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# HEREDITARY HAEMORRHAGIC TELANGIECTASIA IN A BLACK ADULT MALE: CASE REPORT

G.W. KITONYI, P.M WAMBUGU, H.O. OBURRA and J.M. IRERI

## SUMMARY

**Hereditary haemorrhagic telangiectasia, (HHT) or Rendu-Osler-Weber disease is a genetic autosomal dominant disorder that is characterised by telangiectasias, (small vascular malformations), in mucocutaneous tissues and arterial venous malformations, (AVMs), in various internal organs. Although HHT is relatively common in whites, the disorder has been reported to be rare in people of black African descent. Majority of HHT patients present with recurrent epistaxis, which in a significant proportion of patients is severe, warranting repeated blood transfusions and iron supplementation. Telangiectasias are most frequent on the tongue, hands, nose, lips and the gastrointestinal tract (GIT). AVMs occur in internal organs, particularly the lungs, brain, and the liver. Early and correct diagnosis of HHT is crucial as patients derive benefit from certain specific treatment modalities. Besides, AVMs which occur in various organs pose serious complications that may lead to death and therefore require early detection. We report a 55 year old black African male with HHT who presented with severe recurrent epistaxis and haematochezia leading to severe anaemia requiring repeated blood transfusions. His son, daughter and a maternal uncle experience milder recurrent epistaxis. The management of this patient and a brief review of the clinical features and management of HHT is presented. Our aim is to raise awareness of the occurrence of HHT in Kenya, in order to enhance early diagnosis and appropriate management.**

## INTRODUCTION

Sutton first described the disorder now known as HHT in 1864. Further descriptions of HHT were made by Rendu, Osler and Weber in 1896 (1). The disorder is thus also known as Osler-Weber-Rendu syndrome. HHT occurs primarily in Whites, with an average prevalence of 1:3500, (2,3). However cases of HHT have been reported in Asia (4), Arabia (5), and amongst the Afro-Caribbean's of the Netherlands (6).

HHT is an autosomal dominant disorder which shows variable penetrance and expressivity. Four genetic forms have been described, involving gene mutations in chromosomes 9, 12, 5, and 7 respectively, in the order of their discovery (7). The mechanisms underlying the formation of telangiectasies and AVMs are not completely understood, but there appears to be abnormal angiogenesis leading to vascular fragility, easy rupture and haemorrhages (1).

The condition is characterised by telangiectactic lesions involving the skin and mucous membranes. Lesions are commonly present in the hands, fingers, nares, lips and the GIT. Because there is no extravasation of blood, telangictasias blanch on pressure unlike purpuric lesions caused by platelet disorders. Recurrent epistaxis is the chief presenting complaint in over 90% of patients,

arising from telangiectactic lesions over the inferior turbinate and the nasal septum (8). GIT lesions are common along the large and small intestines and commonly cause persistent haemmorrhage and iron deficiency anaemia. Although epistaxis is often the most prominent and problematic feature of HHT, it has become increasingly clear that systemic AVMs are equally serious and are the cause of death in a significant proportion of patients (5). These AVMs are cumulative and progressive. They may be pulmonary in 5-30% of patients, cerebrovascular, (5-27%), and less commonly, hepatic (9). It is recommended that patients be investigated for systemic AVMs whenever possible, so that they can be treated, to preempt complications (10). However there is some controversy about prophylactic screening for cerebrovascular lesions. Pulmonary AVMs (PAVMs) are more common in patients with chromosome 9 mutations (11). The PAVMs predispose patients to paradoxical emboli, particularly to the brain where they may lead to abscess formation. Rupture of PAVMs may also cause haemoptysis or massive fatal pneumothorax (5). Hepatic AVMs are usually asymptomatic but portal hypertension, liver failure and hepatic encephalopathy have been reported occasionally (1).

