Non-Familial Hereditary Hemorrhagic Telangiectasia In A Middle-Aged South Asian Male- A Case Report

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Abstract: Background: Hereditary Hemorrhagic Telangiectasia (HHT) also known as Osler-Weber-Rendu syndrome is an autosomal dominant disease with a prevalence of 1 in 5000 to 10,000. It is characterized by mucocutaneous and visceral telangiectasias with multiorgan involvement- resulting in anemia causing a continuous blood transfusion requirement. Case Description: A 45-year-old diabetic male with a history of recurrent epistaxis since 6 years of age presented with anemic heart failure. Upper GI endoscopy and contrast-enhanced CT abdomen were suggestive of multiple telangiectasias in the oral cavity, oropharynx, and jejunal angiodysplasias with duodenal erosions. The patient was diagnosed with HHT based on three out of four Curacao criteria- Recurrent spontaneous epistaxis, Telangiectasias, and Visceral lesions. The patient was treated with oral Thalidomide and Packed Red Cell transfusions. Epistaxis was conservatively managed with topical medications while the patient underwent Argon Plasma Coagulation for gastrointestinal bleeding. According to hematological opinion, Bevacizumab therapy was planned but due to non-affordability, the family decided to continue with the existing treatment and the patient succumbed a month later. Early diagnosis with a low threshold of suspicion is important to improve the quality of life and life expectancy for this disease. [Bharadwaj S Natl J Integr Res Med, 2024; 15(1):57-60, Published on Dated: 26/01/2024]

Key Words: Bevacizumab, Curacao Criteria, Hereditary Hemorrhagic Telangiectasia, Osler-Weber-Rendu Syndrome, Recurrent Epistaxis, Thalidomide

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Introduction: Hereditary Hemorrhagic Telangiectasia (HHT) also known as Osler-Weber-Rendu syndrome is an autosomal dominant disease with 2 per 10,000 persons an estimated prevalence worldwide[1]. HHT is characterized by mucocutaneous and visceral telangiectasias with multiorgan involvement, resulting in anemia requiring repeated blood transfusions. Definitive diagnosis is made when the patient is observed to be positive for at least three of four criteria as defined by the Curacao Criteria, namely epistaxis, multiple telangiectasia, visceral lesions, and family history with one or more first-degree relatives affected.

Hereditary Hemorrhagic Telangiectasia is characterized by the lack of normal capillary connections between an artery and a vein, leading to the formation of direct artery-to-vein shunts. In mucocutaneous tissues, these small abnormal vessels are known as telangiectasias, while larger ones in solid organs are called arteriovenous malformations (AVMs). Telangiectasias are often asymptomatic but can sometimes bleed. In contrast, the primary concern with AVMs in solid organs is typically direct artery-to-vein shunting rather than bleeding. In this case report we describe a rare case of HHT without a positive family history who presented with recurrent epistaxis and anemic heart failure.

Case Study: A 45-year-old diabetic male with a history of recurrent epistaxis since 6 years of age presented with easy fatigability, pedal edema, and dyspnea on rest, which worsened after 1 month. History of multiple blood transfusions with iron replacement has been present since 10 years of age.

On examination, severe pallor was noted with bilateral pitting pedal edema and a systolic murmur in the aortic area on cardiac auscultation.

Routine blood investigations revealed recurrent bi-cytopenia with normal platelet counts and severe microcytic hypochromic anemia. Peripheral blood smear revealed severely hypochromic microcytic RBCs with anisopoikilocytosis, leptocytes, elliptocytes, tear drop cells, and occasional nucleated RBCs.

