Lesson 302: PreAnesthetic Considerations for a Patient With Hereditary Hemorrhagic Telangiectasia

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Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before the termination date below. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours
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Professional Gaps

Hereditary hemorrhagic telangiectasia (HHT) is an uncommon familial multisystem vascular disorder that affects patients of all ages. Patients with HHT develop abnormal blood vessels that are predisposed to hemorrhage and other complications. Often these complications require surgical intervention. Knowledge of the pathophysiology and anesthetic issues specific to the disease allows the anesthesiologist to anticipate challenging management concerns and guide perioperative management, thereby decreasing morbidity and mortality in this patient population.

Learning Objectives

At the end of this activity, the participant should be able to:

1. Describe the pathophysiology of HHT.
2. List the most common clinical features of HHT.
3. Identify the most frequently involved organ systems.
4. Describe diagnostic criteria.
5. Become aware of treatment options.
7. List potential perioperative complications.
8. Specify anesthetic problems associated with managing patients with HHT.
9. Identify important components of the preoperative evaluation.
10. Develop an anesthetic plan for a patient with HHT.
Case History

A 68-year-old man presented with recurrent epistaxis for more than 40 years. He had undergone septodermoplasty approximately 18 months before the latest admission. The patient experienced relief of symptoms for 15 months before again developing epistaxis requiring emergency surgery. Intraoperative examination of his nasal cavity revealed newly developed telangiectatic vessels in the superior portion of the nasal vault, as well as ingrowth of new vessels into the septodermoplasty. Laser coagulation therapy and bevacizumab (an anti-angiogenesis chemotherapeutic agent that targets a protein found in many cancer cell types) were used to control acute bleeding, but were ineffective in providing long-term relief. As a result, the patient was scheduled for repeat septodermoplasty. Preoperative assessment identified a long history of anemia that required iron supplementation and multiple transfusions. The patient also reported a history of bilateral plantar bleeding, as well as multiple telangiectases of the nose, eyelids, lips, outer ears, and feet. He had a history of embolization to control bleeding colonic telangiectases and reported a magnetic resonance imaging (MRI) study that revealed no intracranial pathology. Anesthetic records from his most recent treatment, with laser coagulation therapy, were reviewed and revealed an episode of epistaxis occurring during induction of anesthesia.

Additional medical conditions identified during the preoperative evaluation included well-controlled hypertension and chronic atrial fibrillation. His home medication list was limited to lisinopril (10 mg once daily) and metoprolol (50 mg twice daily). The patient was 73 inches tall and weighed 138 kg. Vital signs were all within normal limits. His oxygen saturation was 98% on room air. Preoperative complete blood count revealed a hematocrit of 32% and a platelet count of 308 k/mcL. Basic metabolic panel and coagulation studies were within normal limits.

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Hereditary hemorrhagic telangiectasia (HHT) is often referred to as Osler-Weber-Rendu syndrome, derived from the names of Sir William Osler, Henri Rendu, and Frederick Weber, who described this familial multisystem vascular disease in the late 19th century.1 Of note, Benjamin Babington, inventor of the laryngoscope, was among the first clinicians to describe the most common features of HHT.2 The estimated prevalence is 1:5,000.3

HHT is a genetic disorder inherited as an autosomal dominant trait. The majority of cases are associated with an abnormal gene on either chromosome 9 or 12. Both of these genes code for a protein involved in angiogenesis. Inheritance of a single gene mutation results in the formation of abnormal blood vessels in the skin, mucous membranes, and various organs. These vascular malformations lack capillaries and thus contain a direct communication between the high-pressure arterial systems and the thin-walled low-pressure venous system. High pressure causes dilatation of the venules, forming fragile masses of thin convoluted vessels with an increased risk for rupture and hemorrhage.4 Only a small percentage of blood vessels are abnormal in patients with HHT. Furthermore, manifestations of HHT may not develop until later in life. Malformations vary in size and are termed telangiectasia if they involve small blood vessels and arteriovenous malformations (AVMs) when they involve larger blood vessels. The location of these vascular malformations in the body dictates the problems patients encounter.
Clinical Features and Manifestations

