International Journal of Pediatric Otorhinolaryngology 73S (2009) S61–S64

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Pediatric otolaryngologic manifestations of bleeding disorders

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ARTICLE INFO

Keywords:
Bleeding disorders
Otolaryngology
Pediatric
Diagnosis
Treatment

ABSTRACT

Objective: In 1930, considering the diseases of the blood and lymphatic glands in relation to otolaryngology, Goldsmith and McGregor stated that "… the otolaryngologist has frequently to deal with bleeding from the nose and throat …". After approximately 8 decades, in particular preoperatively, the use of universal coagulation screening in children is still controversial. Aim of the present review was to offer a concise but complete discussion of clotting disorders with pediatric otolaryngological interest recognizing: (i) vascular disorders, (ii) platelet disorders, (iii) disorders of coagulation, and (iv) thrombosis.
Methods: An exhaustive review of literature was performed to investigate available data and evidences regarding pediatric otolaryngologic manifestations of bleeding disorders.
Results/Conclusions: Modern otolaryngologists should be familiar with common bleeding disorders since many have head and neck manifestations. This knowledge allows the choice of appropriate pre-operative screening of surgical patients. The most important component of the preoperative assessment is the bleeding history that directs further laboratory evaluation. All otolaryngologic surgical procedures in children with bleeding disorders should be carried out with the close co-operation of the Haematology Department.

Contents

1. Introduction

In 1930, Goldsmith and McGregor [1] wrote in their paper "*A Consideration of diseases of the blood and lymphatic glands in relation to otolaryngology*" that "… the otolaryngologist has frequently to deal with bleeding from the nose and throat …". They also concluded that "… as such pathological conditions rest primarily on alterations of the blood or blood-forming organs … it must be remembered that the correct diagnosis of many obscure cases of haemorrhage from the mucosa of the nose and throat can only be made after skilled analysis of the completed blood picture …". Livingstone [2] stated that blood contains within itself not only the clotting factors that will initiate, accelerate and limit coagulation as required, but also a series of safety devices to prevent coagulation occurring within the vessels and for dissolving fibrin which is no longer useful. After approximately 5 decades, in particular preoperatively, the use of universal coagulation screening in children is still controversial [3]. Shaw et al. [3] considered 842 coagulation screening tests of pediatric patients referred from the Otolaryngology Department at Children's Hospital of Pittsburgh. Twenty-three cases (2.7%) showed abnormal prothrombin times (PT), partial thromboplastin times (PTT), or closure times (CT). Within this sub-population, 16 presented with prolonged PTT (70%),

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0165-5876/$ – see front matter

3 presented with both a prolonged PT and a prolonged PTT (13%), 1 with a prolonged PT (4%), 1 with increased CT (4%), 1 with prolonged CT and PTT (4%), and 1 with prolonged PT, PTT and CTs (4%). These 23 referral patients led to one type 1 Willebrand's disease diagnosis, 4 low Willebrand factor diagnoses and 1 platelet aggregation abnormality diagnosis.

In order to offer a concise but complete discussion of clotting disorders with pediatric otolaryngological interest, we decided to follow the classification approach proposed by Murphy [4] who recognized: (i) vascular disorders, (ii) platelet disorders, (iii) disorders of coagulation, and (iv) thrombosis.

2. Vascular disorders

The vascular disorders are characterised by easy bruising and bleeding into the skin and mucous membranes. Murphy [4] synthesised vascular disorders as follows: (i) congenital (hereditary haemorrhagic telangiectasia, connective tissue disorders), (ii) acquired (due to severe infection as septicaemia, meningococcal infections, measles, typhoid), (iii) allergic (Henoch-Schonlein purpura, connective tissue disorders), (iv) drug-induced, and (v) others.

