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CASE REPORT

Streptococcus constellatus-associated Lemierre's syndrome presenting with extensive venous sinus thrombosis in a child

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Introduction

Lemierre's syndrome is a distinctive clinical syndrome characterised by septicaemia and septic thrombophlebitis of the internal jugular vein that occurs several days after a sore throat in a previously healthy individual (Karkos et al, 2009). A systematic review of 84 cases by Karkos et al (2009) identified tonsils (37%), pharynx or upper respiratory tract (30%), chest or lower respiratory tract (25%) as the most common sites of primary infection, as well as the middle ear or mastoid, larynx, dental, paranasal sinuses and orbits.

Classically, *Fusobacterium necrophorum* has been associated with Lemierre's syndrome, although other organisms, including *Fusobacterium nucleatum*, *Klebsiella pneumoniae*, *Trueperella bernardiae*, *Bacteroides stercoris*, *Campylobacter urealyticus*, *Streptococcus constellatus*, *Streptococcus anginosus* and *Streptococcus pyogenes*, have also been reported (Karkos et al, 2009; Yamaguchi et al, 2010; Shimada et al, 2014; Raymond et al, 2016; Kaiho et al, 2017; Yaita et al, 2018; Sacco et al, 2019; Rohowetz et al, 2020). This article describes a case of Lemierre's syndrome in a child associated with *Streptococcus constellatus*, part of the milleri group of streptococci.

Case report

A previously healthy 10-year-old girl presented with a few days' history of right-sided neck pain and swelling, fever, eye pain, drooping of eyelids and headache. Assessment revealed a temperature of 39.1°C, pulse rate 115/minute, blood pressure 110/59 mmHg and oxygen saturations of 97% in air. On examination, she had torticollis, tenderness over the jaw, trismus, proptosis and limitation of right eye movements. She was admitted with a provisional diagnosis of deep-seated neck tissue infection or inflammation and suspected right-sided orbital cellulitis.

Blood investigations on admission showed a C-reactive protein level of 397 mg/litre, which increased to 467 mg/litre 2 days later. Her white cell count was 27.9×10^9/litre, neutrophil count was 23.7×10^9/litre and platelet count was 310×10^9/litre. Intravenous co-amoxiclav was started after obtaining a blood culture. At day 5 growth of a Gram-positive organism was identified, later confirmed as *Streptococcus constellatus*, which was sensitive to both penicillin and clindamycin.

Contrast-enhanced computed tomography of the head, neck and orbits the next day showed right posterior paraspinal muscle inflammation without abscess, and extensive venous thrombosis in the right sigmoid sinus, internal jugular, facial and posterior paravertebral veins (Figure 1). Lemierre's syndrome was diagnosed and the patient was monitored in the high dependency unit. Antibiotics were switched to intravenous clindamycin, meropenem and metronidazole. Therapeutic doses of intravenous heparin were started.

Following discussion with a paediatric neurologist, magnetic resonance imaging of the neck and venogram were undertaken (Figures 2–4). In addition to the thrombosis seen on computed tomography, there was sagittal venous sinus and right cavernous sinus thrombosis, as well as two small septic emboli in the brain. No neck collection was identified.

The patient was transferred to the paediatric neurology centre as a result of persistent fever, worsening of torticollis and increasing swelling of the neck. A central line was inserted with the same antibiotics continued initially then changed to metronidazole and ceftriaxone to complete a full 4 weeks of intravenous therapy, followed by a further 2 weeks of oral metronidazole and co-amoxiclav. Intravenous heparin was changed after 7 days to subcutaneous enoxaparin to complete 3 months therapy. The patient made a full recovery and her blood parameters normalised. She was reported to be doing well without sequelae at clinic follow up.

