RO Bibliography

1st trimester 2020

TOPICS

Qual Life Res. 2020 Jan 6.

Hereditary hemorrhagic telangiectasia and health-related quality of life: a qualitative investigation.

Martinent G[1], Carrot M[2], Chirac A[2], Dupuis-Girod S[3], Fargeton AE[3], Blois Da Conceição S[4], Fourdrinoy S[5].

Author information

Abstract

OBJECTIVE:

The purpose of the study was to arrive at an accurate description of health-related quality of life of hereditary hemorrhagic telangiectasia patients.

METHODS:

Thirteen semi-structured interviews were conducted in patients with hereditary hemorrhagic telangiectasia.

RESULTS:

Qualitative grounded theory analyses were performed using the participants' transcripts and revealed the following six categories: Impact of physical symptoms on daily life, Quality of family and social life, Emotional and psychological outcomes related to the disease, Knowledge having a severe disease and coping strategies to manage such disease, Recognition of the disease by professional colleagues and superiors, and Knowledge and understanding from health professionals in medical care.

CONCLUSION:

The definition of quality of life that emerged from the participants' transcripts was essentially related to health. Individuals with hereditary hemorrhagic telangiectasia mainly focused on the physical, psychological and emotional impacts of the symptoms and their consequences on professional life and social activities. Family relationships were also highlighted in the participants' transcripts. As such, HHT patients used coping strategies to manage their disease. Finally, a particularly salient issue referred to the lack of knowledge concerning the rare nature of this disease and the ensuing inherent sense of misunderstanding.

DOI: 10.1007/s11136-020-02415-7

1. Orphanet J Rare Dis. 2020 Jan 7;15(1):5.

Hereditary haemorrhagic telangiectasia and pregnancy: a review of the literature.

Dupuis O[1,2], Delagrange L[3], Dupuis-Girod S[4,5].

Author information

Abstract

BACKGROUND:

Hereditary haemorrhagic telangiectasia (HHT) is a dominantly inherited genetic vascular disorder that has prevalence of 1:5000 to 1:8000, and which is characterised by recurrent epistaxis, cutaneous telangiectasia, and arteriovenous malformations (AVMs) that affect many organs including the lungs, gastrointestinal tract, liver, and central nervous system. The aim here was to carry out a review of the literature on HHT complications during pregnancy in order to guide management decisions.

MAIN BODY:

A literature review was carried out to analyse all publications on complications that occurred during pregnancy in women with HHT. The PubMed/Medline and Scopus databases were searched. The complications observed in HHT women during pregnancy were then described. The authors identified 5 case series and 31 case reports that describe the evolution of 1577 pregnancies in 630 women with HHT. The overall maternal death rate described in the case series was estimated at 1.0% of pregnancies in the case series and 2 maternal deaths occurred in 31 pregnancy case reports. Severe maternal complications occurred in 2.7 to 6.8% of pregnancies in the case series. Severe complications occurred mostly in the second and third trimester in non-diagnosed and non-screened HHT patients. Severe complications were related to visceral involvement. The most frequent complications were related to pulmonary arteriovenous malformations (PAVMs) (haemothorax (n = 10), haemoptysis (n = 4), and severe hypoxaemia (n = 3)). Neurological complications were related to PAVMs in one case (right to left shunt) and to cerebral arteriovenous malformations (CAVM) and intracranial haemorrhage in 2 cases. Complications were related to hepatic arteriovenous malformations (HAVMs) in 8 cases (acutely decompensated heart failure due to hepatic involvement (n = 1), dyspnoea related to heart failure (n = 5), and hepatobiliary necrosis (n = 2)).

CONCLUSION:

Based on the literature review, most pregnancies in HHT women occur normally. However, these pregnancies should be considered high-risk, given the potential life-threatening events related to AVM rupture. Furthermore, there is currently no international consensus regarding the medical follow-up of pregnancy in women with HHT and the aim here was to carry out a review of the literature in order to guide screening and management decisions for this rare disease.

DOI: 10.1186/s13023-019-1286-z

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2. Case Rep Obstet Gynecol. 2020 Mar 3;2020:2746947.

Osler-Weber-Rendu Disease Uncovered by Preeclampsia in a Case Report.

Ouachaou J[1], Mimouni H[1], Maarad M[1], Mellagui Y[1], Oulad Amar A[2], Bkiyar H[1], Kamaoui I[2], Housni B[1].

