Cauterization for epistaxis in hereditary hemorrhagic telangiectasia

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Abstract. Cauterization for epistaxis in hereditary hemorrhagic telangiectasia. Problem/objectives: Epistaxis is the most common manifestation of hereditary hemorrhagic telangiectasia (HHT); it is present in >90% of HHT patients >45 years old. Depending on severity, treatment consists of managing bleeding via medical and surgical methods. The aim of our study was to evaluate the efficacy and safety of endonasal surgical arterial cauterization to treat chronic epistaxis in patients with HHT who are no longer responding to first-line therapies.

Methodology: Five patients were included in our study. The day before surgery, all patients underwent devascularization embolization of the external carotid arterial branches involved in nasal bleeding. The primary efficacy endpoint of treatment was assessed by the Epistaxis Severity Score (ESS), which was systematically evaluated preoperatively in our department, as well as every 3 months postoperatively. Data were collected retrospectively from the medical records of patients.

Results: Endonasal surgical arterial cauterization was associated with a ≥50% reduction in the ESS up to 9 months postoperatively. In one of our patients, cerebrospinal fluid (CSF) leakage occurred intraoperatively during cauterization of the posterior ethmoid artery. Closure of the dural skull base defect was successfully performed intraoperatively.

Discussion: Although our results are preliminary and included few patients, they support a role for endonasal surgical arterial cauterization as a second-line treatment method for chronic epistaxis in patients with HHT.

Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease and Osler-Weber-Rendu syndrome, is an autosomal dominant vascular disease with incomplete penetrance characterized by localized angiodyplasia. This is manifested as epistaxis, mucocutaneous and gastrointestinal telangiectases, and arteriovenous malformations (AVM) in the pulmonary, cerebral, or hepatic circulation.¹ In Europe, the frequency is estimated to be between 1 in 5,000 to 8,000 persons, although it is higher in some regions, such as the Jura region in France, Funen Island in Denmark, and certain Caribbean islands.² Three there are two main HHT types: 1 and 2, which are caused by mutations in the endoglin (ENG) and ALK1 (also known as ACVRL1) genes, respectively.³ In around 2% of all HHT patients, the origin of the disease is a mutation in SMAD4, leading to a combined syndrome of juvenile polyposis and HHT (JPHT).⁴ A common property of all these genes is that they code for proteins involved in the transforming growth factor β (TGF-β) signaling pathway, which is critical to the proper development of blood vessels. It is generally accepted that ENG or ALK1 haplo-insufficiency causes HHT, but other poorly understood mechanisms are necessary to trigger the formation of vascular lesions.⁵

The most common clinical manifestation of HHT is epistaxis, which is present in >90% of patients >45 years old.⁶ Spontaneous and recurrent episodes of epistaxis strongly interfere with patients’ quality of life and become a permanent, constant annoyance. It can be a social handicap as well as physically disabling, since patients may be at risk of developing chronic anemia as well as severe acute anemia.⁷ Epistaxis occurs secondary to telangiectasias that develop on the nasal mucosa and become sensitive to the slightest trauma as well as to the simple friction of inspired air. It can occur at any age but increases in frequency with time, and it is hormonally influenced (i.e., by puberty, pregnancy, and menopause).⁸ There is considerable heterogeneity in the severity of epistaxis in patients with HHT.⁹ The severity can be assessed by the Epistaxis Severity Score (ESS score).¹⁰ The ESS is determined by a questionnaire that comprises six items (Figure 1): (1) frequency, (2) duration and (3) intensity of epistaxis; (4) use of medical care to stop the bleeding; (5) occurrence of anemia; and (6) whether blood transfusion was ever performed.
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## Material and methods

All patients with HHT who were admitted to the otolaryngology department of Erasme hospital (Brussels, Belgium) between February 2012 and June 2013 and treated by endonasal surgical arterial cauterization were included in this study. They had in common an inadequate response to less-invasive treatments, as described in the Introduction.

Data collection and analysis were performed retrospectively. The primary outcome was assessment of the efficacy of the treatment, as measured by the ESS. A preoperative assessment was done, and assessments were performed every 3 months as part of the postoperative follow-up period.

