 DOI: 10.2478/acm-2018-0016

Severe Recurrent Epistaxis - The Main Symptom of Hereditary Haemorrhagic Teleangiectasia.

Case report

LUCANSKA M[1], HAJTMAN A[1], PECOVA R[2]

[1]Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava and Martin University Hospital, Martin, Slovak Republic
[2]Department of Pathological Physiology and Biomedical Centre, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin, Slovak Republic

Abstract

Hereditary haemorrhagic telangiectasia (HHT), also known as Rendu-Osler-Weber syndrome, is of dominant autosomal inheritance. Pathologic changes of vascular walls cause recurrent episodes of bleeding from many organ systems. Recurrent epistaxis is the first and the most frequent symptom of HHT. The causal therapy is not known but there are many therapeutic procedures improving the overall condition.

We present a case of a 76-year-old man suffering from HHT, frequently hospitalized and treated for massive nose bleeding. In past a selective arterial embolization was performed thrice; nonetheless, the intensity and frequency of epistaxis remained unchanged. Anterior nasal package and electrocoagulation were performed repeatedly as the "first aid" treatment. In the article we also mention other therapeutic modalities for this diagnosis; unfortunately, their efficacy remains inadequate.

Keywords: Hereditary haemorrhagic teleangiectasia, Rendu-Osler-Weber syndrome, epistaxis

INTRODUCTION

Rendu-Osler-Weber syndrome or hereditary haemorrhagic telangiectasia is of dominant autosomal inheritance (1). This rare systemic fibrovascular dysplasia causes an alteration in the elastic and muscle layers of vessel walls, making them more vulnerable to spontaneous ruptures and injuries (1). Mucocutaneous teleangiectases, arteriovenous malformations, and recurrent spontaneous ruptures of vessels causing repeated bleeding are the most characteristic symptoms. HHT is spread worldwide; the prevalence varies between countries (2). The highest frequency of HHT is in the Netherlands Antilles (1:1331) (2), recent epidemiologic studies in Japan, France, and Denmark showed the incidence of 1:5,000 -1:8,000 (3).

Several mutations in 2 genes, endoglin on chromosome 9 (HHT type 1) and activin receptor-like kinase-1 on chromosome 12 (HHT type 2), are associated with HHT (2).

Teleangiectases are mainly localized in the mucosa of the nasal and oral cavity, gastrointestinal system, and in the skin of fingertips. Arteriovenous malformations occur mostly in lungs, liver, and central nervous system (4). Teleangiectases in face, hands, and oral cavity occur approximately between the ages of 30 and 40 (4). The first and most frequent symptom of the disease is recurrent epistaxis which occurs approximately in the 12th year

Address for correspondence:
MUDr. Miroslava Lučanská, Clinic of Otorhinolaryngology and Head and Neck Surgery, Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Martin University Hospital, Kollárova 2, 036 01 Martin, Slovakia.
Phone: 00421 43 26 33 282; E-mail: miroslava.zarska@gmail.com

of life, the frequency and intensity of bleeding increases with age (4). Severity of epistaxis varies widely from mild self-limited nosebleeds to severe life-threatening nasal haemorrhage (5).

The clinical diagnosis of HHT is based on the Curaçao criteria. Three out of four criteria are required for a definite clinical diagnosis of HHT, two criteria are considered "possible" HHT, and 0 or 1 criterion makes the diagnosis unlikely (6). The four Curaçao criteria include epistaxis, teleangiectases, mainly on the hands, face, and in the mouth, arteriovenous malformations in major organ systems and a family history of HHT (7).

Several therapeutic approaches have been investigated but they are mostly palliative and have had variable results (8). Treatments for HHT range from medication and conservative management to more aggressive surgeries (9).

A range of interventions can be performed including nasal packing, hormone therapies, monoclonal antibodies, local sclerotherapy, diathermy, and coagulation or cautery techniques (10).

The Nd:YAG laser coagulation and argon – plasma coagulation is usually the first option for patients with HHT (11). Other therapeutic modalities include fibrin glue application, transarterial embolization, brachytherapy, ligation of arteries supplying nasal cavity and insertion of nasal obturators (12, 13, 14, 15, 16).

