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Fusobacterium necrophorum, an emerging pathogen of otogenic and paranasal infections?

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Abstract

Fusobacterium necrophorum is a rare causative agent of otitis and sinusitis. Most commonly known is the classic Lemièrre's syndrome of postanginal sepsis with suppurative thrombophlebitis of the jugular vein. We report five patients diagnosed recently with a complicated infection with *F. necrophorum* originating from otitis or sinusitis. Two patients recovered completely, one patient died due to complications of the infection, one patient retained a slight hemiparesis and one patient had permanent hearing loss. Diagnosis and management are discussed. A possible factor in the emergence of *F. necrophorum* is proposed.

Keywords: Emerging pathogen, *Fusobacterium necrophorum*, Lemièrre's syndrome, otitis, sinusitis
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Introduction

Fusobacterium necrophorum is an anaerobic, non-spore forming pleomorphic Gram-negative rod which is considered a commensal of the animal and human upper respiratory, gastro-intestinal and female genital tract. It can cause a variety of human infections, but is most commonly known as the main cause of postanginal sepsis with suppurative thrombophlebitis of the jugular vein (Lemièrre's syndrome). Less well known is the otogenic variant with mastoiditis and intracranial complications such as meningitis, abscesses and sinus thrombosis [1]. We report five patients with a recent diagnosis of complicated infection with *F. necrophorum* originating from otitis or sinusitis with significant morbidity and mortality.

Case 1

A 9-year-old healthy girl, presented to the emergency department with fever, headache and vomiting. Two weeks before presentation the general practitioner had diagnosed an acute otitis media which was treated with co-amoxiclav for 7 days. The fever persisted intermittently with otalgia. One day before admission she developed otorrhoea and vomiting. On admission she was acutely ill with a temperature of 39.6°C, purulent discharge of the right ear, postauricular tenderness and nuchal rigidity. Cerebral spinal fluid revealed neutrophilic pleocytosis (2399/μL). Empiric antibiotic treatment was started with ceftazidime. A computed tomography scan of the brain showed total obliteration of the right mastoid, thrombosis of the sigmoid sinus and epidural empyema of 8 mm in the posterior surface of the temporal bone. Gram staining of the middle ear fluid showed pleomorphic Gram-negative rods, suggestive for the presence of *Haemophilus influenzae*. Gram staining of the cerebrospinal fluid did not reveal any bacteria. Shortly after admission an urgent mastoidectomy was performed. Post-operatively the patient did not regain consciousness (Glasgow Coma Scale E1M1Vtube) and there were no pupillary light reflexes. The

cultures after 1 day were negative. Antibiotic therapy was switched to meropenem. Repeated computed tomography of the brain revealed massive cerebral oedema with brainstem herniation. There was a progressive loss of all brainstem reflexes despite maximal therapy and treatment was withdrawn. The patient died 24 h after admission. Autopsy of the brain showed cerebral oedema with herniation, thrombosis of the sigmoid sinus and the transverse sinus and there was purulent discharge mainly in the posterior cranial fossa. The cultures taken during life (middle ear fluid and mastoid) and from the autopsy revealed *F. necrophorum*, identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS; Microflex, Bruker Daltonik, Bremen, Germany).

Case 2

A previously healthy, 9-year-old girl presented to the emergency department with the suspicion of meningitis. Nine days before admission she started with topical treatment (dexamethasone–framycetin–gramicidin eardrops, Sofradex®; Sanofi-aventis Netherlands B.V., Gouda, the Netherlands) for otitis and otorrhoea. Five days before admission she developed high fever, headache and vomiting and, consecutively, neck pain and stiffness 2 days before admission. She appeared acutely ill, but was fully conscious. Cerebrospinal fluid examination revealed a marked neutrophilic pleocytosis (1 280 000/μL). Empiric antibiotic therapy was started with ceftazidime. When pleomorphic Gram-negative rods were seen in the Gram staining of the cerebrospinal fluid, the antibiotic therapy was switched to meropenem. Computed tomography of the brain showed mastoiditis with thrombosis of the sigmoid sinus and a small empyema. An urgent mastoidectomy was performed. Post-operatively the patient was admitted to the intensive care department. *Fusobacterium necrophorum* was cultured after 24 h from the cerebrospinal fluid, and identified by MALDI-TOF MS. Antibiotic therapy was changed to penicillin. Magnetic resonance imaging (MRI) showed an additional right-sided pontine infarct. She recovered slowly and after 4 days she was transferred to the paediatric ward. The penicillin was continued for 18 days and then switched to clindamycin for another 3 weeks. The patient experienced no diarrhoeal problems during the use of clindamycin. Tinzaparin was started for the sinus thrombosis and continued for 3 months. After 20 days of hospitalization she was discharged, at that moment she experienced urinary and faecal incontinence and a hemiparesis of the left leg. Six months later the urinary and faecal incontinence had recovered, there was still a very mild hemiparesis of the left leg.

Case 3

A 2-year-old boy presented at the Ear, Nose and Throat Clinic with fever, otorrhoea and mastoiditis. Six weeks prior to admission he underwent adenoidectomy and received tympanostomy tubes in another hospital. Post-operatively he was re-admitted with fever and otitis for which he received several antibiotic treatments including amoxicillin, co-amoxiclav and ceftazidime. One week after discharge his symptoms returned. On admission his temperature was 39°C. Since 2 days he had had otorrhoea and mastoiditis was suspected. A computed tomography scan of the mastoid showed a Bezold's abscess with partial thrombosis of the sigmoid sinus and the right vena jugularis. A cortical mastoidectomy was performed with drainage of the abscess. On admission co-amoxiclav and ceftazidime were given. Gram stains of fluid from the right ear and the right mastoid showed slender, small Gram-negative rods. Anaerobic cultures revealed *F. necrophorum* (shown by using MALDI-TOF MS). No aerobic growth was observed. *F. necrophorum* was also cultured from the Bezold's abscess. Blood culture remained negative. Antibiotic treatment was changed to penicillin. The patient showed good clinical improvement. After 2 weeks he was discharged with clindamycin for 1 month. The patient experienced no diarrhoeal problems during the use of clindamycin.

Case 4

A 42-year-old man with a suspicion of mastoiditis and meningitis was transferred from another hospital to the intensive care unit of our hospital. His symptoms, right ear pain and a sore throat, started a few days before his first admission. One day before admission the patient showed an altered mental status, lateralization and lowered level of consciousness. On presentation he was febrile with tachycardia, a lowered level of consciousness, left muscle weakness and right ear discharge, possibly liquorrhoea. A computed tomography scan of the brain showed otitis and mastoiditis with total obliteration of the right mastoid, subdural empyema, two intraparenchymal abscesses in the right frontal and temporal lobe and a midline shift to the left. No sinus thrombosis was present. Right middle ear cultures were taken and amoxicillin, ceftriaxone and metronidazole were administered. Cultures revealed *F. necrophorum* (identified by Vitek 2; bioMérieux, Marcy l'Etoile, France). Amoxicillin was discontinued. Blood cultures remained negative. A hemicraniectomy was performed to drain the subdural empyema. Subsequently, a loss of sensitivity of his right ear and temporal skin was observed