Pericardial Involvement in Hereditary Hemorrhagic Telangiectasia

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Abstract- Hereditary haemorrhagic telangiectasia is a rare disease characterized by cutaneo-mucous and visceral arteriovenous malformations. Cardiac involvement is uncommon and was presented primarily by hyper-output heart failure. Hemorrhagic pericardial effusion, although is extremely rare, can occur during HHT. We report the case of a 48-years-old woman which was hospitalized in 2015 in internal medicine department, Sfax, Tunisia in 2015 for anicteric cholestasis. She noticed a personnel and familial history of recurrent epistaxis. Biologic findings revealed anemia and moderate cholestasis. Viral investigations and immunologic tests were negative. Abdominal tomography showed multiple arterio-venous shunts of the liver. Liver involvement due to Rendu Osler Weber disease was retained. She was treated by ferrous iron, but she was lost to follow up. She was presented in February 2021, with severe anemia (5 g/dL). Physical examination revealed signs of global heart failure. Biological investigations found anemia, inflammatory biological syndrome, cytolysis and cholestasis. Heart ultrasound revealed an abundant pericardial effusion. Only 500cc of hemorrhagic fluid could be aspirated before the needle became blocked. Unfortunately, one week after, re-accumulation of pericardial fluid and worsening occurred. She underwent a partial surgical pericardial excision with pleuropericardial opening. Analysis of the fluid ruled out any infectious cause of this effusion. Histological examination confirmed the vascular dysplasia with signs of hemorrhage and inflammation. The patient was discharged 1 month after surgery with no other bleeding episodes. For her anemia, she received a transfusion of red blood cells. Then, the patient was treated by iron treatment.

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Keywords: Rendu osler disease; Cardiac involvement; Pericardial effusion; Tamponade

Introduction

Hereditary haemorrhagic telangiectasia (HHT) is a rare genetic disorder characterized by cutaneo-mucous and visceral arteriovenous malformations (AVM) leading to spontaneous and provoked bleeding (1). It can be underdiagnosed because it's extremely rare and not well known. Clinical presentation varies from asymptomatic cases to potentially life-threatening ones. The most common locations affected are the nose, lungs, brain and liver. Cardiac involvement and pericardial effusion are a rare complication of hereditary haemorrhagic telangiectasia. We report a case in this regard.

Case Report

A 48-years-old woman which was hospitalized in 2015 in our department of internal medicine, Sfax, Tunisia for anicteric cholestasis. In her medical history, we found the concept of consanguinity and a history of personnel and familial recurrent nose bleeding episodes. Biological findings revealed anemia and moderate cholestasis. Viral investigations (B and C Hepatitis) and immunologic tests were negative (including anti mitochondria and anti-smooth muscle antibodies). Abdominal tomography showed multiple arterio-venous shunts of the liver with dilation of the hepatic artery, the hepatic veins and the inferior vena cava. Liver

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involvement due to Rendu Osler disease was retained. Treatment by oral ferrous iron was instituted (150 mg/day). Regular biological and radiological monitoring were planned, but the patient was lost to follow up.