Pharmacological Management of recurrent epistaxis also includes Bleomycine injections and Thalidomide administration (17, 18).

Systemic pharmacological therapies, such as low-dose monoclonal humanized antibody bevacizumab, have been explored in recent years with evidence of benefit for patients seeking a non invasive treatment of severe epistaxis prior to considering surgical intervention (18).

Surgical treatment of epistaxis in hereditary haemorrhagic telangiectasia (HHT) has historically been managed with the laser procedure or the septodermoplasty procedure. For transfusion-dependent patients with severe epistaxis we have been performing the Young's procedure or surgical closure of the nostrils (19).

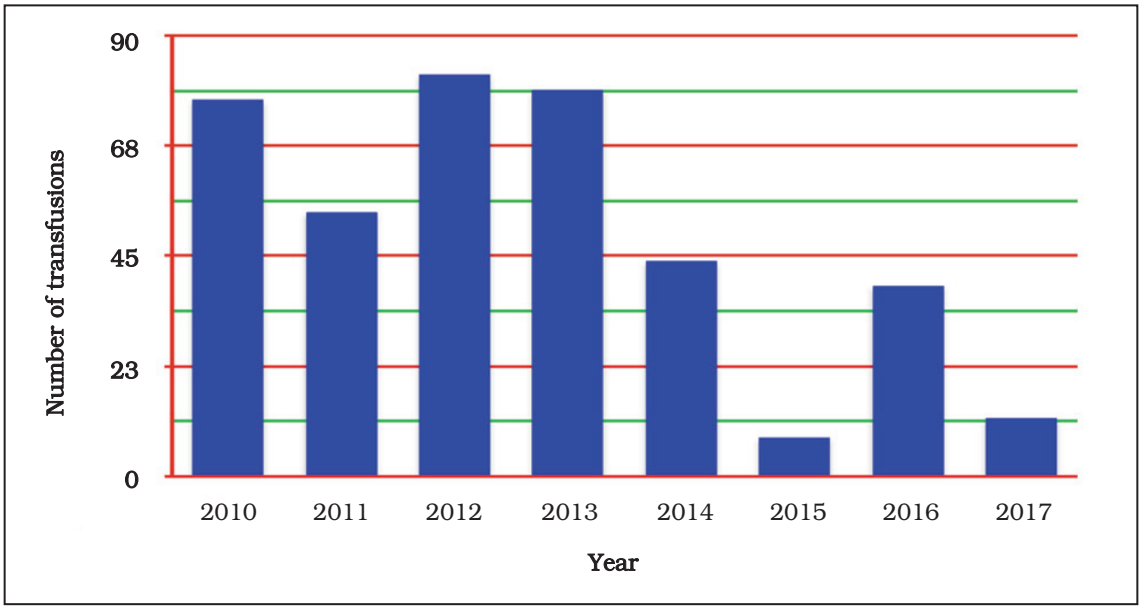
Permanently closing the nares is thought to be effective because it protects the fragile intranasal telangiectasias from the drying effects of air flow (10).

Case Report

During last ten years a 76-year-old man have been regularly referred to our clinic for massive bilateral epistaxis. At the age of 20 recurrent epistaxis connected with physical exertion occurred. The frequency and intensity of epistaxis increased with age. Similar symptoms had been present in the patient's father who died at age of 69 following a massive nose bleeding. Our patient had no children, one sister who suffered from an infrequent mild epistaxis. She had two children – 30- and 31– year-old, respectively, neither with any symptom of the disease.

