CASE REPORT

Pasteurella multocida meningoencephalitis in an immunocompetent adult with multiple cat scratchesDavid Alistair Clarke,¹ Angela McBride,² Michael Kelsey,² Ben Killingley²

¹General Medicine, Whittington Health NHS Trust, London, UK
²Whittington Health NHS Trust, London, UK

Correspondence to
 Dr David Alistair Clarke,
 david.clarke11@nhs.net

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SUMMARY

We present the case of a 49-year-old woman admitted to our Acute Medical Unit with a 2-day history of fever, vomiting and confusion. The patient was alcohol dependent and had sustained several scratches from her pet cat, which her pet dog had licked. She deteriorated in the Emergency Department—developing high fever, worsening confusion and meningism. Blood cultures were taken and broad spectrum antibiotics commenced prior to CT scanning and diagnostic lumbar puncture. Blood cultures and CSF 16S ribosomal PCR confirmed a diagnosis of *Pasteurella multocida* bacteraemia and meningoencephalitis. The patient was successfully treated with 14 days of intravenous antibiotics. *P multocida* is a Gram-negative coccobacillus which frequently colonises the nasopharynx of animals; it is a recognised but very rare cause of meningoencephalitis in immunocompetent adults. This case highlights the need to consider *P multocida* infection in patients with prior animal contact, regardless of their immune status.

BACKGROUND

There are very few reported cases of *Pasteurella multocida* meningoencephalitis in immunocompetent adults. This patient presented with an unusual mode of transmission of her infection and signs that could have easily been dismissed initially in the context of her acute withdrawal from alcohol. The case highlights the need to take a careful history in all patients presenting with sepsis and the importance of awareness of zoonotic transfer of *P multocida* in all patients who present with signs indicating animal contact such as cat scratches.

CASE PRESENTATION

Our patient, a 49-year-old woman with a history of alcohol excess, hyperthyroidism, previous gastric bypass and depression, presented to the Emergency Department in the early hours of the morning with a 3-day history of fever, sore throat, myalgia, vomiting and diarrhoea on a background of recent abrupt withdrawal from alcohol. Her symptoms were initially attributed to alcohol withdrawal with possible superimposed infection and the patient was started on intravenous Co-amoxiclav. However, while in the Emergency Department she developed a worsening headache with associated fever of 39.2°C and a tachycardia at 110 bpm. On examination, she had signs of meningism with mild photophobia and neck stiffness and bilateral arm ataxia, which was attributed to her alcohol excess.

There was no papilloedema. Examination of her skin revealed herpetic lesions around the mouth and eyes, and several cat scratches on her arms and abdomen.

Blood cultures were drawn, and the patient was commenced on empirical intravenous ceftriaxone 2 g twice daily. Due to her confusion, the patient underwent a CT head scan, which was unremarkable. Subsequently, a diagnostic lumbar puncture was performed.

INVESTIGATIONS

Routine blood tests showed a normal white cell count of $6 \times 10^9/L$ ($3.5\text{--}12.0 \times 10^9/L$), raised C reactive protein at 183 mg/L (0–5 mg/L) and low platelet count at $97 \times 10^9/L$ ($140\text{--}400 \times 10^9/L$). Liver function tests were deranged; bilirubin 42 $\mu\text{mol/L}$ (0–21 $\mu\text{mol/L}$), Alanine Aminotransferase (ALT) 68 iU/L (0–33 iU/L) and Alkaline Phosphatase (ALP) 152 iU/L (35–129 iU/L) together with a marked hypokalaemia 2.8 mmol/L (3.5–5.1 mmol/L), mild hyponatraemia 134 mmol/L (135–145 mmol/L), creatinine 64 $\mu\text{mol/L}$ (49–92 $\mu\text{mol/L}$) and urea 1.9 mmol/L (2.1–7.1 mmol/L). Serology for HIV was negative.

Lumbar puncture revealed an opening pressure of 18 mm Hg and purulent cerebrospinal fluid (CSF) with a white cell count of 1505 cells/mm³ (98% polymorphs); no organisms were seen on Gram stain, glucose 0.7 g/dL, protein 2.49 g/dL and lactate 11.7 mmol/L. Real-time PCR for enterovirus and herpes simplex virus 1 and 2 was negative. Auramine stain and PCR for *Mycobacterium tuberculosis* by GeneXpert was negative.

Blood cultures flagged positive at 24 hours, and the Gram stain revealed Gram-negative rods, which were subsequently identified by Matrix Assisted Laser Desorption/Ionization – Time Of Flight (MALDI-TOF) mass spectrometry as *P multocida*. The isolate was sensitive to amoxicillin.

A sample of acute CSF was sent to a referral laboratory for 16S ribosomal PCR, which confirmed the presence of *P multocida* in the central nervous system.