Four diagnostic criteria for HHT have been developed. The first criterion is the presence of spontaneous recurrent epistaxis.The second criterion is the presence of multiple telangiectasias in typical areas. The third criterion is proven positive history in a first degree family member, while the fourth is demonstration of presence of visceral AVMs. When 3 or 4 criteria are met, the patient has definite HHT, while 2 criteria indicate a possible diagnosis of HHT (12). Although platelet function abnormalities have occasionally been reported, haemostatic tests are generally normal in HHT. Recurrent epistaxis in HHT is often a perplexing problem. Bleeding usually occurs before the age of 35 years and becomes increasingly severe. About a third of patients experience severe epistaxis, requiring transfusion support and chronic iron therapy. Parenteral total dose iron (TDI), is preferred over oral therapy in HHT patients. Cautery is commonly used to stop persistent epistaxis but repeated cauterisation has resulted in necrosis of the nasal septum with perforation in some cases. Cryosurgery, laser coagulation, arterial embolisation and arterial ligation are beneficial in patients with refractory epistaxis but they frequently fail because of regrowth of telangiectactic lesions (1). Septal dermoplasty, a surgical technique, where the fragile nasal mucosa is replaced by a sturdy split thickness graft from the thigh, reduces the frequency of epistaxis by one to two years (13). Epistaxis often reoccurs due to regeneration of telangictasias within the graft. Repeat grafting may then be necessary. Oestrogens, antifibrinolytic therapy (10), and trial therapies with antiangiogenic agents such as bleomycin (14) have been of some benefit to patients with severe epistaxis as well as fibrin sealants. In cases of serious GIT haemorrhage, accessible lesions in the stomach, duodenum and colon are often controlled with endoscopic thermal devices and laser coagulation (15). Liver transplants have been performed in some symptomatic cases, (16) while cerebrovascular AVMs often require neurovascular surgery. According to ongoing research, curative therapeutic advances, including gene replacement therapy, may be realistic possibilities in the future (17). The patient reported here exhibits classical features of HHT and serves to highlight clinical and diagnostic features of the condition.

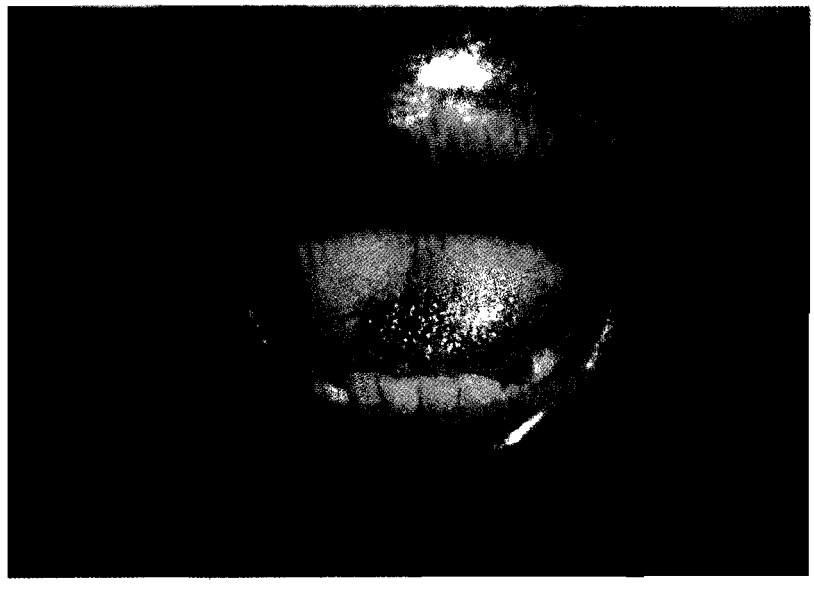
## CASE REPORT

A 55 year- old black African Kenyan man was first seen in November 1998, when he presented with complaints of severe epigastric pains associated with maleana stools. Past medical history obtained then revealed that the patient suffered recurrent episodes of epistaxis dating back to childhood. He had been followed up by an ENT specialist undergoing several cauterisations with good response. On further enquiry he reported that one of his sons, a daughter and a maternal uncle also experienced recurrent but milder episodes of epistaxis. The rest of his family, a wife, a son and a daughter had no history of any bleeding tendency. Stool examination at the time was positive for occult blood and a barium meal revealed an antral gastric ulcer. Helicobacter Pylori antibody test then was negative. The Haemoglobin, (Hb), level was 7.2 g/dl with features of iron deficiency. Diagnosis of peptic ulcer disease, (PUD), was arrived at and treatment for PUD and iron replacement given but stopped when the patient improved. Follow up endoscopy revealed a healed ulcer. He continued with ENT follow up for recurrent epistaxis thereafter. In the year 2002, the patient presented again, this time