Author information

Abstract

Osler-Weber-Rendu disease (OWRD), called hereditary hemorrhagic telangiectasia, is an uncommon genetic illness with the dominant autosomal transmission. It cannot be easily or quickly diagnosed because of both its infrequency and its various associated symptoms. As far as its symptoms are concerned, the patient experiences recurring epistaxis, mucocutaneous telangiectasia, and arteriovenous malformations that can lead to severe undesirable symptoms. In our case, we report a 32-year-old female that was diagnosed with postpartum preeclampsia and whose paraclinical examinations showed that she suffers from hereditary hemorrhagic telangiectasia disease. Management of OWRD includes systematic diagnosis of visceral arteriovenous malformations (AVMs) in regular intervals, measures to prevent complications, and symptomatic treatment.

DOI: 10.1155/2020/2746947

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3. BMJ Case Rep. 2020 Jan 13;13(1). pii: e231120.

Anaesthetic management of a parturient with hereditary haemorrhagic telangiectasia (HHT) and pulmonary haemorrhage requiring urgent caesarean section.

Mac Sweeney C[1], Connolly P[2], Brady AB[3], Cafferkey Á[2].

Author information

Abstract

A 25-year-old gravida 3 para 3 with a history of hereditary haemorrhagic telangiectasia (HHT) and embolised pulmonary arteriovenous malformations (PAVMs) was admitted at 36 weeks gestation with haemoptysis, epistaxis and CT evidence of recent alveolar haemorrhage. An urgent caesarean section was planned. Both previous pregnancies had been delivered by elective lower segment caesarean section (LSCS) under subarachnoid block (SAB) at term.

Preanaesthetic planning involved consultation with our tertiary maternity referral centre, the national HHT centre and our tertiary adult referral centre, which has interventional radiology and cardiothoracic capabilities. A whole spine MRI was carried out to rule out vascular malformation. Following multidisciplinary discussion, the decision was made to proceed with caesarean section in our hospital under SAB. Wide bore intravenous access was sited and blood product availability was ensured in case of acute pulmonary haemorrhage. The LSCS was uneventful. Postoperatively following discharge from the hospital, the patient experienced recurrent episodes of small volume haemoptysis, and had further PAVM embolisation in the national HHT centre. This report highlights the difficulties in managing complex parturients in a non-tertiary referral centre and underlines the importance of communication and multidisciplinary team discussion to determine the most appropriate management.

DOI: 10.1136/bcr-2019-231120

BMJ Full Text

ORL Therapy

1. Angiogenesis. 2020 Feb 28.

Intranasal Efudix reduces epistaxis in hereditary hemorrhagic telangiectasia.

de Jel DVC[1], Disch FJM[2], Kroon S[3], Mager JJ[3], Verdam FJ[2].

Author information

Abstract

BACKGROUND:

Local application of fluorouracil (Efudix, 5-FU) induces sclerosis in patients with sinonasal tumors and superficial basocellular skin carcinoma. As a 'back against the wall' treatment, we investigated the local effect of nasally applied 5-FU and whether this could decrease the burden of severe epistaxis in patients with hereditary hemorrhagic telangiectasia (HHT).

METHODS:

HHT patients with severe and frequent epistaxis, subsequent anemia and a necessity for blood and/or iron infusions were treated with a nasal tampon with 5-FU. This tampon was placed unilaterally in the nasal cavity on the side of the most severe epistaxis and replaced once weekly during 4 weeks. Outcome measures were safety and side effects, the aspect of the nasal mucosa measured with the mucosal HHT score, the epistaxis severity score (ESS), hemoglobin and ferritin plasma levels, and quality of life assessment pre-treatment, one and three months post-treatment.

RESULTS:

Six HHT patients participated. During treatment and follow-up, the nasal mucosa turned more pale and sclerotic and the number of telangiectases diminished. The mucosal HHT score improved and the ESS declined (p = 0.01). The decline of ESS persisted up to 3 months post-5-FU treatment. Moreover, mean hemoglobin levels increased from 6.0 pre-5-FU to 6.8 after one month post-5-FU.

CONCLUSION:

Unilateral application of 5-FU on a nasal tampon diminished the severity and frequency of epistaxis in all HHT patients. This effect sustained up to three months post-treatment, despite the fact that the contralateral side remained untreated. Subsequently, hemoglobin levels increased. Intranasal 5-FU is a promising entity for further research on epistaxis treatment in HHT patients.

DOI: 10.1007/s10456-020-09712-2

SpringerLink FULL-TEXT ARTICLE

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2. Otolaryngol Head Neck Surg. 2020 Jan;162(1):8-25.

