Treatment of Hereditary Hemorrhagic Telangiectasia–Related Epistaxis

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KEYWORDS

• Hereditary hemorrhagic telangiectasia (HHT) • Osler-Weber-Rendu • Epistaxis
• Septodermoplasty • Laser photocoagulation • Young's procedure • Bevacizumab

KEY LEARNING POINTS

At the end of this article, the reader will:

- Know how to diagnose a patient with HHT and discover the key examination findings.
- Know what additional workup is required in a patient with HHT.
- Understand the Epistaxis Severity Score and how it is used.
- Know the nonsurgical options for treatment of mild or moderate epistaxis related to HHT.
- Know the surgical options available for treatment of HHT.
- Understand the role of Avastin (bevacizumab) in treatment of HHT.

Video content accompanies this article at http://www.oto.theclinics.com

INTRODUCTION

HHT is a rare, autosomal dominant disease with prevalence of 1:5000 characterized by formation of multiple mucocutaneous telangiectasias as well as formation of AVMs within the pulmonary, cerebral, and gastrointestinal vasculature. Patients are particularly prone to formation of telangiectasias within the sinonasal mucosa, and recurrent, spontaneous epistaxis is the most common symptom at time of presentation. More than half of patients with HHT will develop troublesome epistaxis by the third decade of life, and severity of epistaxis increases with age. More than 90% of

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What is HHT?

- HHT is hereditary hemorrhagic telangiectasia, also known as Osler-Weber-Rendu disease
- Autosomal dominant inheritance, approximately 1:5000 prevalence
- Recurrent, spontaneous epistaxis is most common presenting symptom
- Spontaneous formation of multiple mucocutaneous telangiectasias
- Patients are also at risk for multiorgan vascular dysplasia with formation of arteriovenous malformations (AVMs) in the brain, lungs, and gastrointestinal (GI) tract

patients with HHT experience recurrent epistaxis at some point in life. Severity and frequency of epistaxis varies widely between patients, from mild, occasional epistaxis to severe, life-threatening nosebleeds. In general, severity of epistaxis increases with age.[1]

ETIOLOGY

What causes formation of telangiectasias and AVMs?

- Mutations in genes associated with transforming growth factor-beta (TGF-β) superfamily signaling pathway
- Dysregulation of vascular endothelial tissue remodeling results in weakened integrity of vessel wall leading to formation of telangiectasias and AVMs
- Three gene mutations have been identified: endoglin (ENG), activin receptor-like kinase (ACVRL1 or ALK1), and MADH4

Various members of the transforming growth factor (TGF)-β superfamily have been implicated in the pathogenesis of HHT. Remodeling of the vascular endothelium within mucosal vessels occurs in a dysregulated fashion, leading to loss of elasticity and dilation of arteriole-venule communications. As a result, fragile and thin-walled telangiectasias form within the nasal cavity in regions with high airflow prone to dryness or repeated mechanical trauma. Telangiectasias tend to congregate along the anterior septum, head of inferior turbinates, anterior lateral nasal wall, and anterior nasal floor. Recurrent and spontaneous epistaxis results from traumatic rupture of the ectatic vessel wall lacking contractile and elastic elements. Elevated plasma levels of vascular endothelial growth factor (VEGF) are present in patients with HHT, which has provided rationale for treatment with VEGF inhibitors in certain cases.[2]

Two distinct mutations account for 90% of cases of HHT: ENG mutation is known at HHT1, and ACVRL1 mutation is known as HHT2.[3] Another gene, MADH4 (mothers against decapentaplegic homolog 4) has been implicated in both juvenile polyposis and a small proportion of cases of HHT.[4] Recently, mutation in bone morphogenetic protein-9 (BMP9) has been described as resulting in a vascular anomaly syndrome with phenotypic similarity to HHT.[5]

Distinct phenotypic variations have been described in HHT1 and HHT2. Patients with HHT1 are more likely to present with epistaxis earlier in life as well as pulmonary AVMs. Patients with HHT2 are more likely to develop hepatic AVMs.[6]