### Figure 1

Epistaxis Severity Score (ESS) questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How often do TYPICALLY have nose bleeding?</td>
<td>Less than monthly, Once per month, Once per week, Several per week,</td>
</tr>
<tr>
<td></td>
<td>Once per day, Several per day</td>
</tr>
<tr>
<td>2. How long do your TYPICAL nose bleeding episodes last?</td>
<td>&lt; 1 minute, 1-5 minutes, 6-15 minutes, 16-30 minutes, &gt; 30 minutes</td>
</tr>
<tr>
<td>3. How would you describe your TYPICAL nose bleeding intensity?</td>
<td>Not Typically Gushing or Pouring, Typically Gushing or Pouring</td>
</tr>
<tr>
<td>4. Have you sought medical attention for your nose bleeding?</td>
<td>No, Yes</td>
</tr>
<tr>
<td>5. Are you anemic (low blood counts) currently?</td>
<td>No, Yes</td>
</tr>
<tr>
<td>6. Have you received a red blood cell transfusion SPECIFICALLY for nose bleeding?</td>
<td>No, Yes</td>
</tr>
</tbody>
</table>

A score of 1-4 is defined as mild epistaxis, 4-7 as moderate epistaxis, and 7-10 as severe epistaxis.

The ESS can be used to select the best treatment for epistaxis and to evaluate its efficiency over time. Although different therapeutic, medical, and surgical modalities exist, none are curative. The aim of treatment is to reduce the frequency and intensity of epistaxis, thereby improving the quality of life of patients. First-line treatment of chronic epistaxis in patients with HHT include: atraumatic nasal packing, laser photocoagulation, and sclerotherapy. The use of more-invasive surgical techniques is justified when the patient is not responsive to these treatments. One of these is endonasal surgical arterial cauterization. It is frequently described in the literature but has never been evaluated. The aim of our study was to evaluate its efficacy in treating moderate-to-severe epistaxis in patients with HHT. Prior to surgery, all patients underwent angiography to assess the degree of involvement of the different vascular territories in endonasal pathology. Angiography also allowed us to embolize the involved branches of the external carotid artery prior to surgery, which greatly reduced intraoperative bleeding.
Endonasal cauterization in patients with HHT

Particles, and temporary proximal occlusion was achieved with 1-2 mm Gelfoam® particles (Pfizer, New York, NY, USA) (Figure 2). Bilateral sphenopalatine devascularization was performed in all patients, while unilateral devascularization only in the territory of the ascending palatine artery (AP) was performed in one patient (Table 1).

Endonasal surgery

Following identification of the vertical part of the palate bone, at the level of the middle turbinate tail, a vertical mucosal incision was made. A subperiostal mucosal flap was elevated, revealing

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Embolization</th>
<th>Surgical cauterization</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SPx2</td>
<td>SPx2, AEx2, PEx2</td>
</tr>
<tr>
<td>2</td>
<td>SPx2</td>
<td>SPx2, AEx2, PEx2</td>
</tr>
<tr>
<td>3</td>
<td>SPx2</td>
<td>SPx2, AEx2</td>
</tr>
<tr>
<td>4</td>
<td>SPx2, right AP</td>
<td>SPx2, AEx2, right PE</td>
</tr>
<tr>
<td>5</td>
<td>SPx2</td>
<td>SPx2, AEx2, PEx2</td>
</tr>
</tbody>
</table>

SP: sphenopalatine artery; AE: anterior ethmoid artery; PE: posterior ethmoid artery; AP: ascending palatine artery; x2: bilateral.

Figure 2

Digital subtraction angiography (DSA) of the left external carotid artery (LECA). (a) Prembolization, LECA DSA, showing characteristic mucosal blush and hypervascularization, mainly from branches of the maxillary artery. (b) Postembolization LECA DSA, showing almost complete devascularization of the mucosa from the maxillary artery.
Six months after surgery. Four out of five patients showed a reduction in the ESS ranging from 50.8% to 82.3%. One patient presented with a much lower reduction in the ESS of 10%; this patient did not receive complete surgical management because of intraoperative leakage of CSF.

Nine months after surgery. Four of the patients still showed a reduction of ≥ 50% in the ESS, with values ranging from 50.8% to 82.3%. The patient whose score had improved after a 3-month period did not show a benefit from the surgery at 9 months.

Twelve months after surgery. One patient preserved a positive response to treatment, with a 74.2% reduction in his ESS compared to his initial score. The other three patients showed an overall reduction, although to a lesser extent: 37%, 26.8%, and 22.2%.

Intraoperative complications

None of the patients presented any complications during the embolization procedure. During endonasal endoscopic surgery, a CSF leak occurred immediately following cauterization of the posterior ethmoidal artery. The osseous/dural defects were repaired using an inferior turbinate free graft held in place with biological glue (Tissucol®; Baxter Healthcare, Deerfield, IL, USA).

Postoperative complications

All of the patients presented facial pain for up to 3 weeks post-operation. This was attributed to the embolization procedure and responded to mild analgesics.