Clinical Practice Guideline: Nosebleed (Epistaxis) Executive Summary.

Tunkel DE[1], Anne S[2], Payne SC[3], Ishman SL[4], Rosenfeld RM[5], Abramson PJ[6], Alikhaani JD[7], Benoit MM[8], Bercovitz RS[9], Brown MD[10], Chernobilsky B[11], Feldstein DA[12], Hackell JM[13], Holbrook EH[14], Holdsworth SM[15], Lin KW[16], Lind MM[17], Poetker DM[18], Riley CA[19], Schneider JS[20], Seidman MD[21,22,23], Vadlamudi V[24], Valdez TA[25], Nnacheta LC[26], Monjur TM[26].

Author information

Abstract

OBJECTIVE:

Nosebleed, also known as epistaxis, is a common problem that occurs at some point in at least 60% of people in the United States. While the great majority of nosebleeds are limited in severity and duration, about 6% of people who experience nosebleeds will seek medical attention. For the purposes of this guideline, we define the target patient with a nosebleed as a patient with bleeding from the nostril, nasal cavity, or nasopharynx that is sufficient to warrant medical advice or care. This includes bleeding that is severe, persistent, and/or recurrent, as well as bleeding that impacts a patient's quality of life. Interventions for nosebleeds range from self-treatment and home remedies to more intensive procedural interventions in medical offices, emergency departments, hospitals, and operating rooms. Epistaxis has been estimated to account for 0.5% of all emergency department visits and up to one-third of all otolaryngology-related emergency department encounters. Inpatient hospitalization for aggressive treatment of severe nosebleeds has been reported in 0.2% of patients with nosebleeds.

PURPOSE:

The primary purpose of this multidisciplinary guideline is to identify quality improvement opportunities in the management of nosebleeds and to create clear and actionable recommendations to implement these opportunities in clinical practice. Specific goals of this guideline are to promote best practices, reduce unjustified variations in care of patients with nosebleeds, improve health outcomes, and minimize the potential harms of nosebleeds or interventions to treat nosebleeds. The target patient for the guideline is any individual aged ≥3 years with a nosebleed or history of nosebleed who needs medical treatment or seeks medical advice. The target audience of this guideline is clinicians who evaluate and treat patients with nosebleed. This includes primary care providers such as family medicine physicians, internists, pediatricians, physician assistants, and nurse practitioners. It also includes specialists such as emergency medicine providers, otolaryngologists, interventional radiologists/neuroradiologists and neurointerventionalists, hematologists, and cardiologists. The setting for this guideline includes any site of evaluation and treatment for a patient with nosebleed, including ambulatory medical sites, the emergency department, the inpatient hospital, and even remote outpatient encounters with phone calls and telemedicine. Outcomes to be considered for patients with nosebleed include control of acute bleeding, prevention of recurrent episodes of nasal bleeding, complications of treatment modalities, and accuracy of diagnostic measures. This guideline addresses the diagnosis, treatment, and prevention of nosebleed. It will focus on nosebleeds that commonly present to clinicians with phone calls, office visits, and emergency room encounters. This guideline discusses first-line treatments such as nasal compression, application of vasoconstrictors, nasal packing, and nasal cautery. It also addresses more complex epistaxis management, which includes the use of endoscopic arterial ligation and interventional radiology procedures. Management options for 2 special groups of patients, patients with hemorrhagic telangiectasia syndrome (HHT) and patients taking medications that inhibit coagulation and/or platelet function, are included in this guideline. This guideline is intended to focus on evidence-based quality improvement opportunities judged most important by the working group. It is not intended to be a comprehensive, general guide for managing patients with nosebleed. In this context, the purpose is to define useful actions for clinicians, generalists, and specialists from a variety of disciplines to improve quality of care. Conversely, the statements in this guideline are not intended to limit or restrict care provided by clinicians based upon their experience and assessment of individual patients.