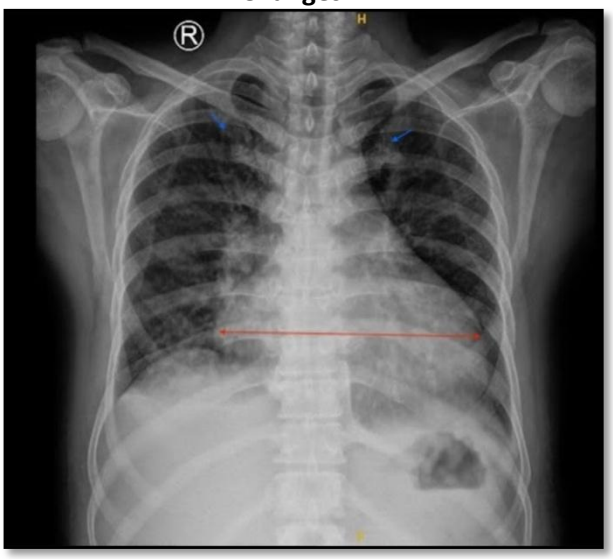
The serology for HIV, Hepatitis B, and C was negative. Two-dimensional echocardiography was suggestive of an ejection fraction of 50% with mildly dilated LV (Left Ventricle), dilated RA and RV, Grade III diastolic dysfunction with mild PAH (Pulmonary Arterial Hypertension), and an RVSP (Right Ventricular Systolic Pressure) of 40 mmHg.

Table 1: Hematological Investigations At The Time Of Admission

Investigation	Results	Reference Range
Hemoglobin (Hb) (g/dL)	2.4	12-18
Total Leukocyte Count (TLC) (/uL)	6090	4000-10000
Absolute Platelets Count (APC) (/uL)	2,22,000	150-410
Urea (mmol/L)	33	15-40
Serum Creatinine (mg/dL)	1.1	0.6-1.2
Na+ (mEq/L)	132	135-145
K+ (mEq/L)	4.5	3.5-5.5
SGPT (U/L)	327	10-49
Total Proteins/Serum Albumin (gm/dL)	6.3/3.1	0.3-1.2/0-0.2
LDH	167	100-250
Direct Coombs test	Negative	Negative

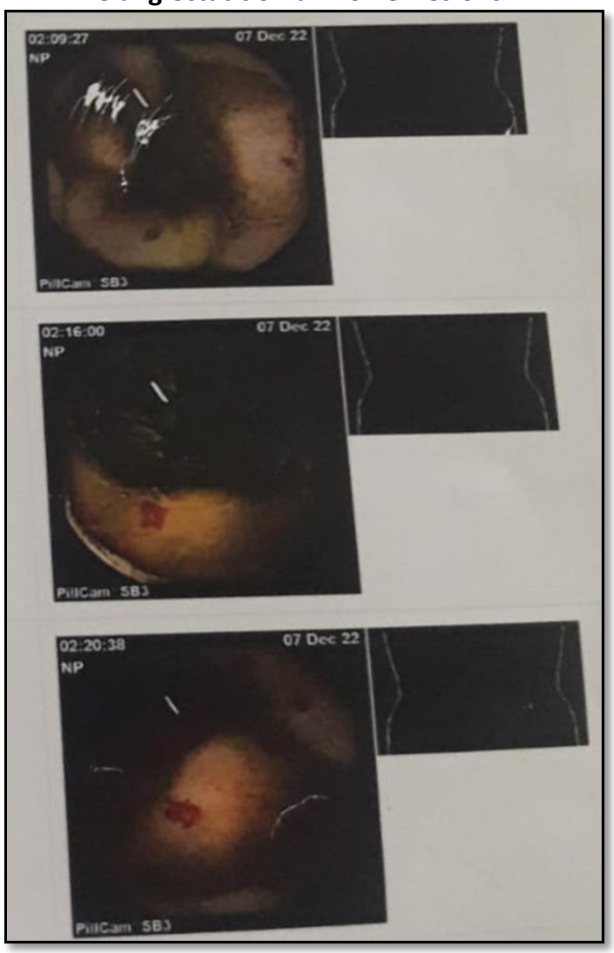
Amongst radiological investigations, an X-ray chest PA view revealed Cardiomegaly with cephalisation and congestive changes. Upper Gastrointestinal (UGI) endoscopy revealed multiple telangiectasias in the oral cavity, oropharynx, and jejunal angiodysplasias with duodenal erosions. Lower GI endoscopy was unremarkable.

Figure 1: X-Ray Chest Posteroanterior View. (A) Red Arrow - Showing Cardiomegaly, (B) Blue Arrows - Showing Cephalisation And Congestive Changes



Contrast-enhanced Computed Tomography (CECT) scan of the abdomen showed focal intramural nodular areas of contrast enhancement in small bowel loops (predominantly jejunal) in left lumbar region with prominent jejunal arteries and dilatation with early filling of draining inferior mesenteric vein, dilated tortuous tuft of vessels in left lumbar and umbilical region. Capsule endoscopy was suggestive of multiple telangiectatic small bowel lesions. CT pulmonary angiography was normal.