In February 2021, she presented with severe anemia. She suffered from asthenia, dyspnea NYHA IV and palpitations. She reported moderate recurrent epistaxis. Examination demonstrated pallor and jaundice. Her pulse was at 103 beats per minute, her blood pressure was at 100/60 mmHg, her respiratory rate was at 26/min. She had jugular venous distension, hepatalgia and bilateral leg edema. Fine rales in both lung bases and heart breath regurgitation murmur were heard. A thrill in cardiac and hepatic area was noticed. Biological findings found hemoglobin level at 5 g/dL with reticulocytes level at 185000/uL, lymphopenia, (Lymphocytes at 790/uL), platelets of 235000/uL, increased erythrocyte sedimentation rate at 30 mm /hour and elevated CRP at 20 mg/dL, cytolysis 3 times than the normal range with cholestasis higher 5 times than the normal range (alkaline phosphatase of 112 units/ L). Computed tomography (figure 1) revealed dilation of trunk of pulmonary artery (measuring 32 mm), enlarged heart predominant on the right side, abundant pericardial effusion, mosaic perfusion appearance of the lung reflecting pulmonary hypertension, enlarged heterogeneous liver (15 cm) with multiple foci of vascular enhancement reflecting arterio-venous shunts, the most obvious of which is located in segment VI measuring 30 mm, dilation of the common hepatic artery and its branches and dilation of portal vein at 13 mm. Serial trans-thoracic doppler echocardiography (figure 2) were practiced revealing large pericardial effusion anterior, lateral and posterior to the heart (21*30*33 mm) with some signs of compromise: partial right atrial collapse and absent respiratory variation of the inferior vena cava (31 mm). The patient remained haemodynamically stable. Emergency percutaneous pericardiocentesis was performed by subxiphoid approach using ultrasound guidance. Only 500 cc of hemorrhagic fluid could be aspirated before the needle became blocked. Unfortunately, one week after, worsening pericardial effusion and re-accumulation of pericardial fluid and cardiac tamponade occurred. The pericardiocentesis wasn't possible. An open surgical procedure was indicated with initial drainage of 800 mL of hemorrhagic fluid. The patient underwent a partial surgical pericardial excision with pleuropericardial opening. Analysis of the fluid ruled out any infectious or neoplastic cause of this effusion. Histological examination of the pericardium revealed vascular dysplasia with signs of hemorrhage and inflammation. The patient was discharged 1 month after surgery with no other bleeding episodes. For her anemia, the patient received a transfusion of red blood cells (RBC). Then, iron treatment was instituted.

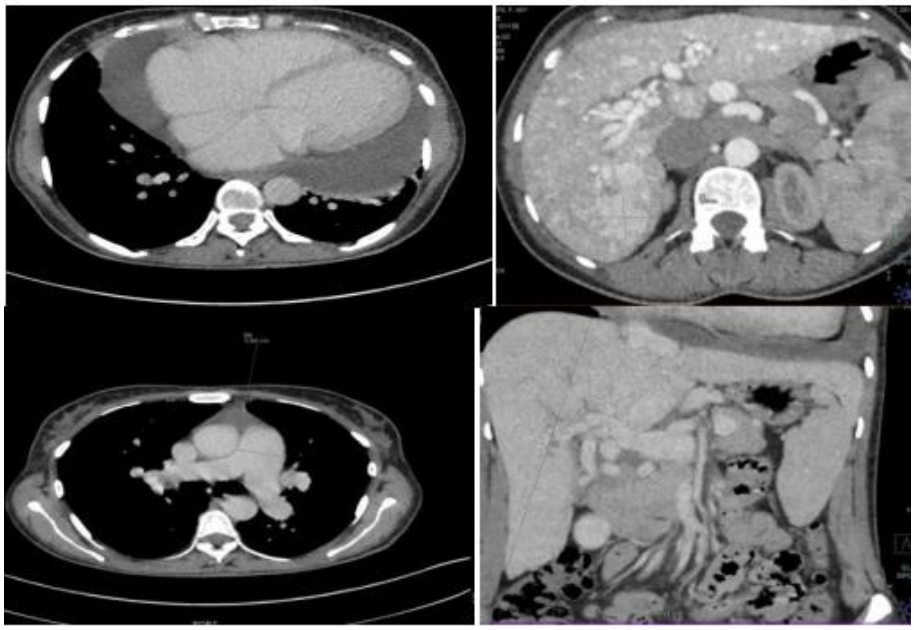

Figure 1. Chest and abdominal computed tomography revealing cardiomegaly with pericardial effusion and heterogeneous liver with multiple arterio-venous shunts