Discussion

It is difficult to compare, in terms of efficacy, the various treatments available for chronic epistaxis in the setting of HHT. The evaluation criteria used are often different. Based on case series and expert opinions published in the literature, the preferred first-line surgical therapy for mild-to-moderate epistaxis in HHT is laser photocoagulation, which has the advantage of being well tolerated and can be repeated. Laser photocoagulation usually results in a reduction in the frequency and intensity of bleeding of ≥ 50% for > 6 months. In addition, it
Endonasal cauterization in patients with HHT

than endonasal surgical arterial cauterization are embolization, septodermoplasty (Saunders’ technique), and definitive closure of the nasal cavities (Young’s technique). Although percutaneous embolization may be very effective in treating idiopathic, traumatic, or tumor-related epistaxis, it is much less effective for severe epistaxis.\textsuperscript{12,13} HHT is a progressive disease; chronic epistaxis may become increasingly disabling in some patients. At present, patients are instructed to rest at home for a given period of time. Thus, issues regarding the management of chronic epistaxis that is no longer responsive to first-line treatments arise. Surgical alternatives to first-line treatments other

is recommended over sclerotherapy, which presents a risk of allergic reactions as well as reflux of particles into the ophthalmic artery.\textsuperscript{12} Although laser photocoagulation is effective in the medium term for mild-to-moderate chronic epistaxis, it is less effective for severe epistaxis.\textsuperscript{13}

HHT is a progressive disease; chronic epistaxis may become increasingly disabling in some patients. At present, patients are instructed to rest at home for a given period of time. Thus, issues regarding the management of chronic epistaxis that is no longer responsive to first-line treatments arise. Surgical alternatives to first-line treatments other than endonasal surgical arterial cauterization are embolization, septodermoplasty (Saunders’ technique), and definitive closure of the nasal cavities (Young’s technique). Although percutaneous embolization may be very effective in treating idiopathic, traumatic, or tumor-related epistaxis, it is much less effective at treating the recurrent nose bleeds that characterize HHT.\textsuperscript{12,13} In the 12-patient series of Layton and colleagues,\textsuperscript{19} only 20-25% of patients had a significant decrease in the frequency and intensity of epistaxis following a single endovascular procedure. More than half of the patients had to be embolized repeatedly in order

**Figure 3**

Epistaxis Severity Score (ESS) questionnaire

<table>
<thead>
<tr>
<th>Table 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent reduction in the ESS over time</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient</th>
<th>3 months</th>
<th>6 months</th>
<th>9 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100%</td>
<td>82.3%</td>
<td>82.3%</td>
<td>74.2%</td>
</tr>
<tr>
<td>2</td>
<td>60.4%</td>
<td>56%</td>
<td>60.4%</td>
<td>26.8%</td>
</tr>
<tr>
<td>3</td>
<td>50.8%</td>
<td>50.8%</td>
<td>50.8%</td>
<td>22.2%</td>
</tr>
<tr>
<td>4</td>
<td>65.2%</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>5</td>
<td>53%</td>
<td>60%</td>
<td>60%</td>
<td>37%</td>
</tr>
</tbody>
</table>
achieve a satisfactory and significant reduction in nosebleeds. About a quarter of patients did not show improvement despite treatment and continued to have severe epistaxis. In this series and that of Fisher and colleagues\textsuperscript{17} (eight patients), only 20% of patients appeared to maintain long-term benefits. This period of time was, however, not properly defined. The ethmoidal arteries, which are not accessible to embolization, contribute substantially to epistaxis; thus, this was likely a factor in failure of the procedure. In our series, the role of the ethmoidal arteries in endonasal pathology was demonstrated by angiography. However, there are risks associated with embolization, such as migration of particles. This risk could increase considerably depending on the level of experience of the operator, and it may vary among institutions. Nevertheless, when performed judiciously, percutaneous embolization could allow for more-complete vascular control, which would limit bleeding during endonasal surgical arterial cauterization. This would make the combined therapy more efficient than embolization.

