CASE REPORT

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Clinical characteristics of hereditary hemorrhagic telangiectasia – case series and review of the literature

Kliničke karakteristike nasledne hemoragijske telangiektazije – prikaz serije bolesnika 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 the HHT signs and symptoms occur and worsen with age. A diagnosis of HHT is based on the Curacao`s criteria. **Case report.** We report a case series of 6 patients diagnosed with HHT, 5 with definite and one with probable diagnosis according to the Curacao criteria. In 5 patients, the recurrent epistaxis occurred in adolescence as the first presentation while one patient presented with melena. The diagnosis was delayed in 5 patients and the presence of HHT was diagnosed during or after the fifth decade. In 4 patients, the overt gastrointestinal bleeding occurred in the later course of the disease. The asymptomatic pulmonary circulation arteriovenous malformations were detected in 2 patients. The cerebral arteriovenous malformations were not detected. **Conclusion.** Hereditary hemorrhagic telangiectasia is a rare disorder affecting multiple organs. It should be considered in the adolescents with recurrent epistaxis and in the differential diagnosis of anemia with signs of the gastrointestinal bleeding in order to shorten the delay in the diagnosis and subsequently improve the outcome of the disease.

Key words:
telangiectasia, herediatary hemorrhagic; diagnosis, differential; hemoptysis; digestive system; hemorrhage; arteriovenous malformation.

Apstrakt

Uvod. Nasledna hemoragijska teleangiektazija (HHT) je redak autosomno-dominantni poremećaj 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. **Prikaz bolesnika.** Ovo je serijski prikaz šest bolesnika sa HHT, pet sa definitivnom i jednog sa verovatnom dijagnozom HHT na osnovu Curaco kriterijuma. Kod pet bolesnika ponavljane epistakse su se javile u adolescentnom dobu kao prva manifestacija bolesti, dok je prvi znak bolesti kod jednog bolesnika bila melena. Kod pet bolesnika dijagnoza HHT postavljena je tek u toku i nakon pete decenije života. Kod četiri bolesnika manifestno gastrointestinalno krvarenje se javilo u daljem toku bolesti. Asimptomatske arteriovenske malformacije plućne cirkulacije uočene su kod dva bolesnika. Cerebralne arteriovenske malformacije nisu uočene ni kod jednog bolesnika. **Zaključak.** Nasledna hemoragijska teleangiektazija je retka bolest koja zahvata više organa. Na ovu bolest bi trebalo misliti kada adolescent imaju ponavljane epistakse i diferencijalno dijagnostički kod anemija sa znacima gastrointestinalnog krvarenja, a u cilju pravovremenog postavljanja dijagnoze bolesti i poboljšanja ishoda iste.

Ključne reči:
teleangiektazija, nasledna, hemoragijska; dijagnoza, diferencijalna; hemoptizije; gastrointestinalni sistem; krvarenje; arteriovenske malformacije.

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as the Rendu-Osler-Weber disease is a rare autosomal dominant disorder with estimated prevalence of one in 5,000 to 10,000 [1–3]. A diagnosis of HHT is based on the Curacao`s criteria published in 2000 [4] that include: epistaxis (spontaneous recurrent nosebleed); multiple telangiectasias at the

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characteristic sites (lips, oral cavity, fingers, nose); presence of visceral lesions (gastrointestinal telangiectasia, pulmonary, hepatic, cerebral, spinal arteriovenous malformations – AVM); 1st degree relative with HHT.

The diagnosis of HHT is definite if 3 criteria are fulfilled, possible or suspected in the presence of 2 criteria and unlikely if less than 2 criteria are seen in the patient [4].

Case report

We report a case series of 6 patients, 5 with definitive and one with suspected HHT.

The majority of the patients (5 out of 6) had the 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 the signs were present from the adolescence. In 4 patients, the overt gastrointestinal bleeding occurred in the later course of the disease. Three patients had melena and one patient hematemesis. Clinical findings are presented in Table 1.

Upon admission, physical examination confirmed the presence of mucocutaneous telangiectasia in all patients.

The lowest hemoglobin level at admission was 14 g/L and the highest one was 95 g/L, while the mean value was 67.5 g/L. The lowest value of mean corpuscular volume (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 of 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 5 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 cauterization of nasal septum varices with acetic acid due to the repeated episodes of epistaxis.