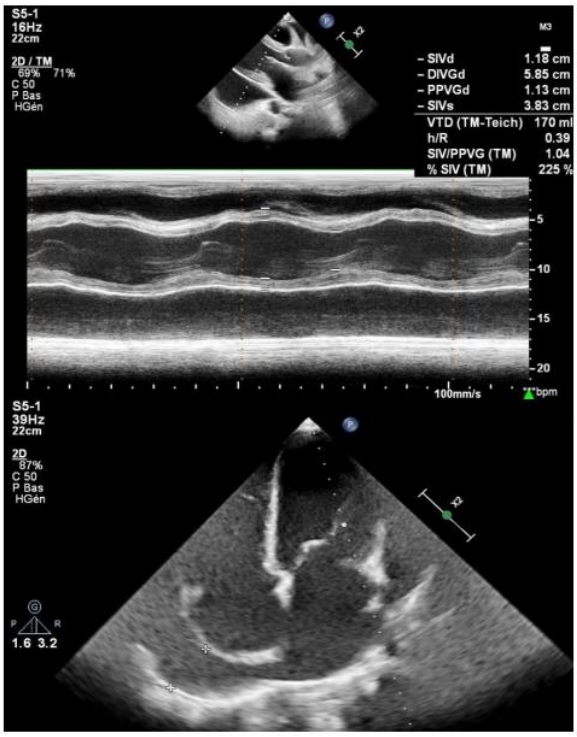

Figure 2. Echocardiographic images generated during diastolic phase of cardiac cycle demonstrating tamponade

Discussion

HHT is an autosomal dominant disease resulting from mutations of endoglin gene which encodes to intra membrane protein called endoglin. This protein was expressed on endothelial cells which stimulates vascular growth and development. Genetic mutation of endoglin leads to development of abnormal immature vessels which easily dilate and rupture (2,3). The diagnosis is based on clinical criteria of Curaçao which combine epistaxis (spontaneous, recurrent), localization telangiectasias multiple (skin or mucous membranes), arteriovenous malformations (pulmonary, hepatic, cerebral) and family involvement. Diagnosis is described as certain in the presence of 3 of the 4 criteria (4-6). Clinical manifestations of HHT were presented by vascular malformations whose rupture causes bleeding. The gravity of bleeding depends on abundance and location of hemorrhage. Repeated epistaxis was present in more than half of patients with this disease (7). Visceral lesions are mainly presented by pulmonary, cerebral, hepatic, spinal and gastrointestinal vascular malformations. The cardiac involvement in HHT is already presented by high-output heart failure complicating arterio veinous malformations in the liver. High cardiac output was defined as greater than 8 L / min (>3.9 L/min/m2 for cardiac index). The main calling symptoms are dyspnea, decreased exercise tolerance, fatigue, palpitations and peripheral edema. Few patients are therefore symptomatic, but complications are potentially serious and fatal (8). A high-output state due to arterio venous malformations in the liver or blood-loss anemia can occur causing increased preload and decreased peripheral vascular resistance. The occurrence of high cardiac output preceded usually the heart failure (9). The rise in filling pressures as well as the progressive dilation of the atrium promotes the development of atrial fibrillation. Transthoracic echocardiography (with measurement of cardiac output) is essential in the baseline and follow-up for all patients with hepatic shunts. If dyspnea appeared, echocardiography should be repeated, and right-left catheterization is considered to obtain invasive measurement of cardiac output and pulmonary pressures. BNP (brain natriuretic peptide) is a poor marker of high cardiac output but remains a good marker for uncompensated heart failure. Treatment of high-output heart failure was based on sodium restriction, administration of diuretics as well as correction of anemia and ACE inhibitors and/or beta blockers prescription. Reversibility of heart failure has been reported in decreased liver shunts (treatment with bevacizumab or liver transplantation) (10). Aortic and coronary artery anevrysms and left ventricular coronary artery fistulas have also been reported (11,12). Pericardial effusion has