Telangiectases tend to develop over time in the skin, especially on the face and hands, and mucous membranes that line the naso- and oropharyngeal cavities and the gastrointestinal (GI) and respiratory tracts. These vascular anomalies often become more numerous with increasing age. They present as small red and purplish blanchable spots on physical exam, laryngoscopy, or endoscopy. Telangiectasia located close to the surface of the skin and mucous membranes tend to rupture easily with bleeding following even slight trauma. Spontaneous and recurrent epistaxis is typically the earliest and most common (>90%) manifestation of HHT. An estimated 25% of HHT patients develop symptoms of GI bleeding. Epistaxis and GI bleeding collectively contribute to a high incidence of iron-deficiency anemia.

AVMs often occur in internal organs such as the lungs (≤50%), liver (>30%), and brain (≤20%). These larger vascular malformations, which typically are congenital and present at birth, can enlarge over time. Bleeding AVMs can create severe, sometimes life-threatening problems. Pulmonary AVM(s) create a right-to-left shunt with a risk for subsequent hypoxemia and paradoxical embolization and/or cerebrovascular accident (CVA). Rupture of a lung AVM can present with hemoptysis or hemotherax. The majority of AVMs within the liver remain asymptomatic. However, depending on the size and connections they form between blood vessels, hepatic AVMs can in rare cases produce high-output congestive heart failure, portal hypertension, hepatic encephalopathy, or liver failure. Cerebral AVMs, which also tend to remain clinically silent, can induce headaches, seizures, CVAs, and/or subarachnoid hemorrhage when ruptured. Women with HHT who are pregnant and have untreated pulmonary AVMs are at increased risk for rupture secondary to increased peripartum blood volume, cardiac output, and vascular distensibility.

<table>
<thead>
<tr>
<th>Table 1: International Consensus Diagnostic Criteria for HHT</th>
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<tbody>
<tr>
<td><strong>Epistaxis</strong>—spontaneous and recurrent</td>
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<tr>
<td><strong>Telangiectases</strong>—multiple at characteristic sites (face, lips, oral cavity, fingers, nose)</td>
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<tr>
<td><strong>Visceral arteriovenous malformations</strong> (lung, brain, liver, spinal) or gastrointestinal telangiectases</td>
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<tr>
<td><strong>Family history</strong>—first-degree relative with HHT according to these criteria</td>
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<tr>
<td>HHT diagnosis is definite if 3 criteria are present; suspected if 2 criteria are present; unlikely if less than 2 criteria are present.</td>
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Diagnosis

Diagnosis of HHT involves criteria summarized more than a decade ago as the International Consensus Diagnostic Criteria for HHT (Table 1). The disorder is highly variable in severity. Affected children may not exhibit all the signs and/or symptoms of HHT, thus diagnostic status may change during the life span. Genetic testing is available but is complex and should be preceded by clinical confirmation.

Screening

Screening recommendations recently have been developed to help clinicians detect cerebral and pulmonary AVMs (PAVMs) before the development of complications. Patients with definite or
suspected HHT should have an MRI with and without gadolinium in childhood, and again as an adult to screen for cerebral AVMs. Screening for PAVMs should begin early in childhood with yearly pulse oximetry measurements obtained in both the supine and sitting positions. Most PAVMs are located in the lower lobes; therefore, these patients often have a higher SpO₂ when supine than when sitting. At age 10 years, a contrast echocardiogram should be obtained to screen for pulmonary shunting. Appearance of bubble contrast in the left heart after 3 cardiac cycles is consistent with PAVMs. The bubble contrast will pass to the left heart much faster with a cardiac shunt. Any patient with a consistent SpO₂ less than 97% or a positive contrast echocardiography test requires a chest computed tomography angiogram to confirm the presence of a PAVM and to determine if its size is sufficient to warrant treatment.

