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Hereditary Hemorrhagic Telangiectasia

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu syndrome, is a rare autosomal dominant genetic disorder characterized by malformed blood vessels, which can result in recurrent and excessive bleeding. These abnormalities, known as arteriovenous malformations (AVMs), commonly affect organs such as the gastrointestinal tract, lungs, liver, brain, and skin. Telangiectasias, the term used when these malformations occur in the skin, are one of the hallmark features of HHT. Due to its genetic basis, the condition can be passed from parent to child, with a 50% chance of inheritance if one parent is affected.

Pathophysiology and Clinical Features

HHT is caused by mutations in genes that regulate vascular development, most commonly in the *ENG*, *ACVRL1*, and *SMAD4* genes. These genetic mutations result in the formation of abnormal blood vessels, characterized by direct connections between arteries and veins without the normal capillary network. This leads to a range of clinical manifestations, including telangiectasias and AVMs, which predispose individuals to recurrent bleeding. The bleeding typically occurs in the skin, gastrointestinal tract, nasal passages, lungs, liver, and, less commonly, the brain.

The most common clinical manifestations of HHT include:

- *Recurrent nosebleeds (epistaxis):* These are often the first sign of the disorder, typically occurring in childhood or adolescence.
- *Telangiectasias*: Small, red, non-blanching macules, usually measuring 2-5mm in size, which are most commonly found on the lips, tongue, and oral mucosa but can also be present on the skin and other mucosal surfaces.
- *Gastrointestinal bleeding*: Resulting in bloody stools or vomiting of blood, this can lead to significant blood loss and iron deficiency anemia.
- *Pulmonary AVMs*: These can lead to hypoxemia, hemoptysis, or paradoxical emboli.
- *Cerebral AVMs*: These are potentially life-threatening and can lead to stroke or hemorrhage if undiagnosed.

Diagnostic Criteria

The diagnosis of HHT is based on clinical criteria, and the most widely used diagnostic guidelines are those established by the Curacao criteria, which require the presence of at least three of the following four features:

- Recurrent nosebleeds.
- Presence of AVMs in internal organs, such as the lungs, liver, or brain.
- Telangiectasias in the skin or gastrointestinal tract.

- A positive family history, with a first-degree relative affected by HHT.

In cases where these criteria are not fully met, genetic testing may be performed to confirm the diagnosis, especially when there is a strong clinical suspicion but an incomplete family history. Additionally, imaging studies, such as MRI or CT scans, are essential for identifying internal AVMs, particularly in the brain, lungs, and liver.

Treatment and Management

Management of HHT focuses on symptom control, prevention of bleeding episodes, and the identification and treatment of potentially life-threatening AVMs. Treatment approaches vary depending on the severity of symptoms and the affected organs.

- ***Prevention and Surveillance***
  The primary strategy in managing HHT is prevention. Routine screening with imaging studies is recommended for early detection of internal AVMs, particularly in the brain, lungs, and liver. An MRI of the brain is typically performed in all newly diagnosed patients to assess for cerebral AVMs, which can be life-threatening if untreated. Pulmonary AVMs may be detected via chest CT or echocardiography, while liver AVMs can be identified using ultrasound or MRI. Early detection allows for timely intervention to prevent serious complications .
- ***Embolization of AVMs***
  When AVMs are identified, particularly those in the brain or lungs, prophylactic treatment is often required to prevent serious hemorrhagic events. Embolization, a procedure in which the abnormal blood vessels are intentionally occluded using a catheter and embolic agents, is commonly used for AVMs in the lungs and brain. This approach can prevent bleeding episodes and improve clinical outcomes, especially when the lesions are at high risk of rupture.
- ***Medical Therapies***
  For telangiectasias or small AVMs that are accessible, local treatments such as laser therapy, electrocautery, or sclerotherapy may be employed to reduce bleeding and improve cosmetic appearance. Lasers, such as the pulsed dye laser, are effective in targeting vascular lesions and shrinking the abnormal blood vessels. In some cases, estrogen therapy, which is believed to promote vascular regression, may be used, particularly in managing mucosal bleeding.
- ***Pharmacological Management***
  For systemic management of bleeding, especially in individuals with gastrointestinal bleeding or those suffering from frequent epistaxis, medications such as tranexamic acid (an antifibrinolytic agent) can be used to reduce bleeding. In cases where iron deficiency anemia is a concern due to chronic blood loss, iron supplementation and blood transfusions may be necessary. Recently, new investigational treatments, such as the use of angiogenesis inhibitors, are being explored for their potential to target the vascular abnormalities at the molecular level.

- ***Surgical Intervention***
  In severe cases, surgical intervention may be required to treat large or complicated AVMs that cannot be managed by embolization or other non-invasive treatments. Surgical removal of large AVMs in the brain or lungs may be necessary, although such procedures are typically reserved for cases that do not respond to other treatments.

Conclusion

Hereditary hemorrhagic telangiectasia is a rare but serious genetic condition that can lead to recurrent bleeding and significant morbidity. Early diagnosis and regular screening are essential for preventing complications associated with AVMs, particularly in vital organs such as the brain, lungs, and liver. Treatment strategies involve a combination of preventive measures, local therapies, medical management, and in some cases, surgical interventions. Advances in genetic testing, imaging technologies, and pharmacological therapies continue to improve outcomes for individuals living with HHT.

References

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