Initial experience of a hereditary hemorrhagic telangiectasia center of excellence

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Abstract

Our objectives in reviewing the initial experience of a hereditary hemorrhagic telangiectasia center of excellence (HHT COE) were to better understand the interventions being performed in the comprehensive care of these patients and to present the early data as a reference for other tertiary centers considering starting an HHT COE. We conducted a retrospective review of consecutive patients referred to our newly developed HHT COE for evaluation and treatment between May 2010 and June 2013. Clinical presentation, otolaryngologic treatments, and other operative interventions were analyzed. One hundred forty-four of the 198 patients (73%) evaluated at the HHT COE had definite HHT based on the Curaçao diagnostic criteria, with 20 additional patients possibly having HHT and undergoing further evaluation to confirm the diagnosis. Sixteen of the 31 patients (52%) referred to otolaryngology required intervention in the operating room for epistaxis. Seventy-two of the 164 (44%) patients with definite or possible HHT required other interventions for internal organ arteriovenous malformations (AVMs), with interventional radiology embolization of pulmonary AVMs being the most common procedure. An HHT COE is important in providing comprehensive care for patients with this rare disease, which has significant clinical sequelae. Having an HHT COE allows for early screening and subspecialty referral within a system of specialists experienced in preventing the morbidity and mortality associated with severe epistaxis and internal organ AVMs.

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Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as *Osler-Weber-Rendu disease,* is an autosomal dominant disease with an estimated prevalence of 1 in 5,000 to 10,000 persons.[1] Primary care physicians are usually the first to evaluate these patients. The most common symptom is epistaxis, and the most common sign is the presence of mucocutaneous telangiectasias, most characteristically in the nasal cavity and on the tongue, lips, and oral mucosa (figure).[2] In addition to affecting the head and neck, HHT is associated with arteriovenous malformations (AVMs) elsewhere in the body, including the brain (15 to 23%), lung (20 to 50%), gastrointestinal (GI) tract (25 to 80%), and liver (32 to 78%).[3-6]

Because of the systemic nature of the disease, medical and surgical care for patients with HHT require a lifelong multidisciplinary team approach. A referral to otolaryngology is often done initially, as recurrent epistaxis occurs in more than 90% of patients and is often the initial symptom prompting medical evaluation.[2] More than 60% of patients with HHT also have facial and oral telangiectasias that can be a source of bleeding requiring intervention.[2]

In addition to the common head and neck manifestations, patients can suffer devastating consequences from visceral AVMs, such as intracranial hemorrhage and stroke, high-output cardiac failure, cerebral abscesses, and massive hemoptysis.[4,6,7] Because of the multidisciplinary care required and the potential for significant morbidity, HHT centers of excellence (HHT COE) have been established to provide better

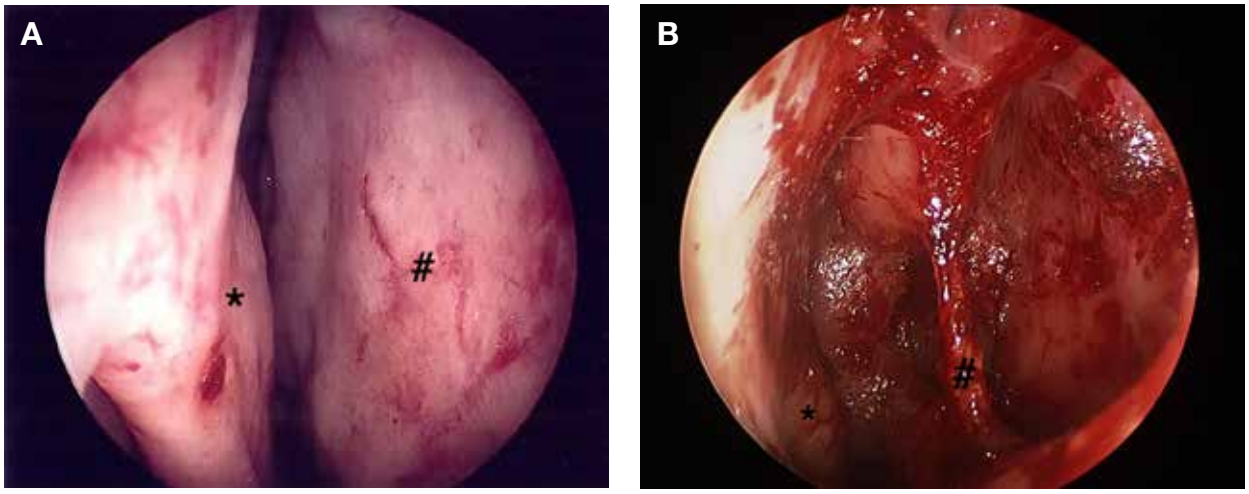

Figure. ***A:*** *Nasal endoscopic image demonstrates multiple telangiectasias along the right lateral nasal wall, turbinates, and septum (* = right inferior turbinate; # = septum).* ***B:*** *This image reveals multiple nasal mucosal telangiectasias and a large septal perforation (* = right inferior turbinate; # = posterior septum).*

care and follow-up for these patients, as well as to treat their vascular malformations before complications occur.