**Treatment**

Treatment for HHT is directed either at relief from symptoms or the prevention of serious complications. No effective therapy currently is available to prevent development of vascular malformations. The recommended treatment options for a telangiectasia and/or AVM depend on both its size and location in the body.

**Table 2: Treatment Options for Common Complications**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Treatment Options</th>
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<tbody>
<tr>
<td>Iron-deficiency anemia</td>
<td>Iron supplementation</td>
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<td></td>
<td>Red blood cell transfusion</td>
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<tr>
<td>Skin telangiectasia (symptomatic or cosmetic)</td>
<td>Laser coagulation therapy</td>
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<tr>
<td>Severe and/or recurrent epistaxis</td>
<td>Keep nasal mucosa moist (humidified air, nasal lubricants)</td>
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<td></td>
<td>Hormonal therapy (estrogens)</td>
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<td></td>
<td>External pressure and/or nasal cavity packing</td>
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<tr>
<td></td>
<td>Laser coagulation therapy</td>
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<tr>
<td></td>
<td>Septodermoplasty</td>
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<tr>
<td></td>
<td>Embolization (emergency control)</td>
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<tr>
<td>Severe and/or recurrent GI bleed</td>
<td>Endoscopic ablation</td>
</tr>
<tr>
<td>Lung AVM (symptomatic and/or feeding vessel ≥3 mm diameter)</td>
<td>Embolization</td>
</tr>
<tr>
<td>Cerebral AVM (≥1 cm diameter)</td>
<td>Embolization</td>
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<tr>
<td></td>
<td>Neurovascular surgery</td>
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<tr>
<td></td>
<td>Stereotactic radiosurgery</td>
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<tr>
<td>Symptomatic liver AVM (CHF or liver failure)</td>
<td>Varies on case-by-case basis</td>
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<tr>
<td></td>
<td>Liver transplantation</td>
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</tbody>
</table>

*AVM, arteriovenous malformation; CHF, congestive heart failure; GI, gastrointestinal*
Anesthetic Management

The vascular anomalies characteristic of HHT are not only prone to rupture but also may produce severe complications from blood shunting. Knowledge of several important anesthetic considerations will help guide perioperative management. Care should be taken to minimize trauma during mask ventilation, laryngoscopy, and endotracheal intubation. Laryngoscopy may induce bleeding; therefore, readily available suction is a key component of induction. Rapid sequence induction may avoid the need for mask ventilation. Instrumentation of the nasal cavity should be avoided if possible, with obvious preference given for placement of an oral endotracheal tube (ETT). Use of a smaller lubricated ETT, with minimally occlusive cuff pressure to decrease mucosal trauma, should be considered. Nasopharyngeal airways also should be avoided due to increased trauma to the mucosa. Use of humidified air during mechanical ventilation may help prevent drying of the respiratory tract mucous membranes that have an increased risk for bleeding.

Given the abnormal arterial connection and the absence of normal vessel wall contractile elements, bleeding from telangiectases can be brisk and difficult to control. A preoperative complete blood count often reveals findings consistent with an iron-deficiency anemia. Given the high frequency of preexisting anemia and increased risk for bleeding during airway manipulation, it is important to communicate early with the blood bank to ensure availability of products before surgery. These patients often have a history of red blood cell transfusions and therefore are at increased risk for alloimmunization and transfusion reactions. The presence of alloantibodies complicate testing for red blood cell compatibility. As a result, early antibody screening and cross-matching is preferred. Use of leuko-reduced blood products may reduce the development of alloimmunization. Anticoagulants should be used with caution. Antifibrinolytic therapy such as tranexamic acid and aminocaproic acid may decrease transfusion needs. The recurrent bleeding that occurs in HHT is caused by vessel wall abnormalities as opposed to a coagulopathy; therefore, patients typically have a normal preoperative platelet count, bleeding time, and prothrombin and partial thromboplastin times.