CT brain imaging on the day of admission was unremarkable. MRI brain on day 3 of admission showed prominent enhancement of the meninges around the whole brain, and a wedge-shaped area of high signal in the centre of the pons showing some restricted diffusion on diffusion-weighted images which did not enhance with contrast. There was no evidence of abscess, but mucosal thickening was noted within the frontal sinus.

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An ultrasound of the liver was performed to exclude liver abscess, given the cholestatic derangement in liver function—this was unremarkable.

DIFFERENTIAL DIAGNOSIS

Given the presentation and supporting investigations, bacterial meningitis was the primary potential diagnosis. Common bacterial pathogens implicated in meningitis were excluded by investigation. After return of positive blood cultures for *P multocida*, which is considered a rare cause of meningoencephalitis in immunocompetent adults, we focused our investigations to isolate this pathogen from the cerebrospinal fluid. Other diagnoses such as viral encephalitis, cerebral abscess or, less likely, liver abscess were considered but ruled out by investigation. The patient was treated concomitantly for alcohol withdrawal.

TREATMENT

The patient was admitted to the Acute Medical Unit for management of a presumed meningoencephalitis with intravenous fluids and intravenous ceftriaxone 2 g twice daily. She was also treated for alcohol withdrawal with a chlordiazepoxide-reducing regimen and intravenous Pabrinex. Due to the herpetic lesions on her mouth and the fact that our initial CSF sample returned sterile intravenous acyclovir 690 mg three times daily was commenced to cover for possible superimposed viral encephalitis. This was continued for 5 days until PCR analysis of CSF for herpes simplex 1 and 2 were confirmed as negative and we had confirmed the presence of *P multocida* in the CSF. The patient required regular oral morphine to control her headache.

After 3 days of intravenous antibiotics, the patient remained intermittently febrile and complained of ongoing headache, confusion and ataxia and hence an MRI brain was performed to assess for cerebral abscess. MRI was unremarkable aside from an area of high signal in the central pons. This was felt to be of unlikely significance and not in keeping with central pontine myelinolysis but given the history of alcohol excess her nutrition was optimised and electrolytes tightly monitored. Intravenous amoxicillin 2 g four hourly was added to the antibiotic regimen. After 5 days, she began to improve clinically, with resolution of inflammatory markers, together with some improvement in cognition and a reduction in headache.

Given the rarity of *P multocida* meningoencephalitis, there were no antibiotic guidelines to follow and hence therapy was guided by antibiotic sensitivities. In total, the patient received 10 days of intravenous ceftriaxone 2 g twice daily and 13 days of amoxicillin intravenous 2 g four times daily with excellent treatment response.

OUTCOME AND FOLLOW-UP

The patient disclosed that her cat had recently scratched her several times and her pet dog had licked these wounds in addition to her face and lips—therefore one of her pets was assumed to be the likely source of infection.

After 14 days of intravenous antibiotics, our patient showed significant improvement, was no longer febrile and her inflammatory markers had returned to normal. However, she displayed ongoing cognitive disturbance, gait disturbance and complained of persistent headache. It was unclear as to whether her slow cognitive improvement was related to her previous alcohol abuse or a partially treated encephalitis. We took the decision to take a repeat lumbar puncture at this point to confirm treatment response and guide any further treatment. Repeat lumbar puncture in a patient who was making clinical progress would

not be considered standard of care but we felt we needed to confirm treatment given the rarity of condition and ongoing symptoms. A CSF sample at day 14 showed a good response to antibiotic therapy with a white cell count of 50 cells/mm³, 15% polymorphs 85% lymphocytes, red cell count 0 cells/mm³ and no organisms seen. Antibiotics were stopped and her slow cognitive improvement attributed to previous alcohol abuse. Her cognition continued to improve, and she was discharged from hospital on day 18.

As she was discharged, the patient felt positive that she would take this opportunity to become abstinent from alcohol and she was encouraged to re-engage with her community alcohol liaison team. We advised that she avoid salivary contact with her animals on discharge.

At month 9 post discharge, the patient reported an ongoing mild headache two to three times per week, which she was managing with simple analgesia. She also reported an increase in her anxiety symptoms and some right-sided hearing loss, which was not reported at the time of her admission. She has not attended for follow-up with our neurology department.