An HHT COE is composed of physicians from multiple fields including otolaryngology, interventional radiology, cardiology, pulmonology, neurosurgery, gastroenterology, hematology, and genetics. Having dedicated providers from multiple specialties is critical when applying to become a COE through the HHT Foundation (**http://hht.org**). Having a dedicated center of experts expedites early subspecialty referral and prompt treatment, and allows coordinated follow-up visits among various specialties.

Since many patients do not become symptomatic until after age 10, an HHT COE also facilitates genetic screening of first-degree relatives to establish early care.[2] Screening with computed tomography (CT), magnetic resonance imaging (MRI), and echocardiography allows the diagnosis of AVMs before the onset of symptoms. Depending on presentation, medical management, embolization, or surgery can be performed to treat significant pulmonary, cerebral, or intra-abdominal AVMs to prevent devastating morbidity and mortality from the vascular malformations.[6,8]

To better care for patients with HHT in the southwestern United States, an HHT COE was established at the University of California, Los Angeles (UCLA) in May 2010 as the 10th COE in the United States. Our objectives in reviewing the initial experience of an HHT COE are to better understand the interventions being performed in the comprehensive care of these patients and to present the early data as a reference for other tertiary centers considering starting an HHT COE.

Patients and methods

Our study was approved by the Institutional Review Board of UCLA. We performed a retrospective review of all patients referred to our HHT COE from its inception in May 2010 through June 2013. Clinical presentation, radiographic imaging, family history, otolaryngologic treatments, and other operative interventions were analyzed.

Patients were initially diagnosed as having definite, possible, or unlikely HHT based on the Curaçao clinical criteria.[9] The 4 Curaçao clinical criteria include: (1) epistaxis, (2) skin or mucocutaneous telangiectasias, (3) other systemic telangiectasias or AVMs such as in lung, brain, or gastrointestinal tract, and (4) family history of HHT in a first-degree relative. A patient is considered to definitely have HHT if at least 3 of the 4 criteria are met. A patient with 2 of the 4 criteria is considered to have possible HHT and to require further workup and follow-up. A patient having only 1 of the 4 criteria is unlikely to have HHT.

Results

Based on the Curaçao clinical criteria, 144 of the 198 (73%) patients referred to and evaluated at our HHT COE over the 3-year period were ultimately diagnosed with HHT. Twenty of these patients met only 2 Curaçao clinical criteria and needed further evaluation before the diagnosis was made, such as with imaging to identify internal organ AVMs. Thirty-four patients had only 1 of the 4 criteria.

Of the 144 patients with confirmed HHT, 31 (22%) were referred to otolaryngology for further management of recurrent epistaxis or persistent oral bleeding. Of these 31 patients, 16 (52%) needed intervention in the

Table. Non-otolaryngology interventions (n = 72)

Intervention	Number of patients
IR embolization of:	
Pulmonary AVM	57
Cerebral AVM	4
Liver AVM	1
Nasal AVM	1
Pelvic AVM	1
Resection of pulmonary AVM	2
Neurosurgical clipping of cerebral aneurysm	2
Brain radiation	7
Excision of cerebral AVM	1
Partial colectomy	1
Bronchoscopy and laser coagulation	1
Upper endoscopy and laser coagulation	2

Key: IR = interventional radiology; AVM = arteriovenous malformation.

operating room, with a mean time to surgery of 3.7 months (range 0 to 11.4).

Fifteen of the 16 patients had potassium titanyl phosphate (KTP) laser photocoagulation treatments for symptomatic nasal telangiectasias, and less commonly, oral telangiectasias. Eleven of these 16 patients had multiple treatments over the 3-year year period examined, with a mean time between laser treatments of 8.3 months (range: 3.5 to 17). The sixteenth patient did not have KTP treatments but had excision of an enlarged telangiectasia from the hard palate for repeated acute hemorrhages that previously required transfusion. She had significant improvement after surgery without recurrence of the lesion for more than a year.

In addition to otolaryngologic interventions, 72 of the 164 (44%) patients with definite or possible HHT were treated for AVMs in other locations or are being followed closely with radiologic imaging for previously treated internal organ AVMs. Several of these patients had interventions for AVMs at multiple locations in the body (table). These interventions included embolization, resection, and radiation therapy for AVMs in the brain, and embolization or surgery for AVMs in the lung or abdomen.

