Case Report

A case of community-acquired *Acinetobacter baumannii* meningitis – has the threat moved beyond the hospital?

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Acinetobacter baumannii is a prolific nosocomial pathogen renowned for its multidrug-resistant nature. We report a case of community-acquired meningitis due to *A. baumannii*. The case highlights the potential pathogenicity of this organism and raises concerns that this highly adaptable organism may soon evolve into a significant community pathogen, too.

Case report

A 48-year-old man was admitted to the emergency department with confusion and pyrexia. Collateral history from an accompanying colleague revealed that the patient had complained of a severe headache that morning, and two generalized seizures were witnessed at his place of work earlier in the day. Emergency medical personnel reported two further seizures during hospital transfer. Initial examination revealed a temperature of 38.5 °C, a blood pressure of 167/105 mmHg, a heart rate of 108 beats min⁻¹ and a respiratory rate of 18 breaths min⁻¹. The Glasgow coma score was 13/15 with verbal and motor impairment. The only other positive finding on examination was severe nuchal rigidity. Results of laboratory tests performed on admission showed the following: white blood cell count 15.4 × 10⁹ cells l⁻¹, haemoglobin 15.3 g dl⁻¹, platelet count 144 × 10⁹ cells l⁻¹, C-reactive protein 35 mg l⁻¹ and random glucose 8.7 mmol l⁻¹. Urea, creatinine and electrolytes were normal and an HIV ELISA (4th generation assay) was non-reactive. Blood cultures were negative. The initial CT scan of the brain showed a small calcified lesion with surrounding gliosis in the right frontal lobe (possibly a calcified granuloma), an old fracture of the left nasal bone, a right frontal hypodensity suggestive of an old infarction and bilateral frontal (non-enhancing) parafalcine collections of cerebrospinal fluid (CSF). None of these lesions suggested an anatomical predisposition to meningitis. A lumbar puncture revealed turbid CSF with neutrophils 2600 cm⁻³, lymphocytes 90 cm⁻³, erythrocytes 103 cm⁻³, protein 13.65 g l⁻¹, glucose 0.5 mmol l⁻¹ and chloride 119 mmol l⁻¹. Gram stain microscopy and bacterial latex antigen (Wellcogen; Remel Europe) testing were negative. Indian ink stain and cryptococcal latex antigen test (CALAS; Meridian Bioscience) were both negative as was serology for syphilis,

toxoplasmosis and cysticercosis. Empiric ceftriaxone 2 g twice daily and dexamethasone 10 mg four times daily was commenced to treat bacterial meningitis. An anticonvulsant (phenytoin) was also given.

By the second hospital day the patient had improved significantly and was no longer confused, but he remained pyrexial with temperatures persistently above 38 °C. At this point, CSF yielded a pure culture of oxidase-negative, nonfermentative Gram-negative bacilli on primary blood agar plates and in brain heart infusion broth. *Acinetobacter baumannii* was subsequently identified using API 20NE (bioMérieux). Antibiotic susceptibilities interpreted according to Clinical Laboratory Standards Institute guidelines (Wikler *et al.*, 2006) were not typical of a hospital-acquired organism. The isolate was susceptible to all commonly used antibiotics, including cephalosporins, aminoglycosides and carbapenems. It was, however, resistant to ceftriaxone/cefotaxime.

The patient's CSF was PCR (Rådström *et al.*, 1994)-negative for *Streptococcus* spp., *Neisseria meningitidis* and *Haemophilus influenzae*.

The treatment regimen was changed to meropenem, dexamethasone was stopped, and the patient defervesced within the next 24 h.

Once the patient was fully conscious, a more detailed history was obtained. He reported a previous diagnosis of hypertension but was not currently using anti-hypertensive medication and denied any other chronic or recent febrile illnesses. He stopped smoking 5 years ago but admitted to abusing alcohol on weekends with occasional blackouts. He arrived in Johannesburg from Limpopo province 2 days prior to admission and had been drinking heavily since arrival. The patient had sustained several injuries over the years. These included scalp and facial lacerations secondary

Abbreviation: CSF, cerebrospinal fluid.

to assault with an axe and broken bottle, respectively. He also sustained a fractured femur in a motor vehicle accident and was stabbed in the back some 30 years ago. In light of this information, closer neurological examination revealed features of a classic Brown-Séquard syndrome from a right-sided spinal cord injury.

A spinal MRI correlated with this clinical picture, showing a small focal intramedullary lesion at T-9 on the right. Brain MRI revealed generalized cerebellar atrophy that we attributed to the chronic alcoholism.

After 14 days of meropenem, a repeat lumbar puncture yielded: neutrophils 5 cm^{-3} , lymphocytes 52 cm^{-3} , erythrocytes 13 cm^{-3} , protein 0.57 g l^{-1} , glucose 7.8 mmol l^{-1} and chloride 122 mmol l^{-1} . CSF cultures remained negative and the patient was discharged without any neurological sequelae.

