CASE REPORT

Complicated *Fusobacterium necrophorum* mastoiditis – More than meets the eye

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ABSTRACT

Otitis media is common in children and *Fusobacterium* species are an emerging causative pathogen. These species have virulence factors which increase the risk of complicated otitis media. We discuss a case of *F. necrophorum* infection resulting in significant intracranial disease to highlight the epidemiology of these infections, risk factors for complicated disease and signs and symptoms to guide diagnosis and investigation.

Key Words: Otitis media, *Fusobacterium necrophorum*, Mastoiditis, Osteomyelitis, Lemierre's syndrome, Cavernous sinus thrombosis

1. CASE PRESENTATION

A previously well three-year-old girl presented to the emergency department (ED) with two days of progressive left-sided orbital swelling. She had become unwell eight days prior with lethargy, fever, left otalgia and vomiting. She had been reviewed by a General Practitioner who prescribed oral amoxycillin 25 mg/kg three times daily. Despite five days of amoxycillin, she experienced ongoing fevers associated with purulent discharge from her left ear.

On presentation, she was febrile to 39 degrees Celsius and tachycardic with a heart rate of 138 beats per minute. She was normotensive but appeared lethargic with signs of moderate dehydration. There was significant left eyelid oedema with discolouration and associated ptosis. Pupils and eye movements were unable to be assessed due to orbital swelling. Full blood examination revealed a normal haemoglobin 119 g/L, raised white cell count 23.7 $\times$ 10^9/L and neutrophil count 16.2 $\times$ 10^9/L with normal platelets 273 $\times$ 10^9/L. C-reactive protein (CRP) was above our test threshold at > 270 mg/L. She received fluid resuscitation with 20 ml/kg of 0.9% normal saline and was commenced empirically on intravenous (IV) ceftriaxone (100 mg/kg 24 hourly) and flucloxacillin (50 mg/kg 6 hourly) for presumptive diagnoses of orbital cellulitis and mastoiditis.

Following computer tomography (CT) and subsequent magnetic resonance imaging (MRI) of her head and neck (see Figure 1), she was diagnosed with left mastoiditis with secondary intracranial abscess, skull base osteomyelitis, cavernous sinus thrombosis, left internal carotid arteritis and associated right internal jugular vein (IJV) thrombosis. A left cortical mastoidectomy was completed with placement of a ventilation tube. Post-operatively IV metronidazole (7.5 mg/kg 8 hourly) was added whilst awaiting culture results. The patient was initially anti-coagulated with a heparin

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infusion which was changed to enoxaparin 20 mg twice daily, several days post-operation. Anti-factor Xa assays were monitored with a target range 0.5-1.0 units/ml and dosing adjusted accordingly.

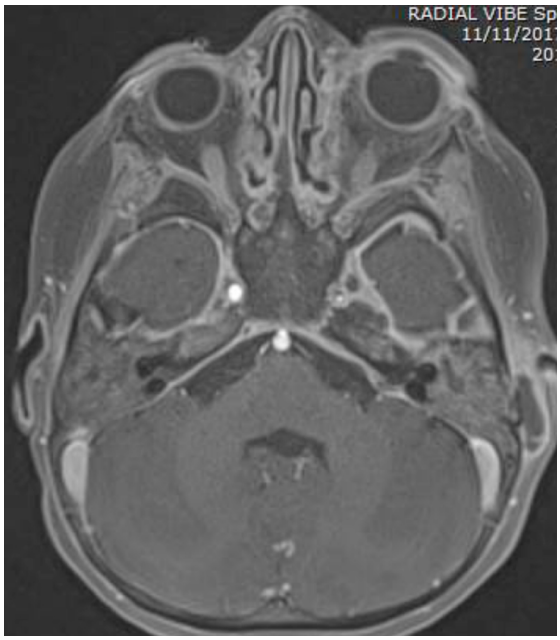

Figure 1. MRI Brain demonstrates evidence acute left mastoiditis with accompanying abscess of the left periauricular soft tissues. Intracranial extradural extension with abscess formation deep to the left sigmoid sinus. Features of secondary skull base osteomyelitis with an abscess underlying the left skull base. Near complete left cavernous sinus and left superior ophthalmic vein thrombosis with marked venous congestion of the left intra-orbital and periorbital soft tissues. Mural thickening and luminal narrowing of the left internal carotid artery.

Intra-operative swabs from her left mastoid cultured *Fusobacterium necrophorum*. Identification was made using a proprietary anaerobe identification kit. Anaerobic sensitivities were not tested, as is protocol at our institution. Blood cultures (Aerobic Paediatric bottle) taken pre and post antibiotics were negative, however, this result is unreliable as anaerobic bottles were not taken.