ACTION STATEMENTS:

The guideline development group made *recommendations* for the following key action statements: (1) At the time of initial contact, the clinician should distinguish the nosebleed patient who requires prompt management from the patient who does not. (2) The clinician should treat active bleeding for patients in need of prompt management with firm sustained compression to the lower third of the nose, with or without the assistance of the patient or caregiver, for 5 minutes or longer. (3a) For patients in whom bleeding precludes identification of a bleeding site despite nasal compression, the clinician should treat ongoing active bleeding with nasal packing. (3b) The clinician should use resorbable packing for patients with a suspected bleeding disorder or for patients who are using anticoagulation or antiplatelet medications. (4) The clinician should educate the patient who undergoes nasal packing about the type of packing placed, timing of and plan for removal of packing (if not resorbable), post procedure care, and any signs or symptoms that would warrant prompt reassessment. (5) The clinician should document factors that increase the frequency or severity of bleeding for any patient with a nosebleed, including personal or family history of bleeding disorders, use of

anticoagulant or antiplatelet medications, or intranasal drug use. (6) The clinician should perform anterior rhinoscopy to identify a source of bleeding after removal of any blood clot (if present) for patients with nosebleeds. (7a) The clinician should perform, or should refer to a clinician who can perform, nasal endoscopy to identify the site of bleeding and guide further management in patients with recurrent nasal bleeding, despite prior treatment with packing or cautery, or with recurrent unilateral nasal bleeding. (8) The clinician should treat patients with an identified site of bleeding with an appropriate intervention, which may include 1 or more of the following: topical vasoconstrictors, nasal cautery, and moisturizing or lubricating agents. (9) When nasal cautery is chosen for treatment, the clinician should anesthetize the bleeding site and restrict application of cautery only to the active or suspected site(s) of bleeding. (10) The clinician should evaluate, or refer to a clinician who can evaluate, candidacy for surgical arterial ligation or endovascular embolization for patients with persistent or recurrent bleeding not controlled by packing or nasal cauterization. (11) In the absence of life-threatening bleeding, the clinician should initiate first-line treatments prior to transfusion, reversal of anticoagulation, or withdrawal of anticoagulation/antiplatelet medications for patients using these medications. (12) The clinician should assess, or refer to a specialist who can assess, the presence of nasal telangiectasias and/or oral mucosal telangiectasias in patients who have a history of recurrent bilateral nosebleeds or a family history of recurrent nosebleeds to diagnose hereditary hemorrhagic telangiectasia syndrome (HHT). (13) The clinician should educate patients with nosebleeds and their caregivers about preventive measures for nosebleeds, home treatment for nosebleeds, and indications to seek additional medical care. (14) The clinician or designee should document the outcome of intervention within 30 days or document transition of care in patients who had a nosebleed treated with non resorbable packing, surgery, or arterial ligation/embolization. The policy level for the following recommendation about examination of the nasal cavity and nasopharynx using nasal endoscopy was an *option:* (7b) The clinician may perform, or may refer to a clinician who can perform, nasal endoscopy to examine the nasal cavity and nasopharynx in patients with epistaxis that is difficult to control or when there is concern for unrecognized pathology contributing to epistaxis.

DOI: 10.1177/0194599819889955

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3. Otolaryngol Head Neck Surg. 2020 Jan;162(1_suppl):S1-S38.

Clinical Practice Guideline: Nosebleed (Epistaxis).

Tunkel DE[1], Anne S[2], Payne SC[3], Ishman SL[4], Rosenfeld RM[5], Abramson PJ[6], Alikhaani JD[7], Benoit MM[8], Bercovitz RS[9], Brown MD[10], Chernobilsky B[11], Feldstein DA[12], Hackell JM[13], Holbrook EH[14], Holdsworth SM[15], Lin KW[16], Lind MM[17], Poetker DM[18], Riley CA[19], Schneider JS[20], Seidman MD[21,22,23], Vadlamudi V[24], Valdez TA[25], Nnacheta LC[26], Monjur TM[26].

Author information

1. Cardiovasc Intervent Radiol. 2020 Feb 4.

Reperfusion of Pulmonary Arteriovenous Malformations Following Embolotherapy: A Randomized Controlled Trial of Detachable Versus Pushable Coils.

Kennedy SA[1,2], Faughnan ME[3,4,5], Vozoris NT[3,4,5], Prabhudesai V[6,3].

Author information

Abstract

PURPOSE:

To compare 1 year post-embolization reperfusion rates in pulmonary arteriovenous malformations (PAVMs) treated with the 0.035″ Interlock™ Fibered IDC™ Occlusion System coils (IDC) (Boston Scientific, Marlborough, Massachusetts) versus 0.035″ Nester coils (Cook Medical Inc., Bloomington, Indiana).

MATERIALS AND METHODS:

A randomized controlled trial was performed randomizing individual PAVMs to treatment with IDC versus Nester coils at the largest hereditary hemorrhagic telangiectasia center in Canada. The primary outcome was CT evidence of reperfusion at 1 year. Secondary outcomes included periprocedural complications, fluoroscopy time and contrast volume.