The septodermoplasty procedure (Saunders’ technique) consists of eliminating the involved nasal mucosa and replacing it with free skin grafts. The technique was evaluated in an uncontrolled, retrospective, case-series study of 67 patients with HHT who presented with severe chronic epistaxis. There was a significant decrease in blood transfusions required 1 year following the intervention, as well as an increase in subjective quality of life. However, >50% of treated patients were lost to follow-up. During the follow-up period of this study (mean 3.9 year) and owing to the recurrence of their symptoms, 15 patients had to undergo several treatments ranging from simple endonasal cauterization to localized repeated septal dermoplasties.\textsuperscript{18} It is difficult to compare this surgical technique directly with ours. Our follow-up period was shorter, the total number of patients was smaller, and our evaluation criteria were different. Nevertheless, we have some idea of the effectiveness and tolerability of our regimen. According to our results, endonasal surgical cauterization reduced the ESS by >50% up to at least 9 months post-surgery in the majority of treated patients (four patients). Only one of our patients rapidly relapsed and presented an ESS score at 6 months post-op that was close to his presurgery score. We attribute this poor result to two factors: (1) During surgery, we were deliberately incomplete in our management. Although both posterior ethmoidal arteries had been shown by angiography to be contributing to epistaxis, we addressed only one side because of the intraoperative occurrence of a CSF leak. (2) The patient was 70 years old at the time of treatment.

HHT is known to be a progressive disease, and telangiectasia lesions increase in number and size with age, which in turn increases the frequency and intensity of nosebleeds. By contrast, the patient with the best response to treatment throughout the follow-up period was the youngest of the series; this patient initially had the lowest ESS.

Although we cannot prove the superiority of our method compared to septodermoplasty, we can compare the side effects. Patients operated on by Saunders' technique develop crusty debris in their nasal cavities that can last for relatively long periods of time. These crusts can regularly become infected, resulting in a foul odor.\textsuperscript{19} The intranasal crusts that developed in our patients after surgery were easily managed and treated by the frequent use of normal saline and topical lubricants. Owing to the aggressive removal of nasal mucosa, septodermoplasty is itself a major source of increased nosebleeds due to the high risk of septal perforation. This risk is even higher upon repetition of the procedure.\textsuperscript{13} However, during endonasal surgical arterial cauterization, the septal mucosa is kept intact. Instead, the major complications of the intervention are related to the course of the ethmoidal arteries along the base of skull. Upon cauterization of any of these, an osseous/dural defect can occur, resulting in CSF leak. Surgeons should be aware of this possibility and be able to correct the defect promptly. The presence of an interventional neuroradiology department in our hospital allowed us, one day prior to surgery, to perform an embolization procedure at the level of the external carotid branches contributing to the epistaxis. This decreased the risk of intraoperative bleeding. However, it had the side effect of exposing patients to the risks inherent to embolization: particle migration to the internal carotid artery and thromboembolic risks. Moreover, embolization results in facial pain, as described by our patients, which was easily treated by mild analgesics.

Patients not affected by HHT who are undergoing endonasal arterial surgery treatment for their epistaxis do not describe such symptoms, but those
who are undergoing embolization do describe facial pain. To secure the patient’s comfort, pre-embolization at the level of the external carotid branches can be avoided.

Definitive closure of the nasal fossae (Young’s technique) is presently the only effective surgical technique for treating chronic epistaxis over the long term. Patients do not develop malodorous infected crusts and generally stop bleeding, thereby decreasing the risk of developing chronic anemia that results in chronic fatigue. Quality of life is improved, as patients’ daily anxiety is greatly diminished. In their series of 43 patients (mean follow-up of 34 months), Richter and colleagues reported good tolerance associated with the procedure in 100% of the cases and bleeding completely stopped in 83% of the patients. Furthermore, a mean increase of 4.83g/dl in the hemoglobin level occurred. Following surgery, the patient loses his/her sense of smell, continuously complains of nasal congestion and obstruction, and experiences oral dryness. Most upsetting of all to the patient, he/she can no longer breathe through his/her nose, which can be a source of ongoing anxiety.

The future of epistaxis treatment in patients with HHT probably lies with drug treatments developed through a better understanding of the pathogenesis of HHT. Antifibrinolytic agents (tranexamic acid) and hormonal therapy (ethinyl estradiol) have each been studied in a double-blinded, randomized, case-control study. Investigators were unable to demonstrate a significant increase in hemoglobin levels but noted a significant subjective improvement in epistaxis severity. These treatments have the disadvantage of increasing the risk of thromboembolism. Experiments with anti-angiogenic agents suggest that they are more promising as potential therapeutic options. Recently, several cases of patients treated with bevacizumab (anti-VEGF) have been reported; however, amelioration of epistaxis was only temporary.

Conclusions

Although our study was limited by the small number of patients and the results are preliminary, endonasal surgical arterial cauterization, preceded or not by devascularization embolization, may have a place as a second-line treatment option for chronic epistaxis in patients with HHT. Although our results were recorded over a short time period, the patients’ quality of life improved substantially post-surgery. In the future, drug treatments are likely to be directed against vascular proliferation.

References

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