Discussion

To our knowledge, this is the first reported case of community-acquired *A. baumannii* meningitis in South Africa. *A. baumannii* is a well-established meningeal pathogen in the neurosurgical setting (Bergogne-Bérézin & Towner, 1996) but has been infrequently described as a cause of primary *de novo* meningitis. To the best of our knowledge, this case brings the total number of *A. baumannii* community-acquired meningitis cases reported in the English literature to six. Other *Acinetobacter* species have also been implicated and recent reviews highlight these cases (Chang *et al.*, 2000; Falagas *et al.*, 2007). Given the taxonomic changes and current subdivision of the genus *Acinetobacter* into genomospecies, it is likely that other cases were due to *A. baumannii*. We accept that genomic species identification using commercial identification systems is problematic (Bergogne-Bérézin & Towner, 1996), although use of such systems in routine microbiology laboratories is widespread and is the basis for identification of our nosocomial isolates. The API profile gave an excellent identification, with a 99% probability and a T value of one. *A. baumannii* has been documented as a cause of pseudomeningitis (Cunha *et al.*, 1999) but our patient's CSF demonstrated clear evidence of bacterial meningitis. The negative Gram stain we attribute to the marked pleocytosis and heavily proteinaceous nature, which may have obscured the bacilli. Our case is in keeping with the clinical scenario of the other cases, where fever and a disturbed level of consciousness were predominant features. Furthermore, the antibiotic susceptibility profile was atypical for a nosocomial strain of *A. baumannii*, a feature consistent with other reported cases.

A. baumannii is generally considered an opportunistic nosocomial pathogen and there is debate as to its mechanisms of pathogenicity and virulence. The epidemiological profile suggests that it is of low virulence and disease is dependent on significant host immunological

impairment. The evidence is now mounting that *A. baumannii* can no longer be exclusively considered a nosocomial pathogen, and is capable of causing profound clinical disease in the absence of traditional nosocomial risk factors. A recent review highlights 80 cases of community-acquired *A. baumannii* infections (Falagas *et al.*, 2007). This review suggests that comorbidities such as chronic obstructive pulmonary disease, renal disease and diabetes mellitus are predisposing factors. Interestingly, heavy smoking and excessive alcohol consumption were also associated with increased risk of disease. Our patient's history concurs and excessive alcohol consumption certainly has an immunosuppressive effect. However, the reported cases of meningitis do not suggest significant comorbidities and our patient was otherwise well. HIV may be a risk factor, especially given the frequency with which such patients seek healthcare services, although in our setting the commonest cause of community-acquired bacterial meningitis in HIV-infected adults is *Streptococcus pneumoniae* (von Gottberg *et al.*, 2006). Our patient was HIV-negative and the use of PCR excluded the common bacterial pathogens. Predisposing immunological factors in the form of complement (C3 and C4) deficiencies and immunoglobulin (IgA, IgG and IgM) deficiencies were actively sought, but all levels were normal. The significant trauma history may provide an explanation for portal of entry and subsequent establishment of infection.

A recent study has revealed that a large portion of the genome of *A. baumannii* consists of pathogenicity islands (PAIs) (Smith *et al.*, 2007). Sixteen PAIs contain genes implicated in virulence, of which the largest appears to contain a type IV secretion apparatus. Type IV secretion systems have been shown to play an important role in other human pathogens, including *Bordetella pertussis*, *Legionella pneumophila*, *Brucella* spp. and *Helicobacter pylori* (Schmidt & Hensel, 2004). Secretion systems allow pathogens to secrete proteins directly into eukaryotic cells, and these proteins then interfere with specific host cell pathways resulting in subversion of host immune responses with subsequent establishment of infection (Nagai & Roy, 2003).

In the case of *A. baumannii*, this may be particularly important and partially explain the opportunistic nature of the organism. PAI genes, like other virulence genes, respond to environmental stimuli and thus may only be expressed under stressful conditions. If one considers the host-pathogen interaction in terms of the damage-response framework (Casadevall & Pirofski, 1999), *A. baumannii* would typically be considered a class 1 pathogen, i.e. causing damage only in situations of weak immune responses. However, the host-pathogen interaction is also dependent on a particular environmental situation where the environment can alter the outcome of the host-pathogen interaction. Prosthetic devices are a prime example where given a particular pathogen and host – irrespective of immune response – the outcome is

modified by the presence of a foreign body. Environmental stimuli may account for differential gene expression and subsequent varied host–pathogen interactions. *A. baumannii* is capable of existing in a range of different environments and it seems plausible that this ubiquitously adaptable organism has acquired a vast array of PAIs to deal with this diversity.

Attempts to characterize the epidemiology of community strains of *A. baumannii* suggest that the community may serve as a potential reservoir for both nosocomial and community-acquired infections (Pancholi *et al.*, 2005; Zeana *et al.*, 2003). We believe a more interesting question is whether hospital strains that disseminate into the community serve as a potential reservoir for community-acquired infections. *A. baumannii* is a hardy organism capable of prolonged survival in the environment, and from a pathogenic perspective, with increasing dissemination of the organism into the community via healthcare-associated infection, it is feasible that *A. baumannii* will now adapt to the hostile environment of a host with a normal immune response. Further study of *Acinetobacter* spp. in terms of host–pathogen interaction, virulence determinants and epidemiological characterization is warranted.

A. baumannii is a significant nosocomial pathogen and it is foreseeable that this highly adaptable organism may soon evolve into a significant community pathogen, too.

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