RESULTS:

Our study was terminated prematurely due to slow recruitment and subsequent expiration of funding. A total of 46 PAVMs in 25 patients (64% female) were included in our study; 26 randomized to Nester coils and 20 randomized to IDC. One patient was lost to follow-up. At a mean follow-up of 421.2 ± 215.7 days, no significant difference in PAVM reperfusion was detected between Nester coils and IDC (0% vs. 5.6%, $p > 0.05$). No major periprocedural complications were noted in either group. Fluoroscopy time (Nester: 15.0 ± 11.8 min vs. IDC 16.0 ± 5.4 min, $p > 0.05$) and contrast volume (Nester: 80.3 ± 36.5 ml vs. IDC 87.3 ± 51.7 ml, $p > 0.05$) utilized did not differ between groups.

CONCLUSION:

No significant difference was detected in PAVM reperfusion rates, periprocedural complication rates, contrast volume utilization or fluoroscopy time following embolization with IDC and Nester coils.

DOI: 10.1007/s00270-020-02422-8

2. Gen Thorac Cardiovasc Surg. 2020 Jan 13.

Emergency surgery for hemothorax due to a ruptured pulmonary arteriovenous malformation.

Naito J[1], Nakajima T[2], Morimoto J[1], Yamamoto T[1], Sakairi Y[1], Wada H[1], Suzuki H[1], Sugiura T[3], Tatsumi K[3], Yoshino I[1].

Author information

Abstract

Pulmonary arteriovenous malformation (PAVM) is a potential cause of hemothorax. The risk of PAVM rupture is reported to be higher during pregnancy for several reasons, including increased body fluid and a change in hormonal conditions. A 34-year-old pregnant woman suddenly felt right chest pain and dyspnea in the 28th week of gestation. Chest X-ray and computed tomography showed massive right pleural effusion. Her vital signs gradually deteriorated with hemorrhagic shock, necessitating emergency surgery. During exploratory thoracoscopy, active bleeding from the middle lobe was noticed and gauze packing was required to maintain her blood pressure. Following conversion to major thoracotomy, wedge resection of the middle lobe was performed with a linear stapler, and finally, her general condition became stable. Her postoperative course was uneventful. A histological examination of the resected specimen confirmed the diagnosis of ruptured PAVM. Her baby was successfully delivered at the 38th week of gestation.

DOI: 10.1007/s11748-020-01291-9

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3. Gen Thorac Cardiovasc Surg. 2020 Jan 13.

Emergency surgery for hemothorax due to a ruptured pulmonary arteriovenous malformation.

Naito J[1], Nakajima T[2], Morimoto J[1], Yamamoto T[1], Sakairi Y[1], Wada H[1], Suzuki H[1], Sugiura T[3], Tatsumi K[3], Yoshino I[1].

Author information

Abstract

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condition became stable. Her postoperative course was uneventful. A histological examination of the resected specimen confirmed the diagnosis of ruptured PAVM. Her baby was successfully delivered at the 38th week of gestation.

DOI: 10.1007/s11748-020-01291-9

SpringerLink FULL-TEXT ARTICLE

Therapeutic strategy

1. PLoS One. 2020 Feb 7;15(2):e0228486.

Bevacizumab for treating Hereditary Hemorrhagic Telangiectasia patients with severe hepatic involvement or refractory anemia.

Vázquez C[1,2], Gonzalez ML[1,3,4], Ferraris A[1,2], Bandi JC[1,3,5], Serra MM[1,2,3].

Author information

Abstract

OBJECTIVE:

To report our clinical experience with bevacizumab in a cohort of Hereditary Hemorrhagic Telangiectasia (HHT) patients with severe hepatic involvement and/or refractory anemia.

METHODS:

Observational, ambispective study of the Institutional Registry of HHT at Hospital Italiano de Buenos Aires. Patients were treated with bevacizumab due to iron deficiency refractory anemia secondary to nasal/gastrointestinal bleeding and/or high output cardiac failure. We describe basal clinical data, bevacizumab schedules, efficacy outcomes and adverse events. Wilcoxon signed ranks test and longitudinal analysis were conducted.