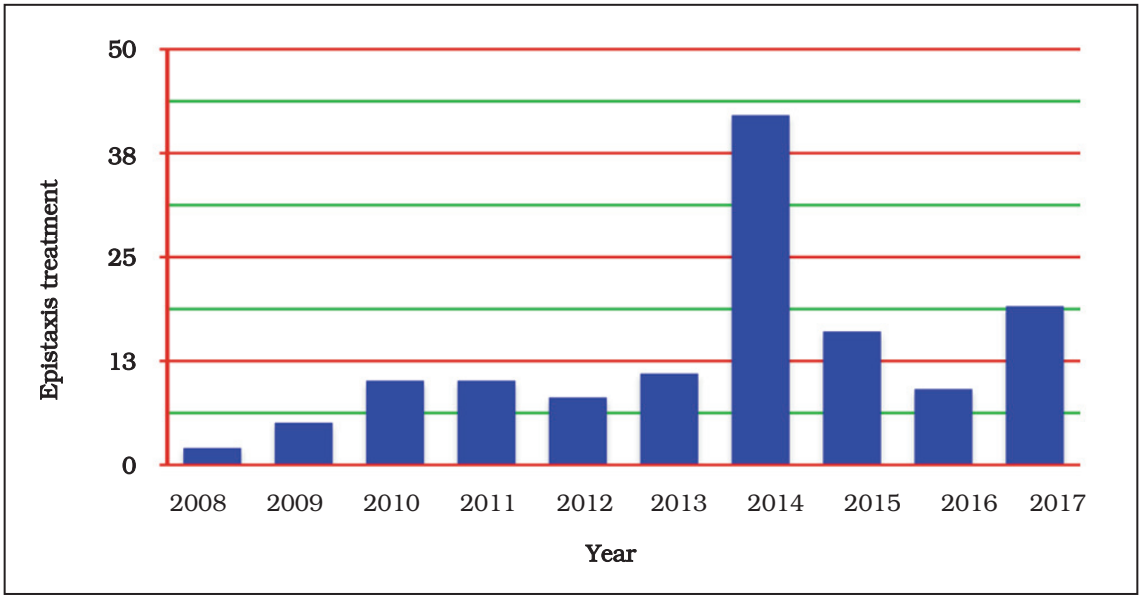
Over the last 10 years, the frequency and intensity of epistaxis grew, the nose bleeding returned approximately once a month. Generally, nasal package was the only way to stop it. Unfortunately, epistaxis returned almost after each removal of the package; after the first treatment the anterior nasal package had to be reinserted 6 or 7 times. Epistaxis was connected with massive blood loss, blood and plasma transfusions were always essential. The bleeding started spontaneously, usually during the evening while in a horizontal position. The frequency of the blood transfusions administration is shown in Table 1.

Table 1: The number of red blood cell transfusions from January 2010 through June 2017



The frequency of the local treatment – the insertion of anterior nasal packages – is shown in Table 2.

Table 2: Anterior nasal packages performed from January 2008 through June 2017



Our patient had numerous telangiectases in the facial region, oral cavity, and hands, especially fingers.

Endoscopy of the gastrointestinal tract showed numerous teleangiectases spread from the distal half of oesophagus to duodenum.

CT scans of the lungs detected interstitial pulmonary process, presumably caused by diffuse pulmonary arteriovenous malformations, ultrasonography of the liver concerned diffuse lesion and haemangioma. CT examination of the brain showed the postmalatic pseudocyst localized in the frontal and parietal lobe. The size of the cyst was 44 × 26 × 22 mm.

The shape of the patient's external nose was markedly changed due to the frequent insertion of nasal package; the common meatus of the nasal cavity was dilated bilaterally. The nasal septum wasn't perforated. However, its frontal part was formed solely by mucosa without the cartilage.