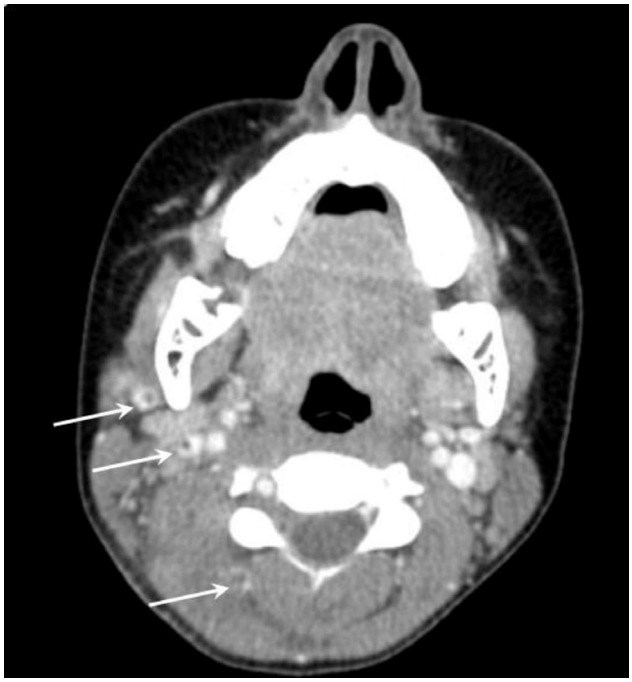

Figure 1. Axial contrast-enhanced computed tomography through the upper cervical spine and mandible. Non-occlusive thrombus seen as filling defects in the right anterior facial vein, internal jugular vein and posterior paraspinal vein (arrows).

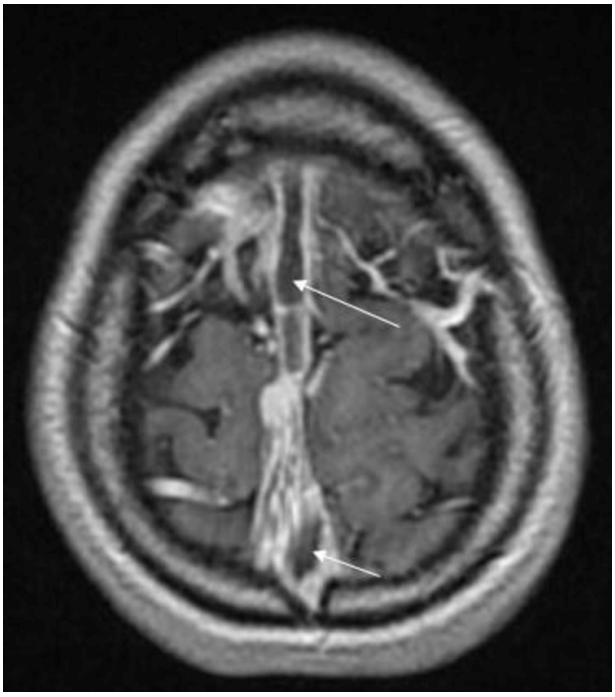

Figure 2. Axial contrast-enhanced T1 magnetic resonance imaging scan through the vertex of the head showing non-occlusive thrombus as a filling defect (arrows) within the superior sagittal sinus.

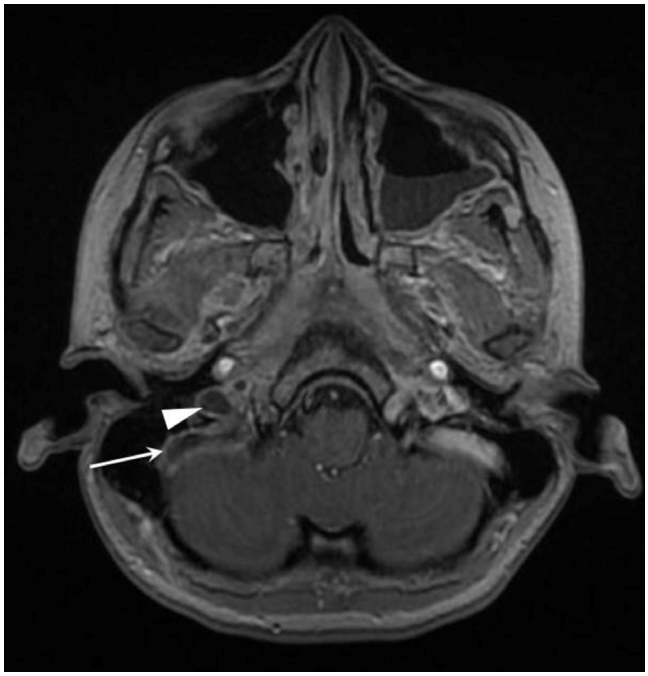

Figure 3. Axial contrast-enhanced T1 magnetic resonance imaging scan through the base of skull showing almost occlusive thrombus in the right sigmoid sinus (arrow) and internal jugular vein (arrowhead).

