CLINICAL APPROACH TO HEREDITARY HEMORRHAGIC TELANGIECTASIA

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ABSTRACT

Background: Hereditary hemorrhagic telangiectasia (HHT or Rendu-Osler-Weber disease) is a rare syndrome, inherited as an autosomal dominant trait with incidence of 1/10000. The clinical manifestations are due to vascular malformations and predisposition to hemorrhages in different organs, the leading symptom being recurrent epistaxis. If diagnosed with HHT, the patient and his relatives and especially children have to be screened for occult vascular malformations.

Case report: A 30 years old woman was treated for cerebral stroke, epistaxis, anemia, arterio-venous malformations for over 6 months. Only at this point she was diagnosed with HHT, after noticing the typical mucosal changes. Focused family history revealed symptoms of HHT in her only child, her father, aunt and two cousins. The child was screened for occult vascular malformations – attainment of the nasal mucosa, lungs, gastrointestinal system, liver and brain. Pulmonary and gastrointestinal arterio-venous malformations were proven.

Conclusion: Any case of recurrent epistaxis should be evaluated for HHT. After confirmation of the diagnosis every patient and close relatives have to be screened for attainment of other organs and followed up in order to prevent severe life threatening complications.

Key words: hereditary hemorrhagic telangiectasia; epistaxis; screening;

BACKGROUND:

Hereditary hemorrhagic telangiectasia (HHT or Rendu-Osler-Weber disease) is a rare disease of the entire vascular system, especially of the capillary vessels. It is inherited as an autosomal dominant trait with incidence of 1/10000 [1, 2].

Clinical manifestation depends on the localization of telangiectases and / or arterio-venous malformations. It is characterised by age related variable expressivity and incomplete penetrance. The most common and typical symptom in 95% of the affected patients is recurrent epistaxis [1, 3]. With variable severity and frequency it occurs at about age of 10/15 [4]. Frequently telangiectasias are observed (up to 95% of the affected) being present at places like skin, hands, face and mouth. Less frequent, but more dangerous is bleeding from the gastrointestinal tract (up to 25%). Up to 50% of the affected suffer from lung AV malformations predisposing to early hemorrhagic or ischemic strokes. AV cerebral malformations are rare (5-20%), but they are also life-threatening. There are also changes in the liver and spinal cord, but they are more difficult to be diagnosed because of their rare bleeding and less frequent complications.

The Curacaocriteria are in clinical use for diagnosis of HHT [2]. It is considered:

Definite when three or more of the criteria below are present
Possible or suspected when two of the criteria below are present
Unlikely when fewer than two of the criteria below are present

- Epistaxis: spontaneous and recurrent
- Telangiectases: multiple on face, lips, oral cavity and fingers
- Visceral AVMs (pulmonary, cerebral, hepatic, spinal and/or gastrointestinal)
- Family history

Molecular diagnosis

Because of locus and allelic heterogeneity confirmation of the diagnosis at the molecular level is complicated. Mutations in two genes HHT1 and HHT2, respectively located in chromosome 9 and 12 are associated with the disease [2, 5], but there are also other, yet undiscovered genes. Mutations in the SMAD4 gene cause syndrome that combine HHT and juvenile polyposis [2]. Until now, the known genes are five or six.

AIM:

The aim of the study is to present a case of a family with epistaxis in three generations and to discuss the clinical approach
METHODS AND PATIENTS:
The objects of the study are 31 years old mother and her 7 years old son. The following methods have been applied: full medical history, general physical examination, biochemical investigation, general otorhinolaryngology examination, X-ray, echocardiography, echography, fibrogastroscopy, CT of thorax and abdomen, MRI of head, genetic counseling.

The first diagnosed person was 31 years old woman with a history of recurrent epistaxis from childhood and anemia. At age of 11 polyposis of sigma and varices of septi nasi have been diagnosed. She was admitted to the hospital for ischemic cerebral stroke. CT of head, X-ray of thorax, echocardiography, rhinoscopy were performed. Additional foramen ovale persistence, ASD type 2 and protein C deficit were diagnosed as possible reason for the condition. Some months later in “St. Ekaterina” Hospital Sofia, AVMs of the lung were visualized. Six months later, based on the family history, facial and mucosal telangiectases (fig. 1 and 2), and clinical manifestations- drumstic fingers, sign of chronic hypoxemia and nasal bleeding (fig. 3 and 4) HHT diagnose was established by otorhinolaryngologist. Operative correction of foramen ovale persistence and AVMs of the lung were performed. Focused family history revealed symptoms of HHT in her only child, her father, aunt and two cousins.

Seven years old child (the son of the woman) was admitted to the hospital for severe respiratory incident with observation of pneumonia (fig. 5). Based on the family history and absence of inflammation markers, HHT was suspected.

From the physical examination cyanosis and chronic hypoxemia (drumstic fingers and nail deformations (fig. 6), telangiectasias on eyes were observed. On CT with contrast performed in “St. Ekaterina” Hospital Sofia multiple AVMs in lungs were found. They are planned for operative correction. Meanwhile because of acute bleeding from the gastrointestinal tract the child was admitted to the St Marina University Hospital. Fibrogastroscopy was performed and telangiectases of stomach and esophagus were proven. On the performed CT of abdomen AVM in the lungs were found (fig. 7). Echography revealed that liver had intact structure.

On the MRI of the head no pathological findings were detected.

DISCUSSION:
Any case of recurrent epistaxis should be evaluated for HHT. After confirmation of the diagnosis every patient and close relatives have to be screened for attainment of other organs and followed up in order to prevent severe life threatening complications [3, 4]. MRI for detecting brain AV malformations, in early childhood– oxymetries, during puberty- contrast echocardiography, antibiotic prophylaxis and /or embolization with relevant evidence should be performed. Pregnancies should be controlled because of the tendency for complications.

Genetic testing of the mother found no known mutation in HHT1 gene. More probably SMAD4 gene is going to reveal molecular diagnosis as if mutation in it are causing combination of HHT and juvenile polyposis. Genetic testings are going to proceed.

Autosomal dominant type of inheritance requires the implementation of genetic counseling to clarify the relevant risks of all affected relatives and their offspring.

CONCLUSION:
Epistaxis is a common symptom in the general population. In individuals with recurrent nose bleeding should be subjected special clinical approach aiming conformation or exclusion of hereditary hemorrhagic telangiectases.
REFERENCES:


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