Osler-Weber-Rendu (OWR) Disease and Heart Failure

Arnon Blum and Rafea Shalabi
Department of Medicine, Baruch-Padeh Poria Medical Center, Lower Galilee Israel. Email: ablum@poria.health.gov.il

Abstract: OWR is a genetic disease, transmitted as an autosomal dominant disorder characterized by arteriovenous malformations predominantly involving the mucocutaneous epithelium. One of the significant complications is the development of arteriovenous fistulas in different organs like the liver and brain. One of the rarest complications of this arteriovenous conduit is a high-output heart failure. We would like to describe a 66 years old woman who was admitted with a high-output cardiac failure who deteriorated clinically and was treated successfully by conservative management.

Keywords: heart failure, high output, A-V malformations
A 66 year old woman was admitted with dyspnea at rest. This symptom started a few months ago as shortness of breath during exercise and got worse with time. In the last week she could not sleep at night due to shortness of breath with orthopnea. She had a family history of Hereditary Hemorrhagic Telangiectasia (HHT), and was hospitalized a few years ago with epistaxis, gastrointestinal bleeding, and she also had a hemorrhagic stroke. During hospitalization in 2007 (when she was admitted with gastrointestinal bleeding) teleangiectases were detected in the stomach.

On physical examination telangiectases were observed on the face, lips, hands, and on the nose. Heart sounds were normal with a holosystolic 2/6 murmur without any pathological heart sounds or clicks. On auscultation there were mild to moderate wet rhonchi without wheezes. There was a +3 peripheral pitting edema in both legs.

Laboratory results showed an iron deficiency anemia (Hemoglobin 10 g%) with elevated alkaline phosphatase and bilirubin levels with normal hepatocellular liver enzymes, but with a prolonged prothrombin time (INR-1.6).

Thyroid function tests were normal.

The electrocardiogram showed a normal sinus rhythm (70 beats per minute) with a normal P-R interval and a normal axis (60°). No signs of myocardial hypertrophy or signs of systolic overload were observed. Echocardiography demonstrated a normal left and right ventricular size and function (Left Ventricular Ejection Fraction 65%–70%) with diastolic dysfunction (restrictive pattern), mild dilatation of the aortic root and the ascending aorta with minimal aortic regurgitation. The Doppler study that evaluated her hepatic venous flow did not show any signs of left to right shunt within the liver or anywhere else around the liver.

Chest X-rays has demonstrated mild to moderate pulmonary edema.

During hospitalization she was treated with diuretics and beta blockers (Normiten 50 mg once daily) and her symptoms improved altogether with weight loss of 5 Kg within 7 days. The orthopnea disappeared, and the dyspnea was relieved. She had no symptoms of heart failure.

**Discussion**

OWR (or HHT) occurs in 0.01% of the population. It is an autosomal dominant disease characterized by angiodysplastic lesions (telangiectases and arteriovenous malformations) that affect many organs, including the skin, lungs, gastrointestinal tract, and brain.1

The genes involved in HHT have been identified as endoglin (HHT type 1) on chromosome 9q33–34, and activin receptor (HHT type 2) on chromosome 12q13. Both genes are involved with the regulation of transforming growth factor (TGF) beta signaling pathway and expression, mainly aimed to endothelial and vascular smooth muscle cells. Endoglin and ALK1 knockout mice die between embryonic days 9–11 due to vascular defects, demonstrating the importance of these proteins in angiogenesis.1,2 This disorder is clinically characterized by cutaneous and muco-cutaneous telangiectases, severe and recurrent epistaxis and gastrointestinal hemorrhage caused by teleangiectases of the nose and upper gastrointestinal tract. Patients also have arteriovenous shunts, most commonly found in the lungs, brain, and liver. Pertinent findings on physical examination in patients with liver involvement vary with the extent of the disease. Patients with small hepatic AVMs may have a normal examination while those with diffuse involvement may have hepatomegaly. Liver function tests are mildly elevated in 75%. The most common laboratory findings are elevated alkaline phosphatase and bilirubin levels with normal hepatocellular enzymes with cholestasis. Angiographic findings include large, tortuous hepatic arteries, and dense, enlarged hepatic veins.

The heart failure syndrome in OWR patients is characterized by an elevated resting cardiac index beyond the normal range of 2.5–4.0 L/min/m². The assumption is that ineffective blood volume and pressure, chronic activation of the sympathetic nervous system and the rennin–angiotensin/aldosterone axis with increased serum vasopressin concentration cause chronic volume overload that gradually develops ventricular enlargement, remodeling and heart failure.

The definition of high–output heart failure is defined by symptoms of heart failure-like dyspnea at rest or with varying degrees of exertion, orthopnea, paroxysmal nocturnal dyspnea, and pulmonary/ peripheral edema) in the presence of normal cardiac index. The elevated cardiac output itself does not lead to symptoms of congestive heart failure. The prolonged increase in blood volume, the continuous increased right atrial pressure, the high pulmonary
High-output heart failure

Medical therapy involves salt restriction, diuretics, anti-hypertensive agents, anti-arrhythmic agents, and digoxin as clinically indicated. The particular clinical manifestation of liver involvement in patients with hereditary hemorrhagic telangiectasia may depend on the predominant type and size of shunt as well as on the effects of an abnormal hepatic blood supply. The majority of patients with liver arteriovenous malformation/shunt have a hyperdynamic circulation resulting from arteriovenous shunting, portal venous shunting, or both. Practically all patients with high-output cardiac failure have shunts from the hepatic artery to the hepatic veins. Chronic high flow from such shunts eventually leads to heart failure. Other factors related to diastolic dysfunction such as older age, hypertension, and coronary artery disease may play a part in precipitating heart failure.

Notably, as we found and as others reported—the clinical manifestations of liver involvement overlap and may fluctuate over time, with spontaneous exacerbations and remissions. The reason for spontaneous improvement is unclear. It may depend on changes in shunting patterns or on the presence of reversible conditions (e.g. anemia or atrial fibrillation). In some cases, pregnancy, which causes a hyperdynamic circulatory state, has precipitated heart failure, with resolution after delivery.

Conclusions
A woman with OWR disease was admitted with high output heart failure that was demonstrated by echocardiography as a diastolic dysfunction with a restrictive pattern.

We would like to suggest that high output heart failure could be presented as a diastolic dysfunction and the management could be conservative.

Disclosures
The authors report no conflicts of interest.

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