Figure 2: Capsule Endoscopy Showing Multiple Telangiectatic Small Bowel Lesions



The patient was diagnosed based on three out of four Curacao criteria: Recurrent spontaneous epistaxis, Telangiectasias, and Visceral lesions; family history was absent.

The patient was treated with oral Thalidomide (100 mg HS) and Packed Red Cell transfusions with diuretics for High Output Cardiac Failure.

Epistaxis was conservatively managed with topical medications while the patient underwent Argon Plasma Coagulation for gastrointestinal bleeding.

Discussion: Recurrent epistaxis, the presenting symptom in our case, is seen in around 90% of HHT patients[2]. 25-30% of patients, usually older, experience some form of gastrointestinal bleeding which can result in severe anemia[3,4].

Pulmonary AVMs can be seen in 50% of patients[5], which form a right to left intrapulmonary shunt and can cause dyspnea, exercise intolerance, hemoptysis, paradoxical emboli, and brain abscesses[6,7], while cerebral AVMs are seen in 10% of the cases, can cause intracranial bleeds, seizures, and focal neurological deficits. High-output cardiac failure, as seen in our patient, ensues due to intrahepatic vascular malformations resulting in porto-venous, arteriovenous, and arterioportal shunting.

20% of HHT patients do not have a positive family history. The diagnosis of Hereditary Hemorrhagic Telangiectasia (HHT) as based on the Curacao criteria is made when 2 or more of the 4 criteria are met: - 1) Recurrent and spontaneous epistaxis; 2) Telangiectasias, often at characteristic sites (lips, finger, mouth, and nose); 3) Visceral Arterio-Venous Malformations (AVMs) commonly seen in the pulmonary, hepatic, cerebral and gastrointestinal circulation; and 4) A family history of a first-degree relative diagnosed with HHT.

The sensitivity of the Curacao criteria is very low for diagnosing HHT in the first decade of life, as most patients are asymptomatic owning to the age-related penetrance of the disorder and hence children with parents affected by HHT must be worked up with a high degree of suspicion even if the Curacao criteria are not met. Furthermore, the Curaçao criteria do not outline specific details such as the frequency of episodes of epistaxis or a specific number of telengiectasia needed to meet the definition. This leads to inconsistent use and uncertainty and thus, more specific definitions of individual criteria can enhance the practical applicability of the Curacao criteria in such patients.

HHT is associated not only with significantly higher rates of premature mortality (before 60 years of age)[1,8] but can also result in serious morbidity that can raise healthcare-related costs and lower quality of life[9]. Improved identification can lead to screening for ArterioVenous Malformations (AVMs) and the use of potentially life-saving treatments[10]. Early diagnosis and prompt treatment can increase life expectancy by 3-7 years[8,9].

Management of HHT is multifold, with systemic therapy aimed at reducing the frequency of bleeding episodes, local and surgical interventions for treating focal vascular malformations, and other supportive therapies such as iron supplementation and blood transfusions to maintain hemoglobin levels in patients.

Intravenous Bevacizumab an anti-Vascular Endothelial Growth Factor (VEGF) agent has shown significant success in reducing bleeding episodes in patients of HHT[11] with minimal side-effects. However in our case, due to the unaffordability of Bevacizumab by the patient, treatment with Thalidomide was pursued which has been known to improve the quality of life of patients of HHT.

Conclusion: HHT has a high degree of morbidity affecting several organ systems, causing a significant impact on quality of life. Often such patients require multidisciplinary care involving the treating physician, otolaryngologist, pulmonologist, neurologist, cardiologist, gastroenterologist, and hematologist. The diagnosis of Hereditary Hemorrhagic Telangiectasia was confirmed as three out of the four Curacao criteria were positive in our patient.

Management of this patient involved a combination of oral Thalidomide, packed red cell transfusions, and Argon Plasma Coagulation for gastrointestinal bleeding.

Continued research and revision of diagnostic criteria, such as the Curacao criteria, are crucial for early diagnosis and management of HHT,

particularly in patients with borderline symptoms. Early diagnosis with a low threshold of suspicion and early institution of genetic studies and targeted therapy is important to improve the quality of life and life expectancy in this disease.

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