AVMs in the lungs are the most common cause of a serious acute complication in patients with HHT. Complications with PAVMs tend to arise from shunting of blood rather than hemorrhage. Shunting of blood through PAVMs effectively bypasses the capillary bed, which typically acts as a filter for impurities (thrombus, bacteria, air bubbles, etc.), and places these patients at risk for paradoxical embolism. Due to the high frequency of PAVMs in patients with HHT, and their potentially devastating complications, antibiotic prophylaxis in accordance with American Heart Association (AHA) guidelines is recommended before dental and invasive procedures to help prevent brain/systemic abscess formation. All IV fluids should be bubble-free to avoid air emboli. Micropore filters help remove microaggregates during transfusion therapy. PAVMs also can result in hypoxemia depending on the magnitude of the shunt fraction. Positive pressure ventilation can increase alveolar-arterial oxygen gradients. Therefore, maintenance of spontaneous ventilation may optimize oxygenation in the presence of PAVM(s). A preoperative contrast echocardiogram is important to screen for PAVMs.

Cerebral AVM(s) affect an estimated 10% of patients with HHT and usually are asymptomatic. Rupture can result in intracerebral hemorrhage and/or subarachnoid hemorrhage and possibly a hemorrhagic CVA. These vascular malformations generally represent high-flow, low-resistance shunts when vascular intramural pressure is less than systemic arterial pressure, and rupture does not appear to be clinically associated with acute or chronic hypertensive episodes. However, high-pressure arterial flow in cerebral AVMs results in dilatation of the venous component of these malformations with subsequent increased risk for developing aneurysms. Hypertension is a widely accepted risk factor for aneurysm
rupture. It seems reasonable to implement measures to avoid sudden increases in systemic arterial blood pressure that can increase aneurysm transmural pressure and potentially cause rupture. Often this aim includes achieving an adequate depth of anesthesia before endotracheal intubation, as well as use of adjunctive agents such as opioids and/or lidocaine, to further attenuate the sympathetic response to laryngoscopy, tracheal intubation, and tracheal extubation. Furthermore, the low-resistance characteristic of cerebral AVMs can divert blood flow away from adjacent brain tissue (“steal phenomenon”) and can lead to ischemia. Avoidance of hypotension and maintenance of normal or even increased systemic arterial blood pressure may optimize perfusion of adjacent tissues. Hyperventilation can potentially shunt additional blood flow to the low-resistance malformation, and therefore, maintenance of normocarbia is ideal for these patients.13

Spinal AVMs develop in 1% to 2% of patients with HHT and almost always cause neurologic symptoms.4 Common symptoms suggesting a possible spinal AVM include back pain, sensory loss, and weakness in the lower extremities. If the preoperative assessment reveals the presence of any concerning neurologic symptoms, it is reasonable to obtain an MRI scan to exclude a spinal AVM before neuraxial anesthesia.

Management of the Case Presented

The patient had a recent negative MRI for intracranial pathology. A previous contrast echocardiogram was reviewed with no evidence of PAVMs. Basic metabolic panel and coagulation studies were within normal limits. Red blood cell compatibility testing revealed a positive antibody screen. A formal crossmatch identified 2 compatible units of packed red blood cells before surgery. A large-bore peripheral IV catheter was inserted and a lactated Ringer’s infusion was started. Care was taken to ensure all IV fluids were free of bubbles. The patient was premedicated in the holding area with 2 mg of IV midazolam.