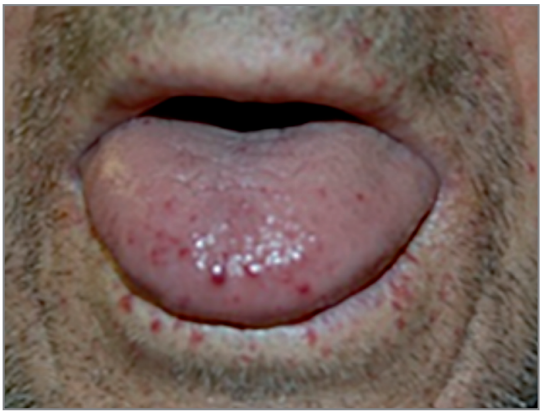


Fig. 1: Telangiectasia of the tongue and lips

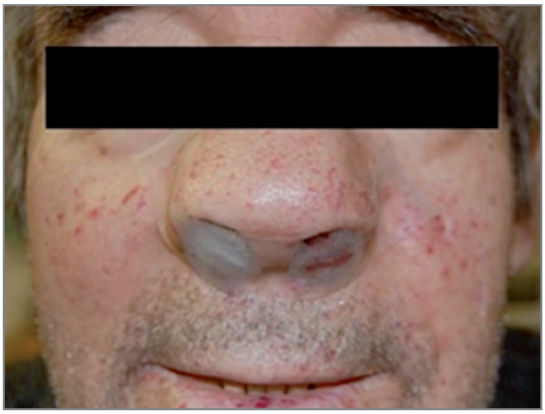


Fig. 2: Telangiectasia of the face, extended external nose with anterior nasal package

The mucosa of the nasal cavity was pale with numerous red teleangiectases.In addition to numerous nasal packages, selective arterial embolization was performed repeatedly. First, in June 2010, the left superior labial artery and the left sphenopalatine artery were embolized. Next, in September 2010, the embolization of the left sphenopalatine artery was performed again and in December 2011, facial artery on the left side and sphenopalatine artery on the right side were embolized. This therapeutic modality had no efficacy, the frequency and intensity of epistaxis remained unchanged. Next, numerous nasal packages, sometimes connected with electrocoagulation in cases of moderate bleeding, were performed. The patient died at the age of 76.

DISCUSSION

As already mentioned, recurrent epistaxis is the main symptom of hereditary haemorrhagic telangiectasia. Nowadays, Nd:YAG laser coagulation and argon – plasma coagulation is the first treatment for patients with this diagnosis (11). This therapy, performed in local anaesthesia, is well tolerated by patients.

According to recent studies, low dose of Thalidomide seems to be safe and effective for the reduction of epistaxis. However, further studies are necessary. Unfortunately, none of these procedures means complete restoration. The treatment is only focused on diminution of frequency and intensity of bleeding (17).

Duncan et al. treated a patient with severe recurrent epistaxis. Bleomycine was repeatedly injected into the damaged mucosa, there was no episode of epistaxis during the next two years (18).

Mucosal treatment includes transmucosal injections of fibrin glue or Aetoxisclerol – a sclerosing agent used in phlebology. Haemostatic gels can contribute to the treatment of epistaxis (20).

The efficacy of endovascular embolization varies from 20% to 80%. The wide variation in the results is presumably due to varying definitions of successful treatment and various length of observation. In patients with HHT we often see the hypertrophy of ethmoid arteries and other collaterals, which is probably the reason of the low efficacy of embolization. Elden et al. recommend endovascular embolization as the last therapeutic option when other possibilities fail (21).

Ghilezan et al. studied the efficacy of brachytherapy used in 43 patients during 20 years. Regardless of the dosage recurrent epistaxis reappeared approximately two years after the treatment. In four patients septal perforation was formed after brachytherapy (22).

Kim JY et al. used endoscopic cryotherapy for the treatment of recurrent epistaxis due to HHT. Their treatment strategy resulted in successful management of symptoms and no associated complications (9).

Recently, a case of patient treated with radiofrequency and fibrin sealant was reported. Radiofrequency ablation of telangiectasia is a save, effective and well tolerated technique even in patients who underwent other previous treatments (23).

Fiorella et al. performed septal dermoplasty to 67 patients, the necessity of blood supply was statistically significantly lower (24). From August 2011 through March 2014 the North American Study of Epistaxis in HHT was performed. There were 121 adult patients suffering from HHT. Patients received twice-daily nose sprays for 12 weeks with either bevacizumab 1% (4 mg/d), estriol 0.1% (0.4 mg/d), tranexamic acid 10% (40 mg/d), or placebo (0.9% saline), there were no significant between-group differences in the use of topical intranasal treatment with bevacizumab vs estriol vs tranexamic acid vs placebo and epistaxis frequency (25).