Hereditary haemorrhagic telangiectasia (HHT), also known as Osler-Weber-Rendu disease, is an unusual disorder with autosomal dominant inheritance. Early linkage studies identified two loci that are situated at 9q34.1 (HHT-1, Endoglin) and at 12q11-q14 (HHT-2, ALK1) [5]. Subsequent studies reported that bone morphogenetic protein receptor II (BMPRII) and MADH4 gene mutations can cause HHT phenotype [6]. The incidence of HHT varies from 1 : 5000 to 1 : 8000 [5]. The genetic defects lead to multiple vasculopathies, especially of the capillary vessels, but also in the vessels of parenchymatous organs. Diagnosis of HHT is currently based on clinical findings like epistaxis, family history, telangiectases and visceral vascular malformation. These criteria of the Scientific Advisory Board of the HHT Foundation International (the so-called Curacao criteria) [7] specify that diagnosis of HHT is definite if 3 criteria are present, possible or suspected if 2 criteria are positive [8]. The disease is most commonly found in middle-aged patients [9]. It is still unclear to which extent the entire spectrum of HHT is expressed in children and adolescents. In 2006, Folz et al. [8] considered 15 children and adolescents from 9 families that had consulted the University of Marburg (Germany) with the tentative diagnosis of HHT. Recurrent epistaxis was present in 10/15 patients with a minimum age of 4 years for the first occurrence. They concluded that epistaxis therapy should be conservative with nasal creams. Besides local measures high dose anti-fibrinolytic agents (i.e. tranexamic acid) have shown efficacy at the time of epistaxis [6]. If conservative therapies fail to provide satisfactory reduction of epistaxis, surgical treatment should be considered: Nd:YAG laser provides good results in this age group. Folz et al. [8] stated that the results were also better than in the adult population, which might be due to the fact that the density of nasal telangiectases is less in children with HHT than in adults. Telangiectases within the nasal mucosa were present in 4 cases of their series: none of these patients was younger than 9 years. Cutaneous telangiectases and other vascular abnormalities of the skin were evident in 5/15 patients and were found on the fingers, arms, lower lip, trunk and neck. Visceral arterio-venous malformations were found in 4/15 cases (brain in 2 patients, lung in 2 patients). Folz et al. [8] concluded that, apart from treating epistaxis, the role of otolaryngologist is to analyse predilection sites for HHT manifestations in the head and neck area and to initiate consultation with pediatricians, radiologists (in particular for visceral vascular malformation diagnosis) and geneticists.

Henoch-Schönlein purpura (also referred to as anaphylactoid purpura) is the most distinguished of the hypersensitivity vasculitides. Purpuric lesions are generally seen over the lower extremities and buttock region but can occur anywhere, including the face [10].

3. Platelet disorders

Patients with platelet disorders usually bleed into superficial sites such as the skin, mucous membranes, genitourinary or gastrointestinal tract [11]. Bleeding is uncommon with platelets count above 50×10^9/litre, and severe spontaneous bleeding is unusual with platelet counts above 20×10^9/litre [4].

3.1. Thrombocytopenia

This is caused by reduced platelet production in the bone marrow or excessive peripheral destruction of platelets (see Table 1).

Autoimmune thrombocytopenic purpura (AITP) is due to immune destruction of platelets. Thrombocypenia is reasonably caused by the deposition of immune-complexes on platelets, but the shortened platelet survival is probably due to acute development of platelet auto-antibodies [4]. AITP is a relatively common hematologic disorder in children (an annual incidence of about 4 per 100,000 children), often following a viral infection. The morbidity and mortality associated with AITP generally revolve around patients who develop life-threatening haemorrhages (usually intracranial). Yue [12] studied otolaryngological manifestations of 90 patients (of which 50 were under 16 years) with AITP evaluated at the Pingdingshan Haematological Institute (People's Republic of China) over 10 years. Epistaxis was the most common complaint, followed by gum, buccal, conjunctive, tongue, lips, eyelids, facial and throat bleeding. Other conditions included: hearing loss, vertigo (or dizziness), tinnitus, facial paralysis. Sale et al. [13] described the rare case of a patient with chronic otitis media who developed idiopathic thrombocytopenic purpura with bleeding from the ear and ipsilateral nostril as a post-myringotomy complication. Acute AITP in children usually remits spontaneously. It is still not clear whether steroids and high-dose intravenous immunoglobulin treatment is effective in minimizing the period of thrombocytopenia or in reducing the incidence of chronic AITP, which develops in 5–10% of children [4].

Table 1
Causes of thrombocytopenia (modified from Murphy [4])

Platelet impaired production	Generalized bone marrow failure	Leukemia Aplastic anaemia Megaloblastic anaemia Myeloma Myelofibrosis Marrow infiltration by solid tumours
	Selective reduction in megakaryocytes	Drugs Viral infections Chemicals
Excessive destruction	Immune	Autoimmune thrombocytopenic purpura Secondary immune thrombocytopenia Autoimmune neonatal thrombocytopenia Post-transfusion purpura
	Coagulation	Disseminated intravascular coagulation (DIC) Thrombotic thrombocytopenic purpura Haemolytic uraemic syndrome
Sequestration	Hypersplenism	
Dilutional loss	Massive transfusion of stored blood	