We performed the head and paranasal sinuses computed tomography (CT) in 2 patients and the cerebral arteriovenous malformations (AVM) were not diagnosed, but nasal mucosa polyposis in the right nostril was diagnosed in 2 and bilateral edema of lower turbinate (concha) in one patient. In both patients, 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 the reduced number of epistaxis episodes (Figure 1). The other patient did not accept the suggested procedure.

Table 1

Clinical findings in hereditary hemorrhagic telangiectasia (HHT) patients

Patient No	Sex F/M (age)	Epistaxis	Gastrointestinal bleeding	MCT	Hgb (g/L)	Diagnosis at admission	Curacao criteria (n)	Treatment	Improvement
1	F (54)	+	+	+	87	HHT	3	BT, APC, embolization	Yes
2	F (50)	+	-	+	14	Anemia	3	BT, APC cauterization	Yes
3	F (62)	-	+	+	95	HHT	2	BT, APC	Yes
4	M (70)	+	-	+	48	HHT	3	BT, APC	Yes
5	M (57)	+	+	+	70	Anemia	3	BT	Yes
6	M (62)	+	+	+	91	HHT	3	BT, APC	Yes

F – female; M – male; MCT – mucocutaneous telangiectasia; Hgb – hemoglobin at admission; BT – blood transfusion; APC – argon plasma coagulation.

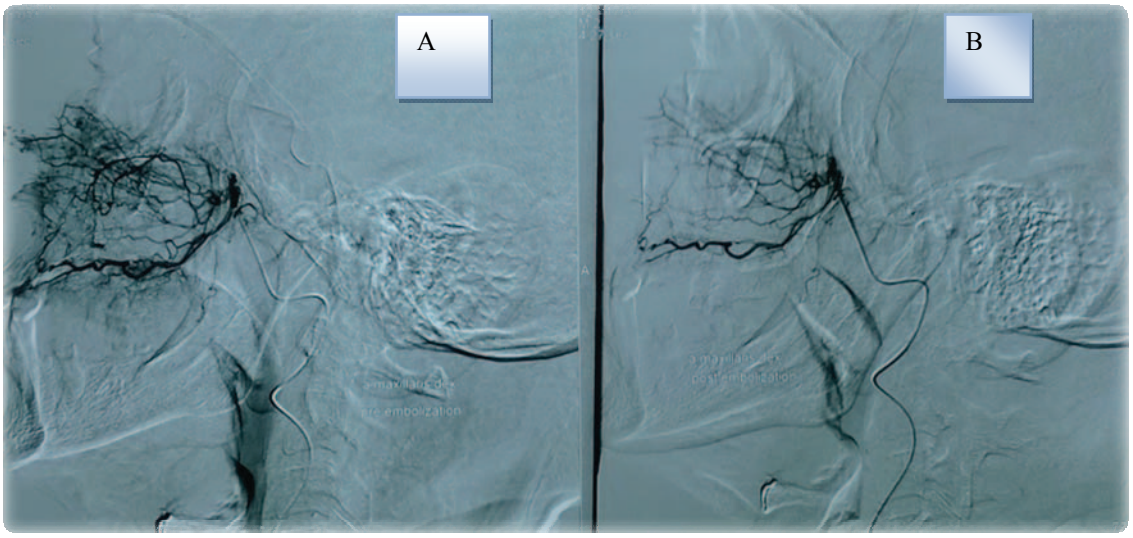

Fig. 1 – (A) Before and (B) after embolisation of right maxillary artery.

Esophagogastroduodenoscopy revealed the presence of esophageal in one and gastric telangiectasia in all patients, while 5 patients had duodenal telangiectasia. In 4 patients, a colonoscopy revealed the presence of telangiectasia in the cecum and on the ileocolonic valve (Figure 2). In 2 patients double balloon endoscopy was performed and jejunal telangiectasia was diagnosed. Five patients underwent endoscopic argon plasma coagulation (APC), and in one patient the procedure was repeated, but a significant reduction in the transfusion frequency was not achieved since the lesions were diffuse. In this patient with a gastrointestinal (GI) bleeding as the first presentation of HHT and repeated unsuccessful APC, a treatment with thalidomide was suggested, but informed consent was not obtained.