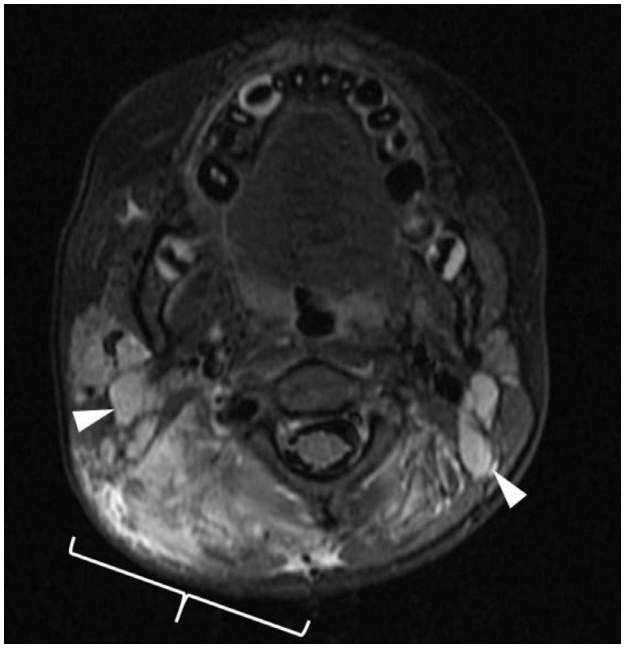

Figure 4. Axial magnetic resonance imaging (STIR) scan through the upper cervical spine and mandible showing high signal oedema in the posterior right paraspinal muscles of the neck without abscess (bracketed). Reactive lymphadenopathy is also seen (arrowheads).

Discussion

This is believed to be the first documented paediatric case of Lemierre's syndrome published in the English language associated solely with *Streptococcus constellatus*. Only six cases (all adults) have previously been reported, mostly from Japan (n=4) (Yamaguchi et al, 2010; Shimada et al, 2014; Raymond et al, 2016; Kaiho et al, 2017;

Yaita et al, 2018; Rohowetz et al, 2020). The overall incidence of Lemierre's syndrome varies between 1–10 cases per million person-years, with an estimated fatality rate of 4–9% (Sacco et al, 2019).

The initial presentations described were sore throat (33%), neck mass (23%), neck pain (20%), bone/joint pain, otalgia, otorrhoea, trismus, dental pain, orbital pain, gastrointestinal symptoms and limb weakness (Karkos et al, 2009). Radiological investigations most commonly requested were computed tomography of neck and chest (55%), followed by ultrasound (26%), magnetic resonance imaging or a combination of scans and magnetic resonance venogram (Karkos et al, 2009).

Streptococcus constellatus forms part of the milleri group of streptococci, which consists of three species: *S. anginosus*, *S. constellatus* and *S. intermedius*. These organisms are known to cause infections and indolent abscess in the head and neck region. A review by Riordan (2007) highlighted that organisms such as *Proteus* spp. or *Streptococcus oralis* may not be capable of causing Lemierre's syndrome in isolation, and it is possible that *Fusobacterium necrophorum* may have been present but remained undetected. Lemierre's syndrome can be associated with multiple organisms in the blood, even to the exclusion of *Fusobacterium necrophorum* which is more characteristic. Anaerobic organisms can be difficult to grow, especially in the paediatric setting where a single blood culture bottle is used (Paul et al, 2018) and any previous antibiotic usage would further reduce the chance of isolation. Although blood culture samples showing positive growth of alpha-haemolytic (viridans) streptococci at 5 days may occasionally represent contamination, this would be much less likely with *S. constellatus* and, in the clinical context of upper airway sepsis, is likely to represent a true pathogen. Metronidazole (clinidamycin if allergic) and a β-lactam- with anaerobic activity are recommended to cover polymicrobial infection (Riordan, 2007; Rohowetz et al, 2020). The role of anticoagulation therapy remains controversial in Lemierre's syndrome, although it is often used in cases with identified thrombophlebitis.

Conclusions

Lemierre's syndrome is often referred to as a 'forgotten disease' as it is a rare but potentially life-threatening condition. The best approach is early diagnosis and initiation of appropriate management with antibiotics, radiological investigations, anticoagulants and other supportive therapies. Surveillance studies and evaluation of risk factors for Lemierre's syndrome associated with *S. constellatus* are warranted.

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Learning points

- *Fusobacterium necrophorum* may not always be isolated in patients with Lemierre's syndrome.
- The diagnostic criteria for Lemierre's syndrome are based on a history of recent oropharyngeal infection, clinical or radiological evidence of thrombophlebitis of the internal jugular vein and isolation of an anaerobic pathogen.
- The empirical antibiotic regimen should include anaerobic cover with metronidazole and penicillin for 4 weeks.
- Use of anticoagulation therapy remains controversial and is often used in cases with thrombophlebitis.

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