Acute high output heart failure revealing hereditary hemorrhagic telangiectasia in a pregnant woman

Insuffisance cardiaque aiguë chez une femme enceinte, révélant une maladie de Rendu-Osler

Hereditary hemorrhagic telangiectasia (HHT) is an autosomal dominant disease causing arteriovenous malformations (AVM). Patients with HHT disease have silent or symptomatic AVM most often located in lung, liver, brain and characteristic mucocutaneous telangiectasias [1,2]. Major adverse events in the course of the disease are most of the time hemorrhagic complications. When there is liver involvement, patients may develop heart failure with high cardiac output [3]. There are few data regarding the management of heart failure during pregnancy in HHT. Our case illustrates the success of a conservative management with complete regression of congestive signs, and safe delivery at almost full-term despite severe heart failure.

Case report
A 36-year-old woman was referred for breathlessness and itch at 25 weeks of pregnancy. She had a history of recurrent episistaxis and normal delivery of a healthy child nine years before. On physical examination, telangiectasias were observed on her face, lips, hands, and nose. Blood pressure was 120/85 mmHg. A systolic murmur, pulmonary rales, a palpable liver with hepatosplenomegaly and lower limbs edema were noted. Laboratory results showed moderate anemia (hemoglobin 10 g/dL, normal value > 11 g/dL during pregnancy), elevated BNP (320 pg/mL, normal values < 100 pg/mL), and moderate cholestasis and cytolysis. Thyroid function tests were normal. ECG was in sinus tachycardia at 105 bpm. Echocardiography demonstrated a normal left and right ventricular function, a high cardiac index (6 L/min/m²), a 40 mmHg systolic pulmonary arterial pressure (PAP) evaluated from the spectral continuous-wave Doppler signal of tricuspid regurgitation, and enlarged inferior vena cava without inspiratory collapse (figure 1). Right heart catheterization documented high cardiac index at 6.3 L/min/m², and post-capillary pulmonary hypertension with a 25 mmHg mean PAP and a 20 mmHg capillary wedge pressure. We decided to exclude pulmonary embolism by a helical computed tomography and it showed hepatic artery enlargement (11 mm), hepatic venous enlargement, and multiple arteriovenous malformations (AVM) of the liver (figure 2). A diagnosis of hereditary hemorrhagic telangiectasia (HHT) was established and further supported by demonstration of an ACVR1 mutation. There was no pulmonary or cerebral AVM. The patient was admitted in the intensive care unit, and she was given high dose intravenous loop diuretics (furosemide 240 mg/day). This led to a 12 kg weight loss within 10 days, and disappearance of congestive signs, but persisting dyspnea. No invasive treatment was decided on the liver AVM. She was treated with per os furosemide 160 mg/day and rest. The patient had cesarean delivery at 33 weeks of pregnancy because of reappearance of congestive signs while she was still taking the same high dose of furosemide. She gave birth to a healthy baby. Following delivery, the patient needed transient increase in diuretics while hemodynamic status remained stable. She was discharged from the hospital at day 16 after delivery with complete regression of congestive signs and persisting mild dyspnea. Three months after the delivery, heart failure remained asymptomatic with furosemide 40 mg, and no treatment on the liver was necessary.

Discussion
HHT is an autosomal dominant disease with a prevalence of 1/3000 to 1/40,000, depending on the geographical region. It is most often caused by mutations in the Endoglin or ACVR1 genes. Clinical manifestations are recurrent nosebleeds, characteristic mucocutaneous telangiectasias intensifying later in life. HHT-affected individuals commonly have silent AVM most often located in lung, liver and brain. Consensus clinical diagnosis criteria (Curacao Criteria) [1] and international HHT guidelines have been established for the diagnosis and the prevention of HHT-related complications and the treatment of symptomatic disease [2]. Symptoms related to liver involvement are documented in less than 10% of HHT patients, including high output heart failure of various severity [3], portal hypertension, and biliary necrosis. Liver transplantation should be considered in patient with liver AVM that develop biliary necrosis, heart failure or portal hypertension [4]. The pulmonary vascular complications of HHT include pulmonary arteriovenous malformations, pulmonary hypertension associated with high output heart failure and liver vascular malformations and, finally, pulmonary arterial hypertension secondary to HHT [5,6].

In the context of pregnancy, severe complications occur in about 4% of HHT women, mainly hemorrhages due to AVM and

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hemorrhage in the perinatal period [7,8]. Four cohorts indicate that the majority of HHT pregnancies proceed uneventfully but that there are significant maternal risks [7–11]. There are only few cases of acutely decompensated heart failure due to hepatic involvement during pregnancy. In one case, pregnant woman with previously unknown HHT was admitted for preterm labor and cardiac failure. After cesarean, she improved on congestive signs with medical treatment [12]. In a second case, pregnant woman with HHT had severe cholangitis and progressive liver dysfunction after delivery leading to liver transplantation [13]. In two other cases of HHT discovered during pregnancy with liver involvement, congestive heart failure improved spontaneously after delivery [14,15]. In this case, we decided not to introduce aldosterone inhibitors, or beta-blockers, and to lead pregnancy further with only high dose loops diuretics and rest. It is likely that the patient became symptomatic during the second trimester of pregnancy because the physiologic cardiovascular changes induced by pregnancy (increased intravascular volume, venous distensibility, and increased cardiac output) may contribute to the enlargement of AVM [16]. The physiological increase in cardiac output approaches its maximum of 50% by the end of the second trimester. Because of preexisting high cardiac output due to liver AVM, congestive heart failure may occur during pregnancy in HHT women. This may also explain the spontaneous resolution of symptoms observed in some women after delivery. Therapeutic options for pregnant women with high cardiac output with HHT remain controversial. Pregnancy in women with HHT and heart failure is rare, but must be considered at high risk. The management may depend on the

Figure 1
Transthoracic echocardiography
a: M-Mode on left ventricle (LV) showing end diastolic LV enlargement at 33 mm/m² (normal value < 30 mm/m²); b: high cardiac output calculated from the LV outflow velocity showing a 6.23 L/min/m² cardiac index; c: dilated inferior vena cava, measured at 25 mm without inspiratory collapse; d: continuous-wave Doppler signal of tricuspid regurgitation with a pick at 2.86 m/s corresponding to a 32 mmHg pressure difference between right ventricle and atrium in systole.
severity of the disease before pregnancy and there is a need for further study to help management of heart failure with high cardiac output in pregnant women with HHT.

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References