RESULTS:

Twenty adult patients were included from July 2013 to June 2019. Clinical indications were: 13 for anemia, 4 for heart failure and 3 for both. In the anemia group, median pretreatment hemoglobin was 8.1 g/dl [IQR: 7.2-8.4] and median transfusion requirement was 4 units [2-6]. In heart failure group, pretreatment median cardiac index was 4.5 L/min/m2 [4.1-5.6] and cardiac output was 8.3 L/min [7.5-9.2]. Bevacizumab 5 mg/kg/dose every 2 weeks for 6 applications was scheduled. By the end of induction, median hemoglobin at 3 months was 10.9 g/dl [9.5-12.8] ($p = 0.01$) and median transfusion requirement 0 units [0-1] ($p<0.01$), and this effect was more or less sustained during a year. Regarding heart failure group, two patients had complete hemodynamic response and achieved liver transplantation and two had partial response. No serious adverse events were registered.

CONCLUSION:

Bevacizumab is a promising line of treatment for HHT patients with refractory anemia. For patients with high output cardiac failure, bevacizumab may be useful as bridge therapy awaiting for liver transplantation.

DOI: 10.1371/journal.pone.0228486

Epidemiology

1. Clin Microbiol Infect. 2020 Mar 20. pii: S1198-743X(20)30154-3.

Hereditary haemorrhagic telangiectasia and pulmonary arteriovenous malformations in brain abscess patients: A nationwide, population-based matched cohort study.

Bodilsen J[1].

Author information

Abstract

OBJECTIVES:

The extent of hereditary haemorrhagic telangiectasia (HHT) and pulmonary arteriovenous malformations (PAVM) as a risk factor for brain abscess is unknown.

METHODS:

Nationwide and population-based registries were used to identify persons with first-time hospitalization for brain abscess (index date) and population controls matched by age, sex, and residence (1:10). Accounting for competing risks, cumulative incidence curves of new diagnosis of HHT/PAVM after brain abscess were constructed. Next, Cox regression was used for computation of cause-specific hazard rate ratios (HRRs) adjusted for severe liver disease and congenital heart disease as potential confounders.

RESULTS:

HHT/PAVM was prevalent before the index date in 2/1,384 (0.1% [95% CI 0.02-0.52]) brain abscess patients and 6/13,838 (0.04% [95% CI 0.02-0.09]) matched population controls. After the index date, a new diagnosis of hereditary haemorrhagic telangiectasia or pulmonary arteriovenous malformations was made in 15/1,384 brain abscess patients (range 0 days to 17 years) compared with 7/13,812 population controls yielding an adjusted hazard rate ratio of 31.4 (95% CI 9.95-98.9). Cumulative incidence was 1.5% for brain abscess patients and 0.1% for population controls.

CONCLUSIONS:

HHT/PAVM should be considered in patients with cryptogenic brain abscess, although absolute risk is low.

DOI: 10.1016/j.cmi.2020.03.011

ELSEVIER FULL-TEXT ARTICLE

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2. Eur Arch Otorhinolaryngol. 2020 Mar 2.

Hospitalization for epistaxis: a population-based healthcare research study in Thuringia, Germany.

Kallenbach M[1], Dittberner A[1], Boeger D[2], Buentzel J[3], Kaftan H[4], Hoffmann K[5], Jecker P[6], Mueller A[7], Radtke G[8], Guntinas-Lichius O[9].

Author information

Abstract

PURPOSE:

Epistaxis is the most common ENT emergency. The aim was to determine population-based data on severe epistaxis needing inpatient treatment.

METHODS:

Retrospective population-based cohort study in the federal state Thuringia in 2016 performed on all 840 inpatients treated for epistaxis in otolaryngology departments (60.1% male, median age: 73 years; 63.9% under anticoagulation). The association between patients' and treatment characteristics and longer inpatient stay (≥ 4 days) as well as readmission for recurrent epistaxis was analyzed using univariable and multivariable statistics.

RESULTS:

The overall incidence of epistaxis needing inpatient treatment was higher for men (42 per 100,000) than for women (28 per 100,000). The highest incidence was reached for men > 85 years (222 per 100,000). Most important independent predictors for longer inpatient stay were localization of the bleeding not in the anterior nose (OR = 2.045; CI = 1.534-2.726), recurrent bleeding during inpatient treatment (OR = 2.142; CI = 1.508-3.042), no electrocoagulation (OR = 2.810; CI = 2.047-3.858), and blood transfusion (OR = 2.731; CI = 1.324-5.635). Independent predictors for later readmission because of recurrent epistaxis were male gender (OR = 1.756; CI = 1.155-2.668), oral anticoagulant use (OR = 1.731; CI = 1.046-2.865), and hereditary hemorrhagic telangiectasia (OR = 13.216; CI 5.102-34.231).

CONCLUSIONS:

Inpatient treatment of epistaxis seems to be variable in daily routine needing standardization by clinical guidelines and strategies to shorten inpatient treatment and to reduce the risk of readmission.

