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Recurrence of Arterio-Venous Malformations with Life-Threatening Complications in a Pregnant Woman with Hereditary Teleangiectasia

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Hereditary hemorrhagic teleangiectasia (HHT) is an autosomal dominant vascular disorder with incidence of 1 in 2300, characterized by teleangiectasia, arterio-venous malformations, and aneurysms. In this article we presented a case of a 43-year-old woman, diagnosed with HHT and treated with a lobectomy at the age of 5 and with transcatheter coil closure of pulmonary feeding artery at the age of 30, who developed a recurrence of arterio-venous fistulas in the lungs and the brain during pregnancy. The case was complicated by ischemic stroke with hemiparesis. The patient went into premature labor at 35 weeks and the child was delivered by cesarean section. The patient developed severe pulmonary insufficiency with hemothorax post partum, which required transcatheter embolotherapy. During a seven year follow-up, the patient developed progressing intrapulmonary shunt deterioration and hypertrophic pulmonary osteoarthropathy. The case described shows that significant morbidity and mortality may arise during pregnancy from this otherwise relatively benign condition.

Key words: hereditary hemorrhagic teleangiectasia, pregnancy, pulmonary insufficiency

INTRODUCTION

Hemorrhagic hereditary teleangiectasia (HHT), also known as Rendu-Osler-Weber syndrome, is an autosomal dominant vascular disorder with the incidence of 1 in 2300, which makes it a common genetic disease. HHT is characterized by teleangiectases and arterio-venous malformations (AVM) distributed non-randomly in the body. Teleangiectases usually appear in skin, oral and nasal
mucosa, tongue, lips, and the nose. AVMs predominantly occur in the lungs, the central nervous system, the upper gastrointestinal tract, and the liver. The former usually do not manifest before the second or third decade of life; the latter, which are largely congenital, may occur at any age, with life threatening complications due to shunting phenomena and neurologic sequelae. Pregnant women are at particular risk, due to pregnancy-induced changes in the hemodynamic status, which may worsen the course of the disease.

CASE REPORT

The study was performed according to the standards set by the Helsinki Declaration of 1975 regarding the Human Research and was approved by an institutional Ethics Committee. Informed consent was obtained from the patient described in this article.

We present a case of a 43-year-old woman, diagnosed with hereditary hemorrhagic telangiectasia and treated with lobectomy at the age of 5 and with transcatheter coil closure of pulmonary feeding artery at the age of 30, who presented a recurrence of arterio-venous fistulas during pregnancy. The woman was admitted to the hospital with fatigue, dyspnea, and severe right-sided headache in 15 HBD. A 3-dimensional chest computed tomography revealed multiple arterio-venous fistulas (Fig. 1).

A tomography of the head revealed a right parietal mass with surrounding edema and the patient underwent craniotomy. The diagnosis was brain abscess, possibly as a result of recent dental treatment. On the second day after craniotomy, the patient developed a right-sided ischemic stroke with left-sided hemiparesis and ischemia-induced epilepsy. The patient went into a premature labor at 35 weeks and the child was delivered by cesarean section. Seven days after the delivery, the patient developed severe pulmonary insufficiency, was

![Fig. 1. Pulmonary arterio-venous fistulas.](image)
diagnosed with hemothorax, and treated with transcatheter embolotherapy. During the last 7 years of a follow-up, the patient developed progressing intrapulmonary shunt deterioration, teleangiectases on the lips (Fig. 2), AVM in the elbow, hypertrophic pulmonary osteoarthropathy, carbamazepin-induced leukopenia, and digital clubbing (Fig. 3).