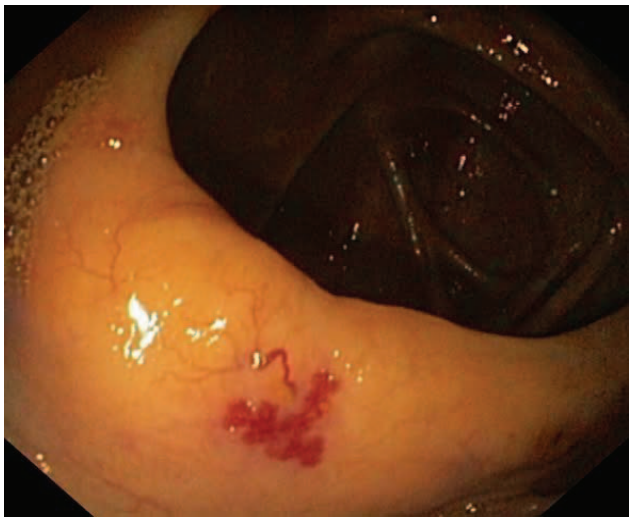

Fig. 2 – Ileocecal valve angiodysplasia.

In 2 patients, the pulmonary AVMs were detected using the chest CT with pulmonary angiography.

Discussion

Our case series included 6 patients, 5 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 the HHT patients with an average of 18 nose bleeds a month [1], while by the age of 30 years, over 90% of patients experienced the recurrent epistaxis [2, 7]. Although epistaxis is an early marker of the disease, diagnosis is usually delayed. According to Pierucci et al. [2], a diagnostic delay is 25.7 years, which is consistent with our results where only one patient was diagnosed in the adolescence.

Mucocutaneous telangiectasia in the 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 numerous and pronounced over time. Bleeding from cutaneous telangiectasia is usually mild to moderate, but in rare cases it is severe and a laser coagulation is indicated [3]. In our study, 5 out of 6 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 the suspected and 80% of patients with the certain HHT diagnosis [5].

Telangiectasia can be localized throughout the GI tract. The stomach and duodenum are the most common sites where GI telangiectasia are diagnosed [1, 8] which is consistent with our results. Telangiectasias were identified in the stomach of all patients, while 5 patients had telangiectasia in the duodenum. The colonic localization was diagnosed in 4 patients, while esophagus telangiectasia was diagnosed in one patient. These results are consistent with the results of other studies [8]. We diagnosed jejunal lesions in 2 patients, as opposed to previously published data where over 50% of patients had jejunal lesions, but this could be explained by a 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 years and can be acute or chronic [1, 8, 9]. In our study, 5 patients had the overt gastrointestinal bleeding and 3 were transfusion dependent. The number of telangiectasia in the gastrointestinal tract is correlating with the average hemoglobin level as previously reported by Longacre et al. [8] Namely, in the patients with more than 20 lesions, mean hemoglobin was 79 g/L while in the patients with less than 20 telangiectasias, mean hemoglobin was 94 g/L.

The pulmonary AVMs were identified in 40%–60% of the HHT patients [1, 10]. Apart from the hemoptysis and hemothorax, neurological disturbances such as a migraine, transitory ischemic attack (TIA), stroke or brain abscess may occur in the patients as a result of communication between the 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 to detect the AVM in the patients with HHT. In our case series, the asymptomatic pulmonary circulation AVMs were detected in 2 patients. The small pulmonary AVMs were not detectable by CT and in the patients with an initial negative finding, CT should be repeated within 3 to 5 years. If AVM is detected in the arterial branch of more than 3 mm in diameter, it is necessary to perform embolization, with a control thoracic CT scan in 6 months [11]. Antibiotic prophylaxis is mandatory in the patients with the pulmonary AVM before the invasive diagnostic procedures, in order to prevent complications [12].

The 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 of the cerebral AVM in the HHT patients. Namely, according to previously published studies, incidence of the 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 the cerebral AVM due to underlying HHT [14].

Conclusion

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

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Conflict of interest

Authors declare that they have no conflict of interest.

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