

Ventriculitis: an unusual cause of sepsis in an elderly patient who presented with persistent fever

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CASE REPORT

A 75-year-old man presented to the Accident and Emergency Department in January 2005 with a 2-day history of fever and productive cough. His medical history included a lung shadow and a right frontal ivory osteoma for which he was being followed up by a chest clinic and an ear, nose and throat surgeon, respectively. Chest radiography on admission revealed right middle lobe consolidation and serum biochemistry was suggestive of inappropriate antidiuretic hormone secretion. He responded initially to oral augmentin and then deteriorated subsequently with fulminant pneumonia. He was intubated and required ventilation in the intensive care unit for around 2 weeks. A catheter specimen of urine, bronchoalveolar lavage, and tracheal