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KLINIČKE KARAKTERISTIKE NASLEDNE HEMORAGIJSKE TELANGIEKTAZIJE - PRIKAZ SERIES LUČAJEVA I PREGLED LITERATURE

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CLINICAL CHARACTERISTICS OF HEREDITARY HEMORRHAGIC TELANGIECTASIA - CASE SERIES AND REVIEW OF THE LITERATURE

Kliničke karakteristike nasledne hemoragijske telangiektazije-prikaz series lučajeva i pregled literature

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ABSTRACT

Introduction: Hereditary hemorrhagic telangiectasia (HHT) is a rare autosomal dominant disorder with estimated prevalence of one in 5,000 to 10,000. The disease has age-related penetrance and HHT signs and symptoms occur and worsen with increasing age. Diagnosis of HHT is based on Curacao’s criteria.

Case series: We report a case series of six patients diagnosed with HHT, five with definite and one with probable diagnosis according to the Curacao criteria. In five patients recurrent epistaxis occurred in adolescence as the first presentation while one patient presented with melena. The diagnosis was delayed in five patients and presence of HHT was diagnosed during or after the fifth decade. In four patients overt gastrointestinal bleeding occurred in the later course of the disease. Asymptomatic pulmonary circulation arteriovenous malformations were detected in two patients. Cerebral arteriovenous malformations were not detected.

Conclusion: Hereditary hemorrhagic telangiectasia is a rare disorder affecting multiple organs. It should be considered in adolescents with recurrent epistaxis and in the differential diagnosis of anemia with signs of gastrointestinal bleeding in order to shorten the delay in the diagnosis and subsequently improve the outcome of the disease.

Keywords: Hereditary hemorrhagic telangiectasia, anemia, epistaxis, melena

ABSTRAKT

Uvod: Nasledna hemoraškij ateleangiektazija (HHT) je redak autosomno-dominantni poremaćaj sa prevalencijom javljanja 1 na 5.000 do 10.000. Bolest je uzrasno zavisna i HHT simptomi i znaci se rano javljaju i pogoršavaju sa godinama. Dijagnoza se postavlja na osnovu Curaco kriterijuma.

INTRODUCTION

Hereditary hemorrhagic telangiectasia (HHT), also known as Rendu - Osler -Weber disease is a rare autosomal dominant disorder with estimated prevalence of one in 5,000 to 10,000 [1-3]. Diagnosis of HHT is based on Curacao`s criteria published in 2000 [4] that include:

- epistaxis (spontaneous recurrent nosebleed)
- multiple telangiectasias at characteristic sites (lips, oral cavity, fingers, nose)
- presence of visceral lesions (gastrointestinal telangiectasia, pulmonary, hepatic, cerebral, spinal AVM)
- 1st degree relative with HHT.

Diagnosis of HHT is definite if 3 criteria are full-filled, possible or suspected in the presence of 2 criteria and unlikely if less than 2 criteria are seen in the patient [4]

REPORT OF A CASE SERIES

We report a case series of six patients, five with definitive and one with suspected HHT. The majority of patients (five out of six) had recurrent epistaxis in their early childhood or adolescence as the first presentation, while one patient initially presented with melena. In 5 patients the diagnosis was delayed and the presence of HHT was diagnosed in the adulthood (during or after the fifth decade) although signs were present from adolescence. In four patients overt gastrointestinal bleeding occurred in the later course of the disease. Three patients had melena and one patient hematemesis. Clinical findings are seen in table 1.

Upon admission, physical examination confirmed the presence of mucocutaneous telangiectasia in all patients.
Lowest hemoglobin level at admission was 14 g/L and highest 95 g/L, while mean value was 67.5 g/L. The lowest value of MCV in the time of admission was 52 fL, the highest 82 fL, and the median 71 fL. The serum iron was in the range 1.9 μmol/L to 15.7 μmol/L, with a mean value of 5.2 μmol/L.

All patients were treated with intravenous iron supplementation while blood transfusion was indicated in five patients. Three patients received multiple transfusions and were classified as transfusion dependent. One patient had one blood transfusion weekly until hemoglobin reached 90.6 g/L.

Three patients underwent cautery of nasal septum varices with acetic acid due to repeated episodes of epistaxis.

We performed head and paranasal sinuses CT in two patients and cerebral AVM were not diagnosed, but nasal mucosa polyposis in the right nostril was diagnosed in two and bilateral edema of lower turbinate (concha) in one patient. In both patients, an arteriography with embolization of nasal blood vessels was suggested aiming to decrease frequency and intensity of epistaxis. In one patient embolization was successfully performed twice leading to reduced number of epistaxis episodes. (Figure 1.) The other patient did not accept suggested procedure.

Esophagogastroduodenoscopy revealed the presence of esophageal in one and gastric telangiectasia in all patients, while five patients had duodenal telangiectasia. In four patients colonoscopy revealed the presence of telangiectasia in the cecum and on the ileocolonic valve. (Figure 2). In two patients double balloon endoscopy was performed and jejunal telangiectasia were diagnosed. Five patients underwent endoscopic argon plasma coagulation (APC), and in one patient the procedure was repeated but significant reduction in transfusion frequency was not achieved since the lesions were diffuse. In this patient with GI bleeding as the first presentation of HHT and repeated unsuccessful APC, treatment with thalidomide was suggested, but informed consent was not obtained.