DOI: 10.1007/s00405-020-05875-2

SpringerLink FULL-TEXT ARTICLE

3. Orphanet J Rare Dis. 2020 Mar 2;15(1):63.

Gender differences in hereditary hemorrhagic telangiectasia severity.

Mora-Luján JM[1,2,3], Iriarte A[1,2,3], Alba E[1,3,4], Sánchez-Corral MA[1,3,5], Cerdà P[1,2,3], Cruellas F[1,3,6], Ordi Q[1,3,4], Corbella X[1,2,3,7], Ribas J[1,3,8], Castellote J[1,3,9,10], Riera-Mestre A[11,12,13,14].

Author information

Abstract

BACKGROUND:

Gender differences in organ involvement and clinical severity have been poorly described in hereditary hemorrhagic telangiectasia (HHT). The aim of this study was to describe differences in the severity of HHT manifestations according to gender.

METHODS:

Severity was measured according to Epistaxis Severity Score (ESS), Simple Clinical Scoring Index for hepatic involvement, a general HHT-score, needing for invasive treatment (pulmonary or brain arteriovenous malformations -AVMs- embolization, liver transplantation or Young's surgery) or the presence of adverse outcomes (severe anemia, emergency department -ED- or hospital admissions and mortality).

RESULTS:

One hundred forty-two (58.7%) women and 100 (41.3%) men were included with a mean age of 48.9 ± 16.6 and 49 ± 16.5 years, respectively. Women presented hepatic manifestations (7.1% vs 0%) and hepatic involvement (59.8% vs 47%), hepatic AVMs (28.2% vs 13%) and bile duct dilatation (4.9% vs 0%) at abdominal CT, and pulmonary AVMs at thoracic CT (35.2% vs 23%) more often than men. The Simple Clinical Scoring Index was higher in women (3.38 ± 1.2 vs 2.03 ± 1.2), and more men were considered at low risk of harboring clinically significant liver disease than women (61% vs 25.3%). These differences were mantained when considering HHT1 and HHT2 patients separetely. Duodenal telangiectasia were more frequent in men than women (21% vs 9.8%). Invasive treatments were more frequently needed in women (28.2% vs 16%) but men needed attention at the ED more often than women (48% vs 28.2%), with no differences in ESS, HHT-score, anemia hospital admissions or mortality.

CONCLUSIONS:

HHT women showed more severe hepatic involvement than men, also among HHT1 and HHT2 patients. Women had higher prevalence of pulmonary AVMs and needed invasive procedures more frequently, while men needed attention at the ED more often. These data might help physicians to individualize HHT patients follow-up.

DOI: 10.1186/s13023-020-1337-5

1. J Clin Med. 2020 Mar 12;9(3). pii: E767.

Impaired Release of Neutrophil Extracellular Traps and Anemia-Associated T Cell Deficiency in Hereditary Hemorrhagic Telangiectasia.

Droege F[1], Pylaeva E[2], Siakaeva E[2], Bordbari S[2], Spyra I[2], Thangavelu K[3], Lueb C[1], Domnich M[2], Lang S[1], Geisthoff U[3], Jablonska J[2].

Author information

Abstract

Hereditary hemorrhagic telangiectasia (HHT) is characterized by mucocutaneous telangiectases and visceral vascular malformations. Individuals suffering from HHT have a significantly increased risk of bacterial infections, but the mechanisms involved in this are not clear. White blood cell subpopulations were estimated with flow cytometry in 79 patients with HHT and 45 healthy individuals, and association with clinicopathological status was assessed. A prominent decrease in absolute numbers of T cells in HHT was revealed (0.7 (0.5-1.1) vs. 1.3 (0.8-1.6), 10^6/mL, $p < 0.05$), and in multivariate regression analysis, hemoglobin level was associated with lymphopenia (OR = 0.625, 95% CI: 0.417-0.937, $p < 0.05$). Although no changes in absolute numbers of neutrophils and monocytes were observed, we revealed a significant impairment of neutrophil antibacterial functions in HHT ($n = 9$), compared to healthy individuals ($n = 7$), in vitro. The release of neutrophil extracellular traps (NETs) against *Pseudomonas aeruginosa* MOI10 was significantly suppressed in HHT (mean area per cell, mm^2: 76 (70-92) vs. 121 (97-128), $p < 0.05$), due to impaired filamentous actin organization (% of positive cells: 69 (59-77) vs. 92 (88-94), $p < 0.05$). To conclude, this study reveals the categories of patients with HHT that are prone to immunosuppression and require careful monitoring, and suggests a potential therapeutic strategy based on the functional activation of neutrophils.