with haematochezia. On investigations he was found to have iron deficiency anaemia with an Hb of 5.2g/dl.The patient underwent colonoscopy which revealed a lesion in the rectum. According to the patient the lesion was shown to him on a monitor during the procedure and was described as a "pimple". The lesion was excised and bleeding stopped. Healing was uneventful. Histology of the lesion was reported as a rectal polyp. The patient improved and continued iron therapy and ENT follow up by different specialists undergoing cauterisation periodically. Iron therapy would be stopped every time the Hb normalised. In the year 2006, the patient was admitted twice to Nairobi's South B Hospital with epistaxis and severe iron deficiency. On each admission he was transfused with several units of packed red cells. In view of the recurrent anaemia and family history of recurrent epistaxis, a haematological disorder was suspected and the patient referred for haematological evaluation. This was just before the second transfusion in October 2006. Physical examination of the patient by a haematologist revealed a well built man with marked pallor of the mucous membranes. Multiple telangiectasias were noted on the tongue, and lower lip, (Figure 1). The patient was unaware of the telangiectasia and therefore did not know when they first appeared. The chest was clear and no neurological deficit was detected. A full blood count revealed an Hb of 4.3 g/dl, with low MCV, MCH, MCHC and a microcytic hypochromic blood picture, consistent with severe iron defficiecy anaemia. The white cell count and morphology were normal, with a mildly elevated platelet count of 616 x 109/L. Coagulation studies revealed a normal bleeding time, normal prothrombin time, normal APTT, and normal thrombin time. Von Willebrand's Factor, (VWF), was normal on two occasions. Stool occult blood was found to be positive. Diagnosis of HHT was made on the basis of 3 criteria; a history of recurrent spontaneous epistaxis, presence of telangiectasias and a positive family history in first degree relatives. In view of the low Hb, and the potential for further immediate epistaxis, the patient was transfused with four units packed red cells, put on iron therapy along with tranexamic acid and allowed home with an Hb of 11.6 g/dl. The patient was counseled appropriately and put on permanent oral iron supplementation. Chest X-ray and liver ultrasound were normal. Due to constraints, it was not possible to do more sensitive pulmonary and central nervous system investigations to rule out asymptomatic AVMs. Over the last one year the patient has had three major episodes of epistaxis which have been managed conservatively. He has not required any further blood transfusions. A trial of oestrogens therapy is being contemplated as well as periodic parenteral iron therapy, to replace the oral therapy. Other management options being considered are septal dermoplasty, if episodes of severe epistaxis increase. Follow up endoscopy to exclude gastrointestinal AVMs is also planned.

**Figure 1**

*Telangiectasias on the patient's tongue and lower lip*



Although the patient was greatly relieved that after many years a diagnosis of his illness had been arrived at, the patient's relatives have been reluctant to present themselves for examination.

## DISCUSSION

Hereditary haemorrhagic telangiectasis is a rare condition in black Africans and as a result, many physicians who practice in black Africa are unlikely to see a case in their lifetime. Indeed this is the first case the authors have seen in a black African. Nevertheless, it is important that physicians recognise the condition, so that the few cases that exist are appropriately managed. Besides, since HHT's mode of inheritance is autosomal dominant, it is probable that there will be a slow increase in the number of cases over the years.

The patient reported here represents a classical picture of HHT. He fulfils the now agreed stringent criteria for diagnosis of HHT (12). The affected relatives conform to the autosomal dominant mode of inheritance of HHT. That the relatives suffer less severe epistaxis is in keeping with the variable penetrance and expressivity of HHT. Although the patient had experienced epistaxis since childhood, there is a clear progression and increase in severity of the condition as expected. In retrospect, the rectal lesion excised at colonoscopy in the year 2002, and which was reported as a rectal polyp, could have been a telangectactasia and ideally the histology should have been reviewed in the light of the diagnosis. Unfortunately attempts to obtain histology review were unsuccessful. It is also of interest that the endoscopy done for PUD did not reveal any telangiectasia. Recurrent iron deficiency in this patient is probably due to both chronic GIT blood loss and recurrent epistaxis.

The patient's management has been conservative so far. However, should he deteriorate, some of the other treatment modalities will be considered. Although it has been recommended that HHT patients who require long term iron supplementation should be managed with periodic TDI (10), dextran TDI iron preparations available in Kenya before the 1980s fell into disrepute because of dextran associated complications. The now available safe sucrose and gluconate TDI iron, which are convenient to administer in chronic iron deficiency, should be made widely available in Kenya, since iron deficiency anaemia is a common condition in our setting. This patient should benefit from these more convenient iron preparations. The patient is also being monitored periodically for the occurrence of AVMs.

The delay in diagnosis of HHT in this patient is not surprising for a condition that is so rare in blacks. Indeed the initial haematologist's impression was that of the more common diagnosis of Von Willebrand's disease, (VWD). VWD was excluded by the repeatedly normal VWF and the presence of persistent blanching lesions, unlike the haemorrhages seen inVWD, which normally change colour and disappear within weeks. No haemostatic abnormalities have been demonstrated in this patient as is the case in majority of other HHT patients. This highlights the importance of having a high index of suscipicion, based on the clinical picture, in arriving at the diagnosis of HHT.

The reluctance of the patient's relatives to be subjected to investigations maybe due to fear of stigma of being labeled with a hereditary disorder, but it could also be due to a perception of the problem as just a minor inconvenience. Either way this trend is likely to hamper prevalence studies of HHT in Kenya.

We believe this is the first documented case of HHT in a black Kenyan and therefore hope that this report will serve to raise the index of suspicion of HHT in our country. The prevalence of HHT in Kenyans remains unknown and we therefore recommend a study, especially among patients with longstanding unexplained recurrent epistaxis, to identify HHT patients so that they can benefit from appropriate management.

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