The closure of the nasal cavity is an effective but very mutilating way of treatment. After the closure breathing through the nasal cavity is no more possible, the nasal mucosa is not irritated by the inhaled air and pollutants. Lund et al. used this method in group of 100 patients. Overall, most patients derived significant benefit from the procedure with complete cessation of nasal bleeding in 94% of cases. Loss of smell and taste was the most frequent post-operative complaint (26). This method cannot be used in patients with septal perforation. Wirsching et al. studied the efficacy of temporary nasal occlusion with hypoallergenic tape. In a group of 20 patients, the application of the tape together with Nd:YAG therapy led to stable haemoglobin levels during the study (27).

Our patient refused surgical treatment, selective endovascular embolization was performed repeatedly. Unfortunately, there was no improvement, the frequency and intensity of epistaxis remained unchanged. The nasal mucosa was damaged, the recurrent epistaxis was always severe, we were led to conclude that any treatment mentioned before would be unsuccessful.

CONCLUSION

Hereditary haemorrhagic telangiectasia is a rare condition, recurrent epistaxis and the bleeding from gastrointestinal tract are the main symptoms, vascular malformations are pathognomonic histological findings. Quality of life is significantly impaired. Unfortunately, there is no causal therapy of HHT. Multiple therapeutic approaches have been tried but they are largely palliative with variable results (8).

REFERENCES

1. Garcia RID, Cecatto SB, Costa KS, Veiga FA, Uvo IP, Rapoport PB. Síndrome de Rendu-Osler-Weber: tratamento clínico e cirúrgico. Revista Brasileira de Otorrinolaringologia 2003; 69 (4): 577-580.

