**Case Report**

A 39-year-old female presented to the emergency department with sudden onset of generalized tonic-clonic convulsions followed by a loss of consciousness. Two days prior to the admission, she had been examined at the emergency department for malaise and low-grade fever following routine haemodialysis. At that time, no significant laboratory abnormalities were found aside from elevated C-reactive protein (CRP). Blood cultures were obtained and the patient was discharged. The patient’s medical history included end-stage renal disease due to systemic lupus erythematosus, and chronic haemodialysis for 4 years. Splenectomy had been performed 17 years prior to the current case of admission due to refractory immune thrombocytopenic purpura. In the years following splenectomy, she suffered from several severe infectious episodes including *Streptococcus* group A osteomyelitis and abdominal abscess, invasive pneumococcal disease with bacteremia, necrotizing pneumonia and meningitis. She was successfully treated with intravenous immunoglobulin monthly until 8 months prior to current admission. On examination, the patient’s heart rate was 85 min⁻¹, temperature was 36.1 °C, blood pressure was 86/35 mmHg and room air oxygen saturation was 96 %. The patient was unconscious, with a Glasgow Coma Scale of 7/15. There was no neck stiffness, or evidence of gross neurological deficit and the rest of her clinical examination was unremarkable.

**Bordetella holmesii** meningitis in an asplenic patient with systemic lupus erythematosus

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**Bordetella holmesii** is a slow-growing, Gram-negative, non-oxidizing bacillus with colonies that produce a brown soluble pigment and was originally described by Weyant et al. (1995) as CDC nonoxidizer group 2 (NO-2). It has recently been shown that *B. holmesii* may be isolated from nasopharyngeal specimens of up to 20 % of patients with pertussis-like symptoms. However, invasive *B. holmesii* has rarely been reported and in the vast majority of cases the patients were immune deficient, mostly as a result of splenectomy or functional asplenia. Clinical presentations have included endocarditis, pneumonia, cellulitis, suppurative arthritis, pyelonephritis and septicemia but no previous reports have documented meningitis secondary to this organism. Here we report what we believe to be the first clinical description of an adult with *B. holmesii* meningitis and bacteraemia with a brief review of published cases.

Laboratory findings revealed an elevated C-reactive protein of 30 mg dl⁻¹, elevated erythrocyte sedimentation rate of 53 mm h⁻¹, white cell count (WCC) of 14 700 μl⁻¹ and platelet count of 21 000 μl⁻¹. Metabolic acidosis with a pH of 7.23 and HCO₃ levels of 11 mmol l⁻¹ were present. Unidentified Gram-negative bacilli (GNB) were isolated from blood cultures taken 2 days previously on initial presentation at the emergency department. A lumbar puncture was performed and cerebrospinal fluid (CSF) analysis revealed an opening pressure of 27 cmH₂O, 7500 polymorphonuclear cells mm⁻³, high protein concentration of 1939 mg l⁻¹ (normal range 200–650 mg l⁻¹) and low glucose of 0.6 mmol l⁻¹. CSF Gram stain revealed GNB. Abdominal ultrasound, chest radiography, transoesophageal echocardiography and computed tomography images of the brain with and without contrast material were unremarkable. Intravenous therapy with ceftriaxone and ampicillin was begun, yet the patient further deteriorated with high fever, additional elevation of WCC and persistent convulsions controlled only with a continuous intravenous diazepam drip, requiring prophylactic mechanical ventilation. Despite the expansion of antibiotic coverage to ceftazidime and vancomycin, the fever persisted with additional elevation of WCC. Finally, treatment with meropenem and fluconazole was started. At this stage, CSF culture yielded an isolate which appeared to be similar to the unidentified GNB isolated from the blood. These organisms were small Gram-negative cocobacilli that produced small convex colonies with a brown soluble pigment on MacConkey agar. The bacterium was positive for oxidase activity and negative for catalase activity and the reduction of nitrate, urea...

