International Journal of Pediatric Otorhinolaryngology 88 (2016) 129–135

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: http://www.ijporlonline.com/

To anticoagulate? Controversy in the management of thrombotic complications of head & neck infections

Jenna Rebelo [a, *], Smriti Nayan [a, b], Karen Choong [c], Martha Fulford [d], Anthony Chan [e], Doron D. Sommer [a]

[a] Division of Otolaryngology-Head and Neck Surgery McMaster University, Hamilton, Canada
[b] Department of Surgery, Cambridge Memorial Hospital, Cambridge, ON, Canada
[c] Division of Critical Care Medicine, Department of Pediatrics, McMaster University, Hamilton, Canada
[d] Division of Infectious Diseases, Department of Medicine, McMaster University, Hamilton, Canada
[e] Department of Pediatrics, McMaster University, Hamilton, Canada

ARTICLE INFO

Article history:
Available online 6 June 2016

Keywords:
Lemierre's
Pediatric
Infection
Thrombophlebitis
Anti-coagulation
Pharyngitis

ABSTRACT

Objective: To review the thrombotic complications of head and neck infections, including Lemierre's syndrome, and their management.
Methods: A retrospective review of pediatric patients presenting to McMaster Children's Hospital from 2009 to 2013 was undertaken. The literature was reviewed for evidence regarding the use of anti-coagulation therapy in this population.
Results: Eleven cases (6 males, 5 females) were identified. The median age was 10.9 (range 14 months −17 years). The most frequent head and neck infection causing a thrombotic complication was mastoiditis (n = 6). All had thrombi identified on imaging, with the most common location being the sigmoid sinus (n = 6) followed by the internal jugular vein (n = 5). All 11 patients were anti-coagulated with low molecular weight heparin (LMWH) within a median of 2 days of diagnosis (average duration 105.8 days). Ten patients (90.9%) had thrombus improvement or resolution within a median of 3.4 months (range 1.0–13.9). Adverse sequelae from the thrombi were MCA infarct (n = 1), septic pulmonary emboli (n = 4), cranial nerve palsies (n = 3) and Horner's syndrome (n = 2). There were no adverse effects from anti-coagulation therapy. Review of the literature revealed anticoagulant use in 63.7% of pediatric cases reported since 2002.
Conclusion: Anticoagulation remains controversial in the management of thrombotic complications from head and neck infections. Based on this case series, certain recommendations can be made regarding the benefits of anticoagulation, which appear to outweigh the risks. Further research is required to establish evidence for consensus in the antithrombotic management of thrombotic sequelae of head and neck infections.

1. Introduction

In 1898, Veillon and Züber, first described a case of human systemic *Fusobacterium necrophorum* infection involving a child who presented with septic arthritis and cerebral abscess secondary to chronic purulent otitis. The classical clinical entity, involving disseminated *F. necrophorum* infection from a pharyngeal (rather than otologic) source, was later described by Courmont and Cade in 1900. However, it was André Lemierre, in his series of 20 cases published in *The Lancet* in 1936, who provided the first clear description of the clinical entity that now bears his name. Lemierre's syndrome, also known as post-anginal sepsis, is classically characterized by a history of pharyngitis followed by fever, internal jugular vein (IJV) thrombophlebitis, septic thrombi to the lungs and/or other remote sites, and isolation of the anaerobic organism *F. necrophorum* from a sterile body site [1].

In recent decades, there has been a paradigm shift in the clinical practice of minimizing antimicrobial use in the treatment of pediatric head and infections such as pharyngitis and acute otitis media (AOM) as the vast majority of these infections are of viral etiology.

* Corresponding author. 1280 Main Street West, 3V1 Clinic, L8S 4L8, Canada.
E-mail address: jenna.rebelo@medportal.ca (J. Rebelo).

http://dx.doi.org/10.1016/j.ijporl.2016.06.013
0165-5876/

Coinciding with this change, there has been an increase in the number of reports of Lemierre's syndrome in the literature [2]. In addition, the literature also has many descriptions of similar thrombotic complications following head and neck infections, which are variants of the classic Lemierre's syndrome as they do not meet the traditional criteria. Currently, there are no consensus guidelines regarding the management of Lemierre's syndrome and it's variants in pediatric patients.

A retrospective case series from a single center and literature review was undertaken. The primary objective of the study was to determine the proportion of classical Lemierre's syndrome vs. variant disease among pediatric patients presenting with infectious thrombi of the head and neck and secondly, to determine which organisms were most responsible for head and neck thrombophlebitis. Through the literature review, we sought to develop recommendations for anticoagulation therapy by determining the indications for anticoagulant use, and to compare the outcomes of patients who were anticoagulated versus those who were not.