2. Grand'Maison A. Hereditary haemorrhagic telangiectasia. CMAJ : Canadian Medical Association Journal 2009; 180 (8): 833–835.
3. Sadick H, Sadick M, Götte K, et al. Hereditary haemorrhagic telangiectasia: an update on clinical manifestations and diagnostic measure. Wien Klin Wochenschr 2006;118(3-4): 72.
4. Sharathkumar A, Shapiro A. Hereditary haemorrhagic telangiectasia. Haemophilia 2008; 14(6): 1269–1280.
5. Sautter NB, Smith TL. Treatment of hereditary haemorrhagic telangiectasia-related epistaxis. Otolaryngol Clin North Am 2016; 49(3):639-654.
6. van Gent MWF, Velthuis S, Post MC, Snijder RJ, Westermann CJJ, Letteboer TGW, Mager JJ. Hereditary haemorrhagic telangiectasia: How accurate are the clinical criteria? Am J Med Genet Part A 2013; 161A: 461–466.
7. Shovlin CL, Guttmacher AE, Buscarini E, Faughnan ME, Hyland RH, Westermann CJ, Kjeldsen AD, Plauchu H. Diagnostic criteria for hereditary haemorrhagic telangiectasia (Rendu Osler Weber syndrome). Am J Med Genet 2000; 91(1): 66–67.
8. Invernizzi, R, Quaglia, F, Klersy, C, Pagella, F, Ornati, F, Chu, F, Balduini, CL. Efficacy and safety of thalidomide for the treatment of severe recurrent epistaxis in hereditary haemorrhagic telangiectasia: results of a prospective phase II clinical trial. The Lancet. Haematology 2015; 2(11), 465–473.
9. Kim JY, Oh JH, Kim GT, Kwon JH. Endoscopic cryotherapy for the treatment of epistaxis due to hereditary haemorrhagic telangiectasia. J Craniofac Surg. 2014; 25(2):120-2.
10. Thomson RS, Molin NL, Whitehead KJ, Ashby S, Johnson L, Ward PD, McRae BR, Wilson KF, McDonald J. The effects of nasal closure on quality of life in patients with hereditary haemorrhagic telangiectasia. Laryngoscope investigative otolaryngology 2018; 3: 178–181.
11. Papaspyrou G et al. Combined therapy for epistaxis by hereditary haemorrhagic telangiectasia: A 3-year follow up study on 45 patients. Journal of Cranio-Maxillo-Facial Surgery 2017; 45(8):1179–82.
12. Richmon JD, Tian Y, Husseman J, Davidson TM. Use of a sprayed fibrin hemostatic sealant after laser therapy for hereditary haemorrhagic telangiectasia epistaxis. Am J Rhinol. 2007; 21:187-91.
13. Robinson AE, McAuliffe W, Phillips TJ, Phatouros CC, Singh TP. Embolization for the treatment of intractable epistaxis: 12 month outcomes in a two centre case series. Br J Radiol. 2017; 90(1080):20170472.
14. Elden L, Montanera W, Terbrugge K. et al. Angiographic embolization for the treatment of epistaxis: a review of 108 cases. Otolaryngol Head Neck Surg 1994;111: 44–50.
15. Pohar C, Mazeron JJ, Ghilezan M et al. Management of epistaxis in Rendu-Osler disease: is brachytherapy effective? International Journal of Radiation Oncology Biology Physics 1993; 27(5): 1073-77.
16. McDermott AM, O'Cathain E, Carey BW, O'Sullivan P, Sheahan P. Sphenopalatine Artery Ligation for Epistaxis: Factors Influencing Outcome and Impact of Timing of Surgery. Otolaryngol Head Neck Surg. 2016; 154(3): 547-52.
17. Willems PWA, Farb RI, Agid R. Endovascular treatment of epistaxis. American Journal of Neuroradiology 2009; 30(9):1637-1645. h
18. Duncan IC, Van Der Nest L. Intralesional Bleomycin Injections for the Palliation of Epistaxis in Hereditary Haemorrhagic Telangiectasia. *AJNR* 2004; 25(7): 1144-1146.
19. Richer SL, Geisthoff UW, Livada N, Ward PD, Johnson L, Mainka A, Henderson KJ, Maune S, White RI Jr, Ross DA. The Young's procedure for severe epistaxis from hereditary haemorrhagic telangiectasia. 2012; 26(5):401-4.
20. Bequignon E, Vérillaud B, Robard L, Michel J, Prulière Escabasse V, Crampette L, Malard O. Guidelines of the French Society of Otorhinolaryngology (SFORL). First-line treatment of epistaxis in adults. Eur Ann Otorhinolaryngol Head Neck Dis. 2017; 134(3):185-189.
21. Elden L, Montanera W, Terbrugge K. et al. Angiographic embolization for the treatment of epistaxis: a review of 108 cases. Otolaryngol Head Neck Surg 1994;111: 44–50.
22. Pohar C, Mazeron JJ, Ghilezan M et al. Management of epistaxis in Rendu-Osler disease: is

brachytherapy effective? International Journal of Radiation Oncology Biology Physics 1993; 27(5): 1073-77.
23. Donato M Pimentel J, Cabral R, Escada P. Radiofrequency for Treatment of Refractory Epistaxis in Hereditary Haemorrhagic Telangiectasia. Acta Médica Portuguesa 2018; 31(1): 63.
24. Fiorella ML, Ross D, Henderson KJ, White RI. Outcome of septal dermoplasty in patients with hereditary haemorrhagic telangiectasia. Laryngoscope 2005;115(2):301–5.
25. Whitehead KJ, Sautter NB, McWilliams JP, et al. Effect of Topical Intranasal Therapy on Epistaxis Frequency in Patients With Hereditary Haemorrhagic Telangiectasia A Randomized Clinical Trial 2016; 316(9): 943–951.
26. Lund VJ, Darby Y, Rimmer J, Amin M, Husain S. Nasal closure for severe hereditary haemorrhagic telangiectasia in 100 patients. The Lund modification of the Young's procedure: a 22-year experience. Rhinology 2017; 55(2): 135-141.
27. Wirsching KEC, Kuhnel TS. Update on clinical strategies in hereditary haemorrhagic telangiectasia from an ENT point of view. Clin Exp Otorhinolaryngology 2017; 10(4): 153–157.

Received:December, 4, 2018
Accepted: December, 20, 2018