal protein or the production of a faulty protein which interferes with normal protein function. Endothelial cell migration, proliferation, adhesion, extracellular matrix composition, and architecture are all altered, thus leading to vascular dysplasia [2]. HHT1, caused by mutations in the ENG gene, and HHT2, caused by mutations in the activin receptor-like kinase 1 (ACVRL1) gene, are the two major subtypes of this condition [3]. Patient gave a positive family history, recurrent epistaxis and multiple telengiectasias were noted, so a clinical diagnosis of HHT was made. Genetic mapping was time consuming and costly and was not done in index case because the diagnosis was direct.

Telangiectasia is a small arteriovenous shunt which involves both dilated arterioles and venules. It presents as a 1–2 mm red spot on the skin and fades when pressure is applied. The initial lesion of HHT, according to Braverman IM et al., is a localised dilation of postcapillary venules, which subsequently join with dilated arterioles [4]. As the vascular lesion develops larger, the capillary segments dissolve, providing a direct arteriovenous contact. A perivascular mononuclear cell infiltration comprising primarily of lymphocytes, is seen.

This condition affects multiple organs and causes a variety of symptoms. Depending on the organ affected, these symptoms include repeated persistent epistaxis, skin lesions, haemoptysis, gastrointestinal haemorrhage, and stroke [5]. Epistaxis, telangiectasia, and a relevant family history are used to diagnose HHT. A positive family history and clinical features of epistaxis, telangiectasia, and visceral lesions are essential for diagnosing HHT. The diagnosis of HHT is definite if all these three features are present. In patients with only two of these clinical features, a high index of clinical suspicion is maintained and regular follow-up is done. If less than two symptoms, HHT can not be ruled out [6]. If patients have frequent episodes of bleed, they may take precautions like restraining from strenuous activities, avoiding violent sports and reporting to hospital in case of any symptoms.

The most common complications of HHT are nasal bleeding and anaemia. This is followed by stroke in young patients with HHT and pulmonary AVM, which is most often caused by paradoxical embolism [7]. Cyanosis, clubbing, migraine, cerebral abscess, embolic stroke, polycythemia, and pulmonary hypertension are all symptoms of lung lesions. Severe headaches and subarachnoid haemorrhage can be caused by AVM in the brain. Coronary arteries and vessels of the eye, spleen, urinary system, and vagina are also rare locations for AVM. The complications of lesions in the brain include TIA/ischaemic stroke, haemorrhagic stroke, and brain abscess. Severe haematemesis, melaena, haematochezia, and hypovolemic shock may result from gastrointestinal lesions, eventually leading to high output failure [8].

Complete blood count, reticulocyte count, erythrocyte sedimentation rate, iron, total iron binding capacity, and serum ferritin must all be included in the haematologic evaluation. Magnetic Resonance Imaging (MRI)/Magnetic Resonance Angiography (MRA), echocardiography, Computed Tomography (CT), colonoscopy, endoscopy, video capsule endoscopy, abdominal doppler ultrasound of the liver, and diagnostic nasal endoscopy are all used to detect AVMs in various organs [9].

The various treatment modalities include the following: humidification, topical moisturising therapy, haemostatic products, antifibrinolytic therapy, ablation therapy, systemic antiangiogenic medicines, and septodermoplasty are used to treat epistaxis. Iron replacement medication, blood transfusions, and antiangiogenic medicines are used to treat gastrointestinal bleeding and anaemia. Pulmonary AVMs are obliterated, and pulmonary artery hypertension is controlled by teamwork of Cardiologist, Pulmonologist, and Vascular Surgeons. Patients with hepatic AVMs who do not respond to medical treatment and develop high-output heart failure require a liver transplant. Embolisation and stereotactic radiosurgery are used to treat cerebral AVMs [1].

HHT is a disease that is inherited as an autosomal dominant trait. The majority of people have a parent who is afflicted with this condition prenatal testing during pregnancy can help detect this condition early in the people who have a positive family history [9]. Drugs that target Vascular Endothelial Growth Factor (VEGF) and the angiogenic pathway are among the most recent developments in treatment of this disease [10]. Aminocaproic acid inhibits the high amount of plasminogen-activator activity in the walls of telangiectatic arteries, resulting in fibrin deposits which plug the bleeding sites [11]. In people with minor symptoms, a topical nasal bevacizumab spray might be utilised [12]. The treatment used in present study was trichloroacetic acid cattery over the haemorrhagic spots. Similar treatment has been done in some studies where they have used trichloroacetic acid cautery, chemical cautery with silver nitrate, Neodymium-Doped: Yttrium Aluminum Garnet (ND:YAG), Potassium Titanyl Phosphate crystal (KTP) laser to cauterise the telengictasias [13].

CONCLUSION(S)

In this case, the patient presented with symptoms of epistaxis and anaemia and was treated with two sittings of local cautery, and iron supplements.The diagnosis of HHT should be made as early as possible to prevent the catastrophic effects of sudden haemorrhage in various organs. The diagnosis requires prompt detailed history taking, positive family history, presence of multiple telangiectasias, frequent episodes of nasal bleed. It requires a multidisciplinary approach with a devoted team of Otorhinolaryngologists,

Pulmonologists, Haematologist, Neurologist, Gastroenterologist, Nephrology specialists and Ophthalmologists having a systematic approach and regular follow-up. The signaling pathways FKBP12, PI3-kinase, and angiopoietin-2 are among the more recent molecular targets. These strategies are now being tested and will open the way for newer approaches to treating HHT.

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