DISCUSSION

P multocida is a Gram-negative coccobacillus, which is a common commensal in the oropharynx of several domesticated or wild animals, and is the most common cause of human skin and soft tissue infection following bites and scratches from cats and dog.¹ Animal bite wound infections are commonly polymicrobial but *Pasteurella* infection can lead to a rapidly progressive cellulitis, usually presenting within 24 hours of injury. However, the organism is commonly sensitive to penicillin therapy and is therefore usually easily treated. Cat bites are more prone to infectious complication than dog bites due to their smaller, sharp teeth causing increased penetrative damage.² Infrequently, inoculation leads to deep or disseminated infections including osteomyelitis, septic arthritis, bacteraemia and meningitis. Infection has also been reported following non-traumatic contact, including kissing and being licked by animals and the pathogen has also been isolated in cases where no animal contact has occurred.^{3–6} *P multocida* meningitis is most frequently reported in infants; it is a very rare cause of adult bacterial meningitis; a recent review article counted only 36 adult cases reported worldwide.⁷ Disseminated infection has more often been reported in those with predisposing factors such as advanced age, immune compromise, cirrhosis, renal replacement therapy or recent neurosurgical intervention.⁸ Although our patient had regular alcohol excess, she did not have evidence of advanced liver disease on biochemical testing or cirrhosis on liver ultrasound. An HIV test returned negative, and no evidence for other immunocompromised was found on investigation.

Empirical antibiotic therapy should be given without delay at first suspicion of bacterial meningitis. Since lumbar puncture is often delayed until after cerebral imaging in patients who are confused or have focal neurological signs at presentation, appropriately administered prior antibiotic doses may render cerebrospinal fluid sterile at culture. If possible, therefore, blood cultures should be drawn prior to antibiotic therapy; 63.2% of 29 patients in one case series of adult patients with *P multocida* meningitis had concurrent bacteraemia.⁶ In our case, as the organisms in the CSF were not viable at culture, we used 16S ribosomal PCR to confirm the presence of *P multocida* in the CSF.

The most common bacterial pathogens causing meningitis in adults include *Streptococcus pneumoniae*, *Neisseria meningitidis*, group B *Streptococcus*, *Haemophilus influenzae* type b

(HiB) and *Listeria monocytogenes*—*S pneumoniae* being the most common organism isolated in adult meningitis. In teens and older children, infection is most common with *N meningitidis*, *S pneumoniae* or HiB, although HiB infection has markedly decreased with the introduction of the HiB vaccine. In neonates, organisms commonly found in the maternal genital tract or gastrointestinal (GI) tract are most commonly implicated such as group B *Streptococcus*, *Escherichia coli* or *L monocytogenes*.⁹ Viral encephalitis decrease in incidence with increasing age but should still be excluded when considering meningitis. Enteroviruses are the most common causative viruses in the immunocompetent followed by herpes simplex type 1 and 2 and less commonly varicella zoster, HIV and Epstein-Barr virus. In the unvaccinated, the mumps virus is a possible cause and the immunocompromised cytomegalovirus. In keeping with the zoonotic theme of our case, patients who disclose contact with rodent droppings or urine should be considered for infection by lymphocytic choriomeningitis virus.¹⁰ We also considered infection with *M tuberculosis* and excluded this with Auramine staining and GeneXpert PCR of CSF samples.

P multocida is usually sensitive to third-generation cephalosporins,⁷ which is recommended as first-line empirical therapy for presumed bacterial meningitis in most UK hospital guidelines. Most, but not all, isolates are sensitive to penicillin and ampicillin,^{11–13} and therapy can therefore be rationalised with antibiotic susceptibility patterns.

Due to the rarity of the disease, randomised clinical trials are not practical, but most case reports have treated patients without focal collections for between 14 and 21 days.^{6,12} Simultaneously with antibiotic therapy, it is important to exclude focal collections, either within or outside of the central nervous system including abscess, osteomyelitis, septic arthritis, otitis media or sinusitis.

Learning points

- ▶ *Pasteurella multocida* is a rare cause of meningoencephalitis in immunocompetent adults but should be considered in patients who disclose the keeping of pets.
- ▶ Patients presenting with *P multocida* meningoencephalitis should undergo work up to exclude any possible source of immune compromise.
- ▶ In all patients presenting with sepsis, a detailed history and careful examination is essential to elucidate risk factors for unusual infections.
- ▶ Blood cultures taken prior to antibiotic therapy can be useful to identify a causative organism in bacterial meningitis.
- ▶ 16S ribosomal PCR can be used to identify the causative pathogen in a sample taken from a sterile site if prior antibiotic therapy has rendered culture unsuccessful.

Some previous studies have attempted to link the causative *P multocida* strain to one isolated from the oropharynx of the suspected culprit pet.^{14,15} We cannot be sure whether our patient acquired her *P multocida* infection via cat scratch, dog lick or dog kiss, but we chose not to apportion blame on either beloved pet, and rather provided advice on discharge to avoid salivary interactions with both animals in the future. This case exemplifies the importance of a meticulous clinical history in patients who present with infectious syndromes. In an era when 60% of human infections are suspected to be zoonotic in origin, and with an estimated 16 million cats and dogs in the UK, the potential for domestic animals to facilitate zoonotic disease should not be forgotten.

Contributors DC and AM contributed equally to the writing of this paper and took care of the patient during their stay. BK and MK were consultants responsible for patient care and reviewed and edited the work for final submission. All authors have reviewed the work prior to publication. MK and BL take joint responsibility for overall content.

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