2. Methods

A retrospective review of Lemierre's syndrome and variant cases presenting to McMaster Children's Hospital, a tertiary referral center, between 2009 and 2013 was undertaken. Approval for the study was obtained from the Hamilton Integrated Research Ethics Board. Pediatric patients under 18 years of age with thrombotic complications from an infection in the head and neck region were included. Consecutive cases were evaluated and relevant data was prospectively obtained by two of the authors (JR and SN) using prescribed tables. Any disagreement was resolved through discussion and consensus.

2.1. Literature search strategy

The literature search was conducted using the following databases: AMED (Allied and Complementary Medicine) 1985 to February 2013, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, and Embase 1974–2013 Week 06. Similar strategies were used when searching all the databases. Relevant articles and abstracts were selected and reference lists reviewed from these sources, and recent review articles or systematic reviews were searched for additional relevant publications.

The search terms “thrombophlebitis”, “pharyngitis”, “*Fusobacterium* infections”, and “Lemierre Syndrome” were combined in a variety of ways to ensure the inclusion of both classical and variant cases (*i.e.* those with no preceding pharyngitis or with no isolation of *F necrophorum*). Classical cases were considered to be those involving all four characteristics of pharyngitis, internal jugular vein (IJV) thrombophlebitis, septic thromboemboli, and *F. necrophorum* confirmed on culture. Similar strategies were used when searching all the databases. Relevant articles and abstracts were selected and reviewed. Reference lists from these sources and recent review articles or meta-analyses were searched for additional relevant publications.

Studies were included in the literature review if they were fully published reports or abstracts of studies evaluating pediatric patients (<18 years of age) presenting with Lemierre's syndrome or a variant of classical Lemierre's. Articles were excluded if they were non-human trials, were published in a language other than English, or included patients greater than 18 years of age.

3. Results

3.1. Patient and infection characteristics

Eleven cases were identified, meeting the criteria of Lemierre's syndrome or variant between 2009 and 2013. The median age was 10.9 years (range 14 months–17 years). Patient demographics are shown in including the types of infections the patients had (Table 1). Recent dental work had been performed in two of the patients. The most common sign on clinical presentation was an area of swelling in the head and neck, as seen in Fig. 1 (face, n = 2; neck, n = 1; mastoid, n = 1; periorbital, n = 1). Other common symptoms were otalgia (n = 3), headache (n = 3), sore throat (n = 2), and fever (n = 2). *Fusobacterium necrophorum* was cultured in only one patient, and no organism was identified in four cases. Culture results are included in Table 1.

3.2. Thrombophlebitis characteristics

All patients had thrombi identified on CT or MR in at least one location, with seven patients having thrombus extension to multiple veins or venous sinuses. Extra-cranial sites of thrombophlebitis included the facial (n = 1), internal jugular (IJV) (n = 7), external jugular (EJV) (n = 2), and brachiocephalic (n = 1) veins, and intracranial thrombi were found in the transverse (n = 3), sagittal (n = 1), sigmoid (n = 6), and cavernous (n = 2) sinuses (Fig. 2). All patients were anti-coagulated (see Section 3.3).

3.3. Management

Medical management included antibiotic and anticoagulant therapy in all patients. The mean time between thrombus identification and initiation of anticoagulation was two days (range 0–21 days). Treatment included low molecular weight heparin (LMWH) in all cases. Additional antithrombotic agents included unfractionated heparin, which was used for initial bridging therapy in three patients, and ASA, which two patients received for long-term treatment. In one patient, the reason for long term ASA therapy was treatment of ischemic internal carotid artery (ICA) infarct. In the second patient, ASA was recommended due to noncompliance with LMWH at home. The average duration of anticoagulation (excluding ongoing ASA use in two patients) was 105.8 days. Ten patients (90.9%) experienced either improvement or complete resolution of thrombus on follow-up imaging. Time from thrombus identification to radiologic evidence of resolution or improvement ranged from 31 to 416 days (median 3.4 months).

Ten patients (90.9%) required some form of surgical management, although in one case, this was limited to wisdom tooth extraction following completion of anticoagulation therapy in a patient with an odontogenic source of infection. Other surgical interventions ranged in invasiveness from a myringotomy and tube (MT) in three cases, to a craniectomy and partial temporal lobectomy in one patient. Other surgical interventions included mastoidectomy (n = 2), endoscopic sinus surgery (ESS) (n = 1), and abscess drainage (n = 4) including one peritonsilar abscess (PTA) and one postauricular subperiosteal abscess. Anticoagulant and surgical treatment is summarized in Table 2. Anticoagulation was generally started within 24 h following the surgery as the risk of the thrombi were felt to be greater than the potential risk of bleeding secondary to anticoagulation.

3.4. Outcome

All patients required hospital admission with six (54.5%) of the patients being admitted to the pediatric intensive care unit (PICU).