exceptionally been described as a manifestation of HHT. Hemorrhagic pericardial effusion secondary to epicardial vascular abnormality is possible but reported in few cases (13). The hypothesis which suggested was about the presence of abnormal microvascular lesions in the pericardium similar to those described in other viscera whose dilation and rupture could trigger inflammation, exudation and hemorrhage in pericardial cavity (7). Kanna B, Das (2004) report a case of HHT-associated hemorrhagic pericardial effusion presenting with pericardial tamponade (13). Kopel and Lage (1998) described a 37-year-old woman with HHT who developed a large pericardial effusion with cardiac tamponade and histological examination confirmed the vascular dysplasia with signs of hemorrhage and inflammation (14). Our patient presented with cardiac tamponade, the most severe complication of HHT pericarditis. Early diagnosis is important to initiate urgent treatment in order to prevent potentially fatal complication. There is no curative treatment for HHT disease and management is primarily aimed at preventing and treating complications (6). In post-surgery, right ventricular failure after pericardiectomy may need ECMO and should be instituted (15). The family survey should be carried out systematically. Child testing remains a matter of controversy: it should be discussed with parents and be the subject of a genetic consultation.

This case reminds us of common and rare complications that can arise from HHT, and that management may be limited highlighting the importance of timely diagnosis (Table)

Table. Summarizing the cases of Hereditary hemorrhagic telangiectasia with pericardial involvement

	Sex	Age	Family history HHT	Clinical presentation	Biological findings	Cardiac manifestations	Pericardial effusion Histologic findings
Kanna B, 2004 (13)	Man	74-year-old	Yes	chest pain, dyspnea, nausea, recurrent epistaxis cutaneous telangiectasias	Martial anemia,	ECG: low voltage QRS complexe T wave abnormalities in the inferior and lateral leads. ChestX ray: cardiomegaly Troponin: <0 echocardiography: pericardial effusion with right ventricular diastolic collapse.	Surgical pericardiotomy: 250ml hemorrhagic pericardial fluid (WBC:220cells/cm3 red blood cells, 141,000 cells/cm3) Pericardial biopsy: tissue inflammatory changes and reactive mesothelial cell hyperplasia
Kopel L, 1998 (14)	Women	7	No	dyspnea lower extremity edema congestive heart failure jugular venous distension cyanosis Cutaneous telangiectases	Normal	Chest X ray : cardiomegaly Echocardiography large pericardial effusion, cardiac tamponade with normal right and left ventricular function	Percutaneuos pericardiocentesis: drainage of 500 mL hemorrhagic pericardial effusion 1week after pericardiocentesis, ➔ cardiac tamponade ➔ surgical procedure: initial drainage of 1000mL hemorrhagic fluid. Pulmonary angiography: tiny arteriovenous shunts distributed diffusely throughout both lungs. Histological examination of the pericardium: vascular dysplasia with signs of hemorrhage and inflammation. lung biopsy: vascular malformations of capillaries postcapillary venules.
Joshua S. Chung (16)	Man	48 year old man	Yes	Tachycardia pitting edema his chest wall	elevated total bilirubin	Chest Xray: enlarged cardiac silhouette, pleural effusions. Computed tomography: thickened pericardium pleural effusions Echocardiogram: thickened pericardium, severely elevated right atrial pressure with dilated vena cava	

Cont. table

Our case	Women	48	Yes	recurrent nose bleeding episodes dyspnea palpitations Tachycardia jugular venous distension, hepatalgia and bilateral leg edema thrill in cardiac and hepatic area	cholestasis severe anemia.	Computed tomography: dilation of trunk of pulmonary artery enlarged heart predominant on the right side, abundant pericardial effusion, Echocardiography large pericardial effusion, right atrial collapse Surgical procedure: initial drainage of 800 mL of fluid Surgical pericardial excision pleuro pericardial opening.	percutaneous pericardiocentesis 500cc hemorrhagic fluid Histological examination pericardium: vascular dysplasia with signs of hemorrhage and inflammation.

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