In two patients pulmonary AVMs were detected using chest CT with pulmonary angiography.
Our case series included 6 patients, five with definite (3 positive Curacao criteria) and one with probable (2 positive Curacao criteria) diagnosis of HHT.

In our study, the most common sign was epistaxis that was present in 5 out of 6 patients. According to different authors, epistaxis is a common sign present in 82-93% of all HHT patients [1,5,6]. Recurrent epistaxis occurs during childhood in more than 50% of HHT patients with an average of 18 nose bleeds a month [1], while by the age of 30 over 90% of patients experienced recurrent epistaxis [2,7]. Although epistaxis is an early marker of the disease, diagnosis is usually delayed. According to Pierucci diagnostic delay is 25.7 years [2] that is consistent with our results where only one patient was diagnosed in the adolescence.

Mucocutaneous telangiectasia in HHT patients are commonly seen on the face, lips, tongue, oral mucosa, gums, conjunctiva and skin of the trunk, hands, and fingers. They usually occur in childhood, and become more numerous and pronounced over time. Bleeding from cutaneous telangiectasia is usually mild to moderate, but in rare cases it is severe and laser coagulation is indicated [3]. In our study five out of six patients had cutaneous telangiectasia. This result is consistent with the results of other studies. In the study of the Irish national center, cutaneous telangiectasia existed in 57% of patients with suspected and 80% of patients with certain HHT diagnosis [6].

Telangiectasia can be localized throughout the gastrointestinal tract. Stomach and duodenum are the most common sites where GI telangiectasia are diagnosed [1,8] that is consistent with our results. Telangiectasias were identified in the stomach of all patients, while 5 patients had telangiectasia in the duodenum. Colonic localization was diagnosed in four patients, while esophagus telangiectasia were diagnosed in one patient. These results are consistent with results in other studies [8]. We diagnosed jejunal lesions in two patients, as opposed to previously published data where over 50% of patients had jejunal lesions, but this could be explained by small sample size in our study [8]. Blood loss from the gastrointestinal tract is presented in 15-30% of patients more often after the age of 30 and can be acute or chronic [1,8,9]. In our study, 5 patients had overt gastrointestinal bleeding and three were transfusion dependent. The number of telangiectasia in the gastrointestinal tract is correlating with the average hemoglobin level as previously reported by Longacre et
Namely, in patients with more than 20 lesions mean hemoglobin was 79 g/L while in patients with less than 20 telangiectasias mean hemoglobin was 94 g/L [8].

Pulmonary AVMs are identified in 40%–60% of HHT patients [1,10] . In patients apart from hemoptysis and hemothorax, neurological disturbances such as a migraine, TIA, stroke or brain abscess may occur [1,5] as a result of communication between arterial and venous blood flow in the pulmonary circulation and subsequent embolization of cerebral blood vessels [1,5]. Therefore, it is essential to conduct screening in order to detect the AVM in patients with HHT. In our case series, asymptomatic pulmonary circulation AVMs were detected in two patients. Small pulmonary AVMs are not detectable by CT and in patients with initial negative finding, CT should be repeated within three to five years. If AVM is detected in the arterial branch of more than 3mm in diameter, it is necessary to perform embolization, with control thoracic CT scan in 6 months [11]. Antibiotic prophylaxis is mandatory in patients with pulmonary AVM before invasive diagnostic procedures, in order to prevent complications [12].

Cerebral AVMs were not detected in any of the patients in our case series that can be explained both by a small number of patients and low incidence cerebral AVM in HHT patients. Namely, according to previously published studies incidence of cerebral AVM varies between 2.3% and 7.7% [5,13]. Also, recent data from an AVM database demonstrated that out of 531 patients 12 (2.3%) had cerebral AVM due to underlying HHT [14].

CONCLUSION

Hereditary hemorrhagic telangiectasia is a rare genetic disorder that should be considered in cases of unexplained recurrent epistaxis of young adults in order to shorten the delay in the diagnosis and subsequently improve the outcome of the disease. HHT should be suspected in cases of an unexplained occult and overt gastrointestinal bleeding. In HHT patients adequate diagnosis and optimal treatment require a multidisciplinary approach.

CONFLICT OF INTEREST: Authors declare that they have no conflict of interest
REFERENCES


**Table 1.** Clinical findings in HHT patients

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Sex (age)</th>
<th>Epistaxis</th>
<th>GI bleeding</th>
<th>MCT*</th>
<th>Hgb†</th>
<th>Diagnosis at admission</th>
<th>No of Curacao criteria</th>
<th>Treatment</th>
<th>Improvement</th>
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<td>1</td>
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<td>+</td>
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<td>+</td>
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<td>BT, APC cauterization</td>
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</tr>
<tr>
<td>3</td>
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<td>+</td>
<td>+</td>
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<tr>
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<td>M (62)</td>
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<td>+</td>
<td>+</td>
<td>91</td>
<td>HHT</td>
<td>3</td>
<td>BT, APC</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*MCT- mucocutaneous telangiectasia, †Hgb-hemoglobin at admission, ‡BT-blood transfusion, §APC-argon plasma coagulation
Figure 1. Before (A) and after (B) embolisation of right maxillary artery

Figure 2. Ileocecal valve angiodysplasia