Discussion

A dedicated center composed of physicians from multiple specialties with experience in HHT allows for early screening, diagnosis, and treatment of patients with this chronic and often debilitating disease. The director of the HHT COE can be a physician of any specialty but must be willing to take a primary care role in the management of HHT in these patients. In addition to routine screening and treatment of visceral AVMs, patients often require extensive counseling on the significance and natural history of their disease, nonoperative management of epistaxis and GI bleeding, and advice on lifestyle modification. This physician must also have a support network of subspecialty physicians to evaluate and treat HHT-specific problems rapidly.

A patient referred to the HHT COE is first seen and examined by the center director, who at our institution is an interventional radiologist. The center director obtains and evaluates all relevant imaging, determines epistaxis severity using a standardized instrument (the epistaxis severity score),[10] and evaluates for other sources of bleeding. Subspecialty referrals are then made as needed.

Early radiologic screening and subsequent treatment of visceral AVMs is performed to prevent catastrophic complications such as stroke, hemorrhage, and brain abscess. After initial evaluation and treatment, the center director and the relevant subspecialist experts follow the patient at regular intervals with history and physical examination, imaging, and continued treatment as needed.

A major benefit of a recognized HHT COE includes easier access to subspecialist providers with experience and familiarity in treating each aspect of the chronic disease. At our HHT COE, patients receive early education from the otolaryngologists on conservative treatments for epistaxis, such as humidification and nasal lubricants.[11,12]

When conservative measures fail, otolaryngologists play a key role in caring for patients' nasal and oral bleeding episodes. In 3 years, 22% (31/144) of patients with confirmed HHT managed at the HHT COE have been referred to otolaryngology, with 16 (52%) of these patients requiring surgery. The most common otolaryngologic intervention performed at our institution is photocoagulation with a KTP laser, which was done in 15 (48%) of the patients referred for refractory epistaxis. Eleven patients required repeat KTP laser treatments over the 3 years, with an average of 8.3 months between treatments. The most common indication for KTP laser treatment was the patient's desire for more aggressive treatment of recurrent epistaxis.

Other otolaryngologic interventions that have been reported to be successful in treating epistaxis include bipolar cauterization, coblation, sclerotherapy, and submucosal bevacizumab injections.[12-14] More aggressive surgical treatments include septodermoplasty and Young's procedure (nasal closure). One drawback with

septodermoplasty is that return of telangiectasias occurs within 2 years. Also, bleeding can still occur from other sites in the nasal cavity not addressed with the surgery, including the turbinates and nasal floor.[12] Young's procedure prevents nasal airflow and improves epistaxis, but results in obligate mouth breathing and loss of olfaction.[12]

In addition to head and neck manifestations of HHT, the lungs are the most common internal organ site for AVMs, with pulmonary lesions occurring in 20 to 50% of patients.[4,6,8] Pulmonary AVMs rarely regress spontaneously and continue to increase in size over time. If not screened, monitored, and treated, patients can suffer from right-to-left shunting, leading to dyspnea, hemoptysis, strokes, brain abscesses, and hemorrhages.[6,8,15] Many patients with HHT have multiple pulmonary AVMs, and mortality from untreated symptomatic patients has been reported to be about 20%.[8,15]

At our institution, all patients with suspected HHT undergo screening for pulmonary AVMs with an ultrasound bubble study or CT of the chest. If an AVM of significant size is found (feeding artery >2 mm), patients then undergo angiography and embolization of the pulmonary AVMs and are followed every 5 years with repeat CT scans of the chest. With our early screening process, 71 of the 164 (43%) patients with possible or definite HHT were found to have pulmonary AVMs, including 57 of the 71 (80%) who were subsequently treated with intervention radiology embolization and 2 (3%) with resection (table).

In addition to pulmonary imaging, all patients with suspected HHT undergo MRI of the brain with contrast. Brain AVMs are thought to affect up to 23% of HHT patients, with potential symptoms that include headache, transient ischemic attacks, seizures, strokes, and hemorrhages.[3,6,14] Twenty-three of our 164 (14%) patients with possible or definite HHT had evidence of brain AVMs on imaging, and 14 of the 23 (61%) were subsequently treated (table).

Conclusion

The development of an HHT COE is important in providing comprehensive care for patients with HHT. An HHT COE consists of a multidisciplinary team of providers with experience treating the disease. Our center involves specialists from otolaryngology, interventional radiology, neurology, pulmonology, cardiology, hematology, dermatology, and gastroenterology, as well as a genetics counselor and a center nurse who helps patients coordinate care between specialists and assists with research. Early screening by experienced providers likely reduces the morbidity and mortality associated with severe epistaxis and internal organ AVMs, as having a dedicated center allows for prompt subspecialist referral and treatments.[8]

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