She continued to spike fevers up to 39°C. Further investigations were performed to detect possible infective metastases including a transthoracic echocardiogram, chest radiograph and an abdominal ultrasound. No evidence of septic emboli was demonstrated.

Four days post-operatively, she was noted to have left sided hypertonia in her upper and lower limbs. Despite therapeutic anticoagulation a repeat MRI of her brain demonstrated multiple bilateral infarctive foci involving the caudate and lentiform nuclei, likely secondary to vasculitis. As her eye swelling improved, a left sixth cranial nerve (CN) palsy was observed as a complication of the cavernous sinus thrombosis.

Two weeks following her operation, there was resolution of fevers with normalisation of inflammatory markers. With ongoing involvement by our Infectious Disease team, IV ceftriaxone and oral metronidazole were continued for a total of 10 weeks without complications. Therapeutic enoxaparin was continued for three months. Repeat neuroimaging demonstrated an improvement of skull osteomyelitis and progressive recanalization of the cavernous sinus with stable ischaemic changes. Due to difficulties in tolerating subcutaneous injections the patient was switched to warfarin (target INR 2-3). She completed a 6-month course of therapeutic anticoagulation with warfarin with resolution of the cavernous sinus and right IJV thrombosis. Mild residual stenosis of the left internal carotid artery and superior ophthalmic vein persisted so the patient will continue on aspirin 4 mg/kg daily for a further twelve months. On clinical follow-up there was complete resolution of her left eye ptosis and left sixth CN palsy with no neurological deficits. She had normal hearing on follow-up audiology.

2. DISCUSSION

This case is a potent reminder that although ear infections are incredibly common, there remains the potential for serious complications. We discuss below the epidemiology of *Fusobacterium* and possible signs that suggest further thought and investigation are warranted.

Fusobacterium species are Gram negative obligate anaerobes that can colonise the oral cavity, upper respiratory tract, gastrointestinal and female genital tract.[1,2] *Fusobacterium* species are increasingly implicated in pharyngitis and otogenic infections in children.[1] Controversy exists as to whether there is a true increase in incidence related to a reduction in antibiotic use for respiratory tract infections, or that improved microbiological detection techniques are facilitating diagnosis.[2–4] *F. necrophorum* possess virulence factors which promote local extension of infection and invasion into surrounding tissues and structures predisposing to intracranial complications and Lemierre's syndrome.[2,3] Intracranial complications secondary to *F. necrophorum* head and neck infection occur more frequently in infants and young toddlers[1,6] and include meningitis, epidural or brain abscesses and cerebral sinovenous thrombosis (CSVT).[1,3,5,6] In one single centre study, Shamriz et al. reported intracranial complications in 8/22 (36.4%) patients, of whom 9/22 (40.9%) stemmed from an otogenic focus.[1] Lemierre's syndrome predominately affects young adults with a review by Rior-

dan finding 89% of cases occurred between 10-35 years old with a median age of 19 years.[2] Complications can be life-threatening with mortality rates of 4.9% reported in Lemierre's syndrome and 6.7% in *F. necrophorum* infection.[2]

Fusobacterium infection in young children can cause a wide spectrum of disease resulting in multiple different presentations.[1,5] Inflammatory biomarkers are usually elevated as seen in our patient, but can be normal.[1,6] Persisting fever, decreased level of consciousness, signs of meningism or ophthalmoplegia should warrant further investigations to exclude intracranial infection or thrombosis.[1,5,7]

In our patient, her presenting features of fever, lethargy, significant eye swelling with limited examination of cranial nerves prompted concerns about intracranial involvement. Evidence of sepsis or respiratory compromise raises concerns of Lemierre's and metastatic infection.[1,5,7] Common sites for distal infection include lungs and joints, however other soft tissues, liver, kidneys, spleen and the central nervous system can be involved.[2] Fortunately, we were able to exclude Lemierre's syndrome and distal infection in our patient with imaging studies.

Early neuroimaging is essential for identification and prompt management of intracranial complications. MRI is the gold standard for identification of intracranial complications, however this modality may be limited by the requirement for sedation in younger children and issues of access and cost.[8] In contrast, CT is more readily available and does not require sedation, but is associated with significant radiation exposure.[8] MR or CT venography are required to assess for CSVT.[9]

Options in the management of complex *Fusobacterium* infections may include surgical drainage of associated abscesses and antibiotics.[2,3] Due to difficulties in identification, purification and manipulation of anaerobes, antimicrobial sensitivity testing is not performed routinely. *Fusobacterium necrophorum* is traditionally sensitive to penicillin, however, beta-lactamase resistance was found in 4% of isolates in a New Zealand analysis using the NCCLS reference agar dilution procedure.[2,3,10] In this analysis, all isolates were sensitive to amoxycillin/clavulanic acid, piperacillin/tazobactam, metronidazole, clindamycin, cephalosporins and carbapenems.[10] Current recommendations suggest treatment with either a beta-lactam/beta-lactamase inhibitor combination, carbapenem or metronidazole.[2,3] Metronidazole has the advantage of good tissue penetration and high oral bioavailability.[2] Broad spectrum cover is recommended in severe infections due to a high likelihood of polymicrobial involvement.[1,3] Recommended treatment durations range between 3 to 6 weeks, however may vary depending on the severity of infection and treatment response.[2] The prolonged duration of treatment in our patient was based on the extent of osteomyelitis and vasculitis with secondary thrombosis, in ongoing consultation with our local Infectious Diseases team.

The role of anticoagulation in *F. necrophorum* infection complicated by CSVT or Lemierre's is controversial and data is lacking.[9] In a literature review by Rebelo et al., amongst 51 documented paediatric cases of Lemierre's disease caused by *F. necrophorum*, 63.7% were on anticoagulants. Interestingly, the authors quote a Cochrane review for CSVT demonstrating no significant difference in morbidity or mortality between anti-coagulated and non-anticoagulated cohorts.[9] Our patient was anti-coagulated for CSVT for six months as per the American College of Chest Physician guidelines with no adverse effects.[11]

Fusobacterium species are a significant emerging pathogen in pharyngeal and otogenic infections in children, often overlooked. Our case describes serious infective sequelae complicating *F. necrophorum* otitis media which initially presented with relatively subtle clinical features. Our experience highlights the importance of a comprehensive clinical examination in otitis media and early neuroimaging if intracranial complications are suspected.

Conflicts of Interest Disclosure

The authors declare no conflicts of interest.

References

[1] Shamriz O, Engelhard D, Temper V, et al. Infections caused by Fusobacterium in children : a 14-year single-center experience. Infection : A Journal of Infection Disease. 2015; 43(6): 663-70. PMid:25929419. https://doi.org/10.1007/s15010-015-0782-x

[2] Riordan T. Human infection with Fusobacterium necrophorum (Necrobacillosis), with a focus on Lemierre's syndrome. Clinical Microbiology Reviews. 2007; 20(4): 622-59. PMid:17934077. https://doi.org/10.1128/CMR.00011-07

[3] Brook I. Fusobacterial head and neck infections in children. International Journal of Pediatric Otorhinolaryngology. 2015; 79(7): 953-8. PMid:25980688. https://doi.org/10.1016/j.ijporl.2015.04.045

[4] Osowicki J, Kapur S, Phuong L, et al. The long shadow of Lemierre's syndrome. Journal of Infection. 2017; 74: S47-S53. https://doi.

org/10.1016/S0163-4453(17)30191-3

[5] Giridharan W, De S, Osman E, et al. Complicated otitis media caused by Fusobacterium necrophorum. Journal of Laryngology and Otology. 2004;118(1): 50-3. PMid:14979974. https://doi.org/10.1258/002221504322731646

[6] Stergiopoulou T, Walsh TJ. Fusobacterium necrophorum otitis and mastoiditis in infants and young toddlers. European Journal of Clinical Microbiology and Infectious Diseases. 2016; 35(5): 735-40. PMid:26951264. https://doi.org/10.1007/s10096-016-2612-1

[7] Van-Munster M, Brus F, Mul D. Rare but numerous serious complications of acute otitis media in a young child. BMJ Case Reports. 2013; 2013: bcr2012008149. PMid:23486343. https://doi.org/10.1136/bcr-2012-008149

[8] Marom T, Roth Y, Boaz M, et al. Acute Mastoiditis in Children: Necessity and Timing of Imaging. The Pediatric Infectious Disease Journal. 2016; 35(1): 30-34. PMid:26398740. https://doi.org/10.1097/INF.0000000000000920

[9] Rebelo J, Nayan S, Choong K, et al. To anticoagulate? Controversy in the management of thrombotic complications of head and neck infections. International Journal of Pediatric Otorhinolaryngology. 2016; 88: 129-35. PMid:27497400. https://doi.org/10.1016/j.ijporl.2016.06.013

[10] Roberts S, Shore KP, Saviour SD, et al. Antimicrobial susceptibility of anaerobic bacteria in New Zealand: 1999-2003. Journal of Antimicrobial Chemotherapy. 2006; 57: 992-998. PMid:16507560. https://doi.org/10.1093/jac/dkl052

[11] Monagle P, Chan A, Goldenberg NA, et al. Antithrombotic therapy in Neonates and Children: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141: e737S-e801S. PMid:22315277. https://doi.org/10.1378/chest.11-2308