Case Report

A rare presentation of ventriculitis and brain abscess caused by *Fusobacterium nucleatum*

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Anaerobic ventriculitis is rare, and usually seen in patients with predisposing factors such as otitis media, mastoiditis, sinusitis or recent neurosurgery. We report what we believe to be the first case of ventriculitis and brain abscess due to *Fusobacterium nucleatum* infection in a man with no significant predisposing factors. He was successfully treated with antibiotic therapy.

Introduction

Anaerobic organisms are rarely isolated from specimens of cerebrospinal fluid (CSF) submitted to the diagnostic microbiology laboratory, despite the recent improvement in laboratory methods for culturing obligate anaerobes. Anaerobic meningitis is not commonly reported and the incidence was approximately 1% in a large study of almost 500 cases of acute bacterial meningitis (Durand *et al.*, 1993). It has been associated with contiguous infection (otitis, sinusitis, pharyngitis, brain abscess), head and neck malignancy, recent head and neck surgery, and central nervous system (CNS) trauma (Tunkel & Scheld, 2005; Heerema *et al.*, 1979; Feldman, 1976). Anaerobic meningitis has also been associated with pathology at other sites including the abdomen (Heerema *et al.*, 1979). Anaerobic ventriculitis is also rare and may follow CNS surgery or shunt infection (Kaufman, 1997). This is in sharp contrast to cerebral abscesses, from which anaerobes can be cultured in 40–100% of cases. The most common anaerobes isolated from cerebral abscesses include *Fusobacterium nucleatum*, *Prevotella* spp., *Actinomyces* spp. and *Bacteroides* spp.

Fusobacterium spp. are non-spore-forming Gram-negative anaerobic bacilli. The most common species isolated from clinical specimens worldwide is *F. nucleatum*, which is currently divided into five subspecies. *F. nucleatum* forms part of the normal oral, gastrointestinal, urogenital and upper respiratory tract flora (Bolstad *et al.*, 1996) and is most commonly associated with periodontal disease. *Fusobacterium necrophorum* causes the life-threatening Lemierre's disease or necrobacillosis, although it has been reported as a cause of sore throat and localized abscesses (Brazier, 2006).

In this paper, we present the case of an immunocompetent patient who recently presented to our hospital with a brain abscess and ventriculitis caused by *F. nucleatum*.

Case report

A 47-year-old male bricklayer, who was previously fit and well, presented to our hospital with a 6-day history of worsening headache and neck pain. On the day prior to admission, he complained of fever, rigors and vomiting and had experienced transient loss of consciousness while passing urine. There were no other neurological symptoms, and he was taking no regular medication. He had no sore throat or symptoms of oral or pharyngeal infection, and had attended a routine dental check-up 6 weeks previously but had required no treatment.

On examination, he was alert and orientated, had a low grade fever and marked neck stiffness but no rash, photophobia, papilloedema or focal neurological signs. The peripheral white blood cell count was $14 \times 10^9 \text{ l}^{-1}$ (neutrophils $13 \times 10^9 \text{ l}^{-1}$) and C-reactive protein was 33 mg l^{-1} . Microscopy of the CSF revealed elevated polymorphs ($2250 \times 10^6 \text{ l}^{-1}$), elevated lymphocytes ($270 \times 10^6 \text{ l}^{-1}$), no red blood cells and no organisms visible on Gram stain. The CSF glucose concentration was low (0 g l^{-1} ; no simultaneous serum glucose available) and CSF protein was markedly elevated ($>2 \text{ g l}^{-1}$). There was no growth on aerobic culture, but CSF inoculated onto fastidious anaerobic broth media, incubated anaerobically for 48 h, grew small white haemolytic colonies that were susceptible to penicillin, metronidazole, co-amoxiclav and meropenem. Biochemical profiling (API Rapid ID 32A for anaerobes; bioMérieux) gave a result consistent with *F. necrophorum*. However, an in-house PCR of the original CSF, and the isolate, performed with primers specific for *F.*

Abbreviations: CNS, central nervous system; CSF, cerebrospinal fluid.

necrophorum (Aliyu *et al.*, 2005) was negative. Thus the isolate was submitted to the anaerobic reference laboratory and identified as *F. nucleatum* by amplified rDNA restriction analysis.

Cerebral imaging (CT head) on admission showed moderate dilatation of the lateral ventricle on the right with 3 mm midline shift to the left. There was a suggestion of some prominent soft tissue at the foramen of Monro. Thus the patient proceeded to MRI, which demonstrated mild dilatation of the right lateral ventricle, surrounded by increased signal (Fig. 1). These features were consistent with ventriculitis, in that there was enhancement of the ependyma and the swollen choroid plexus following the injection of contrast medium (gadolinium). The soft tissue at the foramen of Monro, noted on CT scan, was in keeping with enlargement of the choroid plexus. In addition, a small ring-enhancing structure adjoining the right lateral ventricle was noted (Fig. 1), consistent with a cerebral abscess. The parenchymal lesion and the abnormal choroid plexus exhibited restricted diffusion pattern on the diffusion-weighted imaging. The rest of the brain was normal with no meningeal or pial enhancement.