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2. Arterioscler Thromb Vasc Biol. 2020 Apr;40(4):e87-e104.

Impaired SMAD1/5 Mechanotransduction and Cx37 (Connexin37) Expression Enable Pathological Vessel Enlargement and Shunting.

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Author information

Abstract

OBJECTIVE:

Impaired ALK1 (activin receptor-like kinase-1)/Endoglin/BMP9 (bone morphogenetic protein 9) signaling predisposes to arteriovenous malformations (AVMs). Activation of SMAD1/5 signaling can be enhanced by shear stress. In the genetic disease hereditary hemorrhagic telangiectasia, which is characterized by arteriovenous malformations, the affected receptors are those involved in the activation of mechanosensitive SMAD1/5 signaling. To elucidate how genetic and mechanical signals interact in AVM development, we sought to identify targets differentially regulated by BMP9 and shear stress. Approach and Results: We identify Cx37 (Connexin37) as a differentially regulated target of ligand-induced and mechanotransduced SMAD1/5 signaling. We show that stimulation of endothelial cells with BMP9 upregulated Cx37, whereas shear stress inhibited this expression. This signaling was SMAD1/5-dependent, and in the absence of SMAD1/5, there was an inversion of the expression pattern. Ablated SMAD1/5 signaling alone caused AVM-like vascular malformations directly connecting the dorsal aorta to the inlet of the heart. In yolk sacs of mouse embryos with an endothelial-specific compound heterozygosity for *SMAD1/5*, addition of TNFα (tumor necrosis factor-α), which downregulates Cx37, induced development of these direct connections bypassing the yolk sac capillary bed. In wild-type embryos undergoing vascular remodeling, Cx37 was globally expressed by endothelial cells but was absent in regions of enlarging vessels. TNFα and endothelial-specific compound heterozygosity for *SMAD1/5* caused ectopic regions lacking Cx37 expression, which correlated to areas of vascular malformations. Mechanistically, loss of Cx37 impairs correct directional migration under flow conditions.

CONCLUSIONS:

Our data demonstrate that Cx37 expression is differentially regulated by shear stress and SMAD1/5 signaling, and that reduced Cx37 expression is permissive for capillary enlargement into shunts.

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FULL TEXT

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3. Orphanet J Rare Dis. 2020 Jan 7;15(1):4.

Future treatments for hereditary hemorrhagic telangiectasia.

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Abstract

Hereditary Hemorrhagic Telangiectasia (HHT), also known as Rendu-Osler syndrome, is a genetic vascular disorder affecting 1 in 5000-8000 individuals worldwide. This rare disease is characterized by various vascular defects including epistaxis, blood vessel dilations

(telangiectasia) and arteriovenous malformations (AVM) in several organs. About 90% of the cases are associated with heterozygous mutations of ACVRL1 or ENG genes, that respectively encode a bone morphogenetic protein receptor (activin receptor-like kinase 1, ALK1) and a co-receptor named endoglin. Less frequent mutations found in the remaining 10% of patients also affect the gene SMAD4 which is part of the transcriptional complex directly activated by this pathway. Presently, the therapeutic treatments for HHT are intended to reduce the symptoms of the disease. However, recent progress has been made using drugs that target VEGF (vascular endothelial growth factor) and the angiogenic pathway with the use of bevacizumab (anti-VEGF antibody). Furthermore, several exciting high-throughput screenings and preclinical studies have identified new molecular targets directly related to the signaling pathways affected in the disease. These include FKBP12, PI3-kinase and angiopoietin-2. This review aims at reporting these recent developments that should soon allow a better care of HHT patients.

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Case report

Case Rep Oncol. 2020 Feb 18;13(1):176-181.

Pathologically Complete Response after Triple Therapy in Locally Advanced Esophageal Cancer in a Hereditary Hemorrhagic Telangiectasia Patient.

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Abstract

Hereditary hemorrhagic telangiectasia (HHT) is a disorder characterized by vascular manifestations including mucocutaneous and visceral telangiectasias and arteriovenous malformations. Herein we present the case of a relatively young patient with HHT with an incidentally discovered locally advanced esophageal cancer on endoscopic screening and pathologically complete response after neoadjuvant chemoradiation. This case highlights an unusual tumor response to chemoradiation in locally advanced esophageal cancer, and the surveillance care of HHT patients.

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