DISCUSSION

Hereditary hemorrhagic teleangiectasia was first described by Benjamin Guy Babington in 1865, who called this disorder hereditary epitaxis. Henri Jules Louis Marie Rendu in 1896 differentiated the condition from hemophilia and William Bart Osler in 1901 authored the first comprehensive description of the disease, emphasizing its familial nature. Friderick Parkes Weber in 1907 supplemented the clinical description in a report of a series of cases. HHT has been reported in literature under various names including Babington’s disease, Goldstein’s hematemesis syndrome, Osler’s disease, or the Rendu-Osler-Weber syndrome. Diagnostic criteria of HHT are based on clinical findings and family history. The latter plays a particular role in the diagnosis of genetic disorders as every patient has access to this free, well-proven personalized genomic tool.
The Rendu-Osler-Weber syndrome usually presents with recurrent epitaxis which starts before the age of 10. Multiple teleangiectases on hands, lips, buccal, nasal, and GI mucosa are sources of substantial bleeding, but the onset is generally 5-30 years later than that for epitaxis. In contrast, symptoms from arterio-venous malformations may arise unexpectedly or insidiously at any age, mainly as a consequence of shunting of blood, thrombosis, and emboli rather than a direct hemorrhage. The characteristic clinical presentation of pulmonary arterio-venous malformations (PAVMs) is respiratory failure with cyanosis, exercise intolerance, polycystemia, and clubbing. The second most common visceral location of AVMs is the central nervous system, where they present at any age with seizures, headache, stroke, brain abscess, or intracranial hemorrhage (2, 3).

Although uncommon (occur in 1% of patients with HHT) spinal AVMs manifest as subarachnoid hemorrhage, progressive myelopathy, radicular pain, or sphincter disturbances. Such disorders may complicate the management of laboring women after epidural anesthesia (4). The prevalence of hepatic AVMs is up to 30%. These are most often silent, but occasionally manifest with life-threatening complications, such as a high-output heart failure, portal hypertension, biliary disease, or portosystemic encephalopathy (5, 6).

Pregnant women are at a particular risk of serious complications. Due to hemodynamic changes caused by pregnancy, such as increased cardiac output and intravascular volume, and decreased vascular resistance, pregnant women are at higher risk of hemorrhage form teleangiectases and AVMs. The state of hypercoagulability in pregnancy also increases the risk of thrombus formation. As cesarean section is an elective way to terminate pregnancy in women with HHT, the additional risk of amniotic fluid or air embolism is present. The emboli may go to the lungs and cause normal vessels to constrict, increasing the flow through PAVMs, or may traverse malformation and produce paradoxical emboli in the systemic circulation (7-9). Post partum surveillance is obligatory in these patients, as they may deteriorate also after delivery. The most hazardous are the first two weeks after delivery, when plasma expansion and anemia of pregnancy are substantial (9).

As HHT is a genetic disorder a surveillance and screening of family members of affected individuals is recommended. Early diagnosis and treatment may prevent both chronic and acute complications and should be available to all affected individuals (10). A development of new genomic tools gives a possibility of early molecular diagnosis. Presently, the Rendu-Osler-Weber syndrome is

<table>
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<th>Diagnostic Criteria of hereditary hemorrhagic teleangiectasia.</th>
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<td>HHT is diagnosed if 3 or more of the following criteria are met (1):</td>
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<td>- Epitaxis</td>
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<td>- Teleangiectasia at characteristic sides (tongue, lips, oral cavity, fingers, nose, GI mucosa)</td>
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<tr>
<td>- Visceral lesions including pulmonary, cerebral, gastrointestinal, hepatic, spinal AVMs</td>
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<tr>
<td>- Family history of the first degree relative with HHT by these criteria</td>
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Table 1
linked to two well characterized loci which are responsible for about 70% of HHT cases. Genetic studies of affected families identified genes for two receptors in the TGFβ family: endoglin (ENG) and activin receptor-like kinase 1 (ALK1) whose mutations are responsible for HHT 1 and HHT 2 respectively (10). New mutations have been found on the long arm of chromosome 5 and the short arm of chromosome 7 (11, 12). Although there are some genotype-phenotype correlations, ENG and ALK1 mutations result in similar phenotypes. Therefore, it is not possible to diagnose subtypes of HHT on clinical grounds. To-date, no correlation has been found between the specific ENG or ALK1 mutation and the severity of phenotype.

In conclusion, early diagnosis and treatment combined with watchful surveillance of affected individuals, especially those at higher risk, such as pregnant women, are crucial in the management of HHT. It is a matter of future research to find more about genotype–phenotype correlation, which could change the natural course of the disease.

Conflicts of interest: The authors had no conflicts of interest to declare in relation to this article.

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Received: June 16, 2008.
Accepted: August 25, 2008.

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