The patient was transferred to the operating room and standard monitors were attached in accordance with guidelines from the American Society of Anesthesiologists. He was preoxygenated with care taken to minimize pressure over the nasal bridge. A mild bleed was noted from his nasal pharynx. Rapid sequence induction was performed with atraumatic placement of a lubricated 7.0-mm ETT. The endotracheal cuff was inflated with minimal occlusive pressure. Another large-bore peripheral IV catheter was obtained for additional access. He received antibiotic prophylaxis before incision, according to AHA guidelines. The otolaryngologist performed a repeat septodermoplasty in which the offending nasal mucosa was scraped away and a split-thickness skin graft was applied to the nasal cavity. Maintenance of anesthesia was facilitated with sevoflurane. The patient remained hemodynamically stable throughout the case with an estimated blood loss of 600 mL. He received approximately 2 L of crystalloids and 2 units of packed red blood cells administered using micropore filters. The patient’s trachea was extubated at the conclusion of the case and he was transported to the postanesthesia care unit in stable condition. He was monitored overnight as an inpatient and discharged home the following day without incident.

Summary

Approximately 1.2 million people worldwide have HHT, making the condition uncommon but not rare. These patients develop abnormal blood vessels that often involve multiple organ systems. Complications are common and often require surgical management. Patients with HHT therefore are likely to undergo multiple operations throughout their lifetimes. Perioperative care of patients with
HHT can be especially challenging for the anesthesiologist. Anticipation and preparation for all potential perioperative problems is essential in avoiding life-threatening complications in these patients.

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REFERENCES

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**Post-test**

1. Hereditary hemorrhagic telangiectasia (HHT) is a genetic disease associated with an abnormal gene involved in _____.
   a. cellular differentiation
   b. factor V synthesis
   c. angiogenesis
   d. collagen synthesis

2. Vascular anomalies can develop in which of the following organ systems of patients with HHT?
   a. Skin
   b. Pulmonary
   c. Central nervous system
   d. All of the above

3. The most common manifestation of HHT is _____.
   a. anemia
   b. gastrointestinal (GI) bleeding
   c. hemoptysis
   d. epistaxis

4. According to the International Consensus Diagnostic Criteria for HHT, _____ is consistent with a definite diagnosis of HHT.
   a. family history of first-degree relative with HHT and recurrent epistaxis
   b. history of multiple colonic telangiectases and several telangiectases over the face
   c. history of recurrent epistaxis, telangiectases on the fingers, and a cerebral arteriovenous malformation (AVM)
   d. multiple facial telangiectases and family history of first-degree relative with HHT

5. Potential problems encountered during the anesthetic management of a patient with HHT include _____.
   a. airway bleeding during mask ventilation and endotracheal intubation
   b. epistaxis refractory to treatment with nasal phenylephrine
   c. hypoxemia from pulmonary shunting
   d. all of the above
6. Match the common complication with its recommended treatment option
   a. Recurrent GI bleed → hormonal therapy
   b. Iron-deficiency anemia → iron supplementation
   c. Cerebral AVM (<1cm in diameter) → neurovascular surgery
   d. Lung AVM → estrogen

7. Screening recommendations for patients with definite or suspected HHT include _____.
   a. MRI with/without gadolinium in childhood and again as adult
   b. yearly pulse oximetry measurements obtained in both supine and sitting positions
   c. contrast echocardiogram at 10 years of age
   d. all of the above

8. The preoperative test most often abnormal in patients with HHT is _____.
   a. coagulation study
   b. hematocrit
   c. platelet count
   d. CXR

9. All of the following are airway management recommendations in patients with HHT except _____.
   a. minimize pressure over nasal bridge during preoxygenation
   b. use a larger lubricated ETT with minimally occlusive cuff pressure
   c. use humidified air during mechanical ventilation
   d. spontaneous ventilation is preferred to positive pressure ventilation

10. All of the following are intraoperative anesthetic recommendations in patients with HHT except _____.
    a. maintenance of normocarbia
    b. avoid hypertension/hypotension
    c. ensure all intravenous fluids are bubble-free
    d. antibiotic prophylaxis only for invasive procedures