**Case report**

Abbreviations: CSF, cerebrospinal fluid; GNB, Gram-negative bacilli; WCC, white cell count
and citrate. Commercially available identification systems (API-20-NE, bioMérieux) failed to identify the organism. The isolate was susceptible to ampicillin, third generation cefalosporins and meropenem, with MICs, measured by Etest (bioMérieux), of 0.094, 2.000, and 0.002 mg L⁻¹, respectively. We performed molecular characterization of the CSF isolate using 16S rRNA gene sequencing as previously described (Chakravorty et al., 2007; Gee et al., 2003). An amplified 586 bp fragment of the 16S rRNA gene of the organism showed 100% nucleic acid sequence similarity to several published B. holmesii 16S rRNA gene sequences (GenBank accession numbers: DQ409136.1, AY466116.1, AY466114.1, AY466115.1 and AF469002.1). This BLAST match also corresponded to Bordetella pertussis (99% sequence similarity); to rule this out, specific real-time PCRs to identify B. pertussis, Bordetella parapertussis and the B. pertussis toxin promoter (Knorr et al., 2006) were performed and all were negative. In addition, a throat swab from the patient was tested and found to be PCR-negative for B. pertussis.

With less than 3 weeks of treatment with meropenem, the patient improved, was weaned from mechanical ventilation and was transferred to the rehabilitation department for an additional 3 weeks, after which she was discharged home without permanent neurological deficits.

Discussion

To the best of our knowledge, this is the first reported case of meningitis secondary to infection with B. holmesii. As in most of the previous clinical reports of infection with this organism, our patient was asplenic. In the largest study to date of 26 patients with B. holmesii bacteraemia, 85% were anatomically or functionally asplenic, 12% had other kinds of immune suppression and only one patient (3%) was reported as being previously healthy (Shepard et al., 2004). The clinical picture was characterized by non-specific febrile illness and the outcomes were generally favourable with a 100% survival rate (Shepard et al., 2004). Although there are no established interpretive MIC breakpoints for this organism, antibiotic susceptibility testing on isolates from these patients showed that the MICs of the β-lactam drugs, including the cephalosporins, were high relative to the MIC breakpoints of several other common aerobic Gram-negative bacterial pathogens, while the MICs of the carbapenems, fluoroquinolones and trimethoprim–sulfamethoxazole were low (Shepard et al., 2004).

In addition to the above-mentioned study and excluding previous and recent reports suggesting that B. holmesii may be an emerging respiratory pathogen which has been isolated from nasopharyngeal specimens of immune-competent patients with pertussis-like symptoms (Njamkepo et al., 2011; Mooi et al., 2011; Mazengia et al., 2000; Yih et al., 1999), we found another 16 case reports (including the present case) of invasive B. holmesii infection. Of the 14 patients for whom data were available, 12 (85%) were anatomically or functionally asplenic (Njamkepo et al., 2000; Greig et al., 2001; Lam et al., 2008; McCavit et al., 2008; Panagopoulos et al., 2010; Moissenet et al., 2011), one (10%) had frequently relapsing steroid-sensitive nephritic syndrome (Dörbecker et al., 2007), and one (10%) was previously healthy (Russell et al., 2001). All patients presented with fever; eight had a non-specific febrile illness (Weyant et al., 1995; Njamkepo et al., 2000; Lam et al., 2008; McCavit et al., 2008; Panagopoulos et al., 2010); three had respiratory symptoms (Monnier et al., 2010; Dörbecker et al., 2007; Russell et al., 2001) two of which had X-ray documented pneumonia and respiratory failure (Dörbecker et al., 2007; Russell et al., 2001); one had endocarditis (Tang et al., 1998); two had haemodialysis-associated bacteraemia (Greig et al., 2001 and our patient); one had cellulitis (McCavit et al., 2008); and one had septic arthritis (Moissenet et al., 2011). Different antimicrobial treatment strategies, including β-lactams and erythromycin, were employed resulting in a 100% survival rate. One surviving patient developed pulmonary fibrosis (Russell et al., 2001).

B. holmesii may be an emerging respiratory pathogen in patients with pertussis-like symptoms. Nevertheless, it appears to be a rare invasive disease affecting, almost exclusively, immune-compromised patients, most of whom are anatomically or functionally asplenic. Although the antibiotic susceptibility of B. holmesii to β-lactam drugs, including cephalosporins, appears to be reduced (Shepard et al., 2004), the prognosis appears favourable in most cases of mild or non-specific febrile illness, even when treated with these antibiotics. The present case report is believed to be the first description of a patient with meningitis caused by B. holmesii, which was characterized by a severe clinical course and poor response to conventional treatment. This case emphasizes the broad clinical spectrum of this disease, which may include meningitis and the need for broad-spectrum antimicrobial therapy in severe cases.

References


