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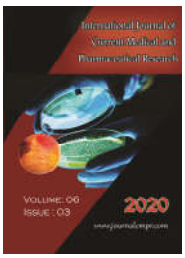

Research Article

TO STUDY HEREDITARY HAEMORRHAGIC TELENGIECTASIA

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ABSTRACT

Introduction: Osler Weber Rendu disease also known as Hereditary Haemorrhagic Telengiectasia(HHT) is a rare autosomal dominant disorder by the presence of multiple arterivenous malformations (AVMs) that lack intervening capillaries resulting in direct connections between arteries and veins.

Case Report: A 60 year old male patient known case of hypertension , Indian origin was brought to the emergency department of our hospital with complaints of severe epistaxis. An attempt was made initially to control bleeding by ice compressions and finally anterior and posterior nasal packing was done.He gave history of similar episodes in the past often accompanied with hemetemesis and malena on and off since childhood Gastroduodenoscopy was done to rule out cause for hemetemesis which showed multiple telengiectasia in fundus, body and antrum of stomach and first part of duodenum estabilishing the diagnosis of HHT.

Conclusion: Patient with osler-weber –Rendu disease may present with uncontrolled bleeding .Resuscitation along with hemostasis is the main stay of treatment. As the bleeding occurs from malformed vessels coagulation tests are normal. Management include blood transfusion,antifibrolytics and surgical hemostasis.

INTRODUCTION

HHT was first described by Henry Gawen Sutton in 1864. With similar symptoms to hemophilia the two diseases were differentiated by Henri Jules Louis Marie Rendu in 1896. William Osler connected the disease's presence in families to establish it as an inherited disorder. In 1907 Frederick Parkes Weber continued the characterization of the disease, writing a report on a series of cases. In 1909, the name hereditary hemorrhagic telangiectasia was coined, but alternate names based on the scientists who first characterized it have also been commonly used. Since its first identification, HHT has been an underdiagnosed disease, affecting more than a million people worldwide. Osler Weber Rendu disease also known as Hereditary Haemorrhagic Telengiectasia (HHT) is a rare autosomal dominant disorder by the presence of multiple arteriovenous malformations (AVMs) that lack intervening capillaries resulting in direct connections between arteries and veins. [1-3]Epistaxis is the most common symptom of HHT and mucocutaneous telengiectasia the most common sign.[1]

Aim and Objectives

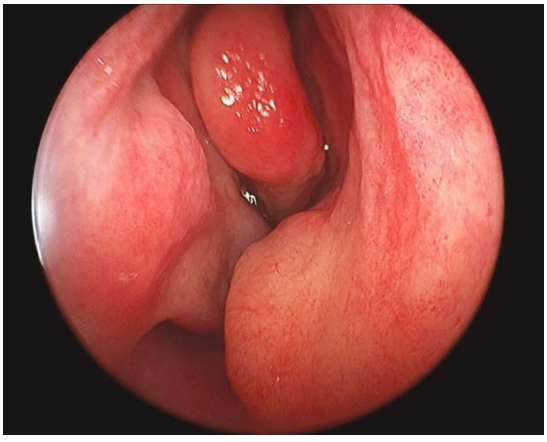
1. To study the case of hereditary haemorrhagic telengectasia
2. To evaluate other associated abnormalities

Case Report

A 60 year old male patient brought to the emergency department of our hospital with complaints of severe epistaxis and hypertension was included in the study. Attempt was made to control bleeding by ice compressions and finally anterior and posterior nasal packing was done. History of hemetemesis and malena was taken. Blood pressure and pulse was recorded.

Gastroduodenoscopy done to rule out cause for hemetemesis which showed multiple telengiectasia in fundus, body and antrum of stomach and first part of duodenum estabilishing the diagnosis of HHT.CT brain done to rule out cerebral arteriovenous malformations.

Newer drugs like Bevacizumab as medical line of management and septodermoplasty was advised



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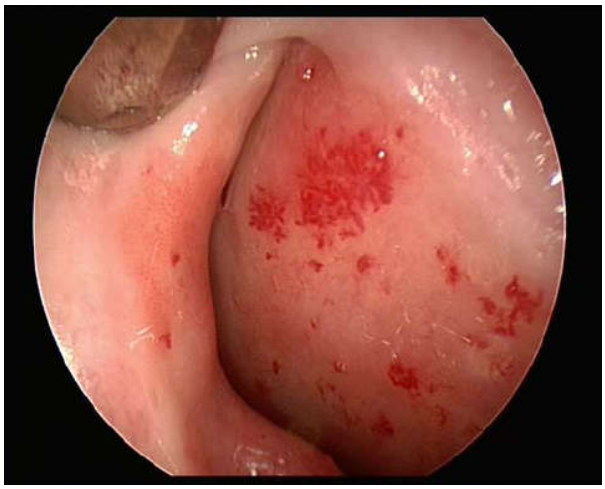

Figure 1 Diagnostic endoscopic images of nasal mucosa of patient

DISCUSSION

The direction in treatment of HHT has moved to a focus on prevention rather than symptomatic treatment, understanding the genetic mechanism behind the disease and the gene mutations is important for appreciating the pharmacology of preventive agents. Gene coding mutations are responsible for HHT, with 3 genes accounting for 85% of clinical cases: (1) HHT type 1 mutation of ENG coding for endoglin, (2) HHT type 2 mutation of ACVRL1 coding for activin receptor-like kinase (ALK), and (3) the combined disorder of juvenile polyposis/HHT mutation in MADH4 that codes for transcription factor SMAD4.[6-8] These predominant gene mutations are involved in the encoded proteins that mediate transforming growth factor beta superfamily signaling, initially thought to be central to the disease's pathogenesis.[9] Various hypotheses for the pathogenesis of HHT have subsequently been proposed, with the predominant conclusion being an impairment of blood vessel formation and/or an imbalance in multiple proangiogenic and antiangiogenic factors.[9,10]

HHT is a rare systemic fibro vascular dysplasia with incidence varying from 1 in 5,000 to 10,00.HHT is manifested by mucocutaneous telangiectases and arteriovenous malformations (AVMs) in different parts of body. [(1-2)] Lesions can affect the nasopharynx, central nervous system (CNS), lung, liver, and spleen, as well as the urinary tract, gastrointestinal (GI) tract, conjunctiva, trunk, arms, and fingers.Impaired signalling of transforming growth factor-ß/bone morphogenesis protein (TGF-β/BMP) as well as vascular endothelial growth factor (VEGF) has been attributed as the primary cause of HHT. [(5,11)] The diagnosis of HHT is made clinically Significant bleeding from gastrointestinal tract may occur in 25% patients older than 60 years and may increase with age. Pulmonary involvement in the form of arteriovenous malformations (AVMs) may be present in 75% HHT1 and 44% HHT2 patients Patients with pulmonary involvement are at high risk of developing cerebral thrombotic and embolic events including stroke, brain abscess, or transient ischemic attacks due to right-to-left shunting Cerebral AVMs may be present 15-20% HHT1 and 1-2% HHT2 patients and may present with seizure, headache or intracranial haemorrhages . Pre-existing anemia due to recurrent bleeding is common and sudden decompensation may lead to heart failure. Uncontrolled bleeding may occur from skin lesions during patient positioning and transport. [(12,13)] Epistaxis may lead to aspiration of blood into trachea causing pulmonary edema. Sudden change in blood pressure may cause bleeding from AVMs anywhere in the body, most serious of which is from cerebral AVM. Gastric distension may occur from ingested blood and may cause reflux and aspiration during induction. Male and females are equally affected .Classic triad of presentation include telangiectases of the skin and mucous membranes, epistaxis, and a positive family history. Epistaxis may be present in upto 95%whereas skin lesions account for 75-90% of presentations [(14)].

In Stable patients, posted for elective surgery, angiogenesis inhibitor or hormone therapy should be considered in selected patients to reduce perioperative bleeding. Careful history and physical examination may indicate any systemic involvement and standard radiological imaging with angiography may be performed to search for hemangiomas in brain, lung, gastrointestinal tract, nose and paranasal sinuses. In unstable patient presenting with severe bleeding focus should be directed to simultaneous resuscitation and hemostasis. [(13)]Blood transfusion forms the mainstay of volume resuscitation in severely volume depleted patient. Epistaxis should be controlled with tight nasal packing immediately followed by cauterisation of bleeding vessels and dermoplasty if required. Since bleeding does not result from a defect in coagulation cascade, but from the malformed vascular structures, platelet or plasma transfusions are of no use and reserved only to supplement the loss. Antifibrinolytics including tranexamic acid and aminocaproic acid [(13)] have been used with success to control epistaxis. In addition to antifibrinolytic effects, tranexamic acid also stimulates the expression of ALK-1 and endoglin, as well as the activity of the ALK-1/endoglin pathway[(15)]. Intraoperatively controlled hypotension should be used to reduce bleeding.

CONCLUSION

Patient with osler-weber –Rendu disease may present with uncontrolled bleeding .Resuscitation along with hemostasis is the main stay of treatment.As the bleeding occurs from malformed vessels coagulation tests are normal.Management include blood transfusion,antifibrolytics and surgical hemostasis. HHT is a disease more commonly associated with significant morbidity rather than mortality. The morbidity of the disease and decreased quality of life are the result of the recurrent and potentially severe epistaxis a majority of patients with HHT experience. During active epistaxis, the effective emergency techniques of locally applied pressure, nasal packing anteriorly and/or posteriorly, and cauterization will likely remain paramount. Medical treatment with antiestrogen therapy has shown promising results in trials from Israel, but further research is needed to determine the long-term side effects and the limitations of lifelong therapy. Research directed toward bleeding reduction and prevention has yet to have a breakthrough. Although initial reports suggest that intranasal bevacizumab is an effective agent, with some studies resulting in decreased ESS and manageable side effects, further research is required with longer treatment periods and follow-up. In the meantime, appropriate management of acute epistaxis coupled with early diagnosis and referral to an ear, nose, and throat specialist should be the mainstay of treatment.

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