Based on the clinical presentation of headache and neck stiffness, intravenous therapy with ceftriaxone 2 g b.d. was initiated. When MRI demonstrated evidence of a cerebral abscess, intravenous metronidazole 500 mg t.d.s. was added. The ceftriaxone was changed to intravenous benzylpenicillin 2.4 g q.d.s. when antimicrobial susceptibility tests were available. In order to allow a prolonged course of intravenous antibiotics, a peripherally inserted central venous catheter (PICC) was inserted.

Ultrasonography of the patient's neck and jugular vessels, performed before the final isolate identification was available, excluded features associated with Lemierre's disease (caused by *F. necrophorum*); there was no evidence of abscess formation, lymphadenopathy or jugular vein thrombosis.

The patient gradually improved for 4 weeks, but then developed pyrexia of 38 °C, associated with nausea and vomiting. Examination revealed no obvious focus of infection. His antibiotic regimen was changed to meropenem 2 g t.d.s. and the PICC was removed. Blood, CSF, urine and stool cultures were performed and yielded no growth. A repeat CT scan of his head showed resolution of

Fig. 1. MRI of brain on admission showing cerebral abscess and ventriculitis. The top row of images shows one Axial T2-weighted image and two Flair images. There is dilation of the right lateral ventricle, minor midline shift to the left and periventricular high signal. The bottom row of images shows one Axial T1-weighted image and two T1 images after gadolinium enhancement. These illustrate enhancement of the ependyma and enlargement of the choroid plexus, consistent with ventriculitis. The arrows point to the gadolinium-enhancing parenchymal high signal lesion, consistent with a cerebral abscess.

ventricular dilatation and no new lesions. The patient subsequently developed a maculopapular rash over his trunk. Antibiotics were changed to linezolid 600 mg b.d., ciprofloxacin 200 mg b.d. and metronidazole 500 mg t.d.s. because of the possibility of beta-lactam allergy and sepsis of unknown cause. He made a full recovery and was discharged home after completing a 6-week course of antibiotics. When reviewed as an outpatient, the patient had made a full recovery with no residual neurological deficits.

Discussion

This clinical case of a patient diagnosed with ventriculitis and a brain abscess due to *F. nucleatum* highlights several important points in the presentation, diagnosis and management of anaerobic cerebral infections. It highlights the importance of anaerobic culture of CSF, without which there would have been no firm diagnosis or antibiotic susceptibility patterns to guide appropriate therapy. It also shows that such infections can occur in patients with no significant past medical history or predisposing injury, as demonstrated in our patient. The radiological imaging was unusual in that ventriculitis, usually seen in the context of postoperative neurosurgical or intraventricular catheter infection, was associated with an isolated cerebral abscess adjacent to the right lateral ventricle. The causative organism, *F. nucleatum*, has not previously been reported as a cause of ventriculitis together with brain abscess. Fortunately, the patient responded fully to appropriate antibiotic therapy alone.

This case highlights the importance of Gram stain and molecular tests in the laboratory identification of bacteria. *F. necrophorum* and *F. nucleatum* differ by one (2-naphthyl phosphate) of 32 biochemical test results on the Rapid ID 32A panel. Downes *et al.* (1999) found this test to poorly discriminate between the two species. The initial laboratory mis-identification of our isolate as *F. necrophorum* may have been avoided if staff had recognized that the cultured isolate did not have the typical Gram-stain appearance of *F. necrophorum*: pleomorphic Gram-negative rods with occasional long pleomorphic forms (Brazier, 2006) whereas *F. nucleatum* resembles slender Gram-negative rods. The isolate in our case was referred to the reference laboratory because our in-house molecular techniques (PCR specific *F. necrophorum*) (Aliyu *et al.*, 2005) gave a negative result for *F. necrophorum*. The initial incorrect speciation in our case led to aggressive treatment with a combination therapy of penicillin and metronidazole instead of metronidazole alone.

In early reports of anaerobic meningitis, identification of most of the causative organisms was to genus level only (Heerema *et al.*, 1979; O'Grady & Ralph, 1976); hence the epidemiology of meningitis and ventriculitis caused by *F. nucleatum* is still unclear. Heerema *et al.* (1979) searched the medical literature and found 17 cases of meningitis caused by *Fusobacterium* spp. among 86 reported cases of anaerobic meningitis, including 4 cases of their own. All cases of

Fusobacterium meningitis had underlying infection (12 patients with otitis/mastoiditis; two with pharyngitis; one case each of sinus, dental and pulmonary origin). We searched the PubMed database and found nine case series or case reports published in the English language of cerebral abscess with *F. nucleatum* and these predominantly involved patients who had undergone cranial or dental surgery or had a history of ENT infection or head trauma.

F. nucleatum meningitis is rarely reported. Chang *et al.* (2004) reported a case of *F. nucleatum* meningitis in a 63-year-old lady following a tooth extraction. She presented after 3 weeks of symptoms with fever, headache, neck stiffness, right eye proptosis and reduced level of consciousness. There was extensive disease with cavernous sinus thrombosis and cerebral infarction and she was treated conservatively with latamoxef. Six months after discharge she had residual hemiplegia.

In summary, cerebral infection caused by *F. nucleatum* is rare and is usually associated with underlying causes. To our knowledge, this is the first reported case of *F. nucleatum* ventriculitis and brain abscess in a patient with no significant past medical history or predisposing factors. This report illustrates the importance of considering anaerobes as cause of meningitis. It underlines the usefulness of molecular techniques in diagnosis of infections with *Fusobacterium* species and the potential success of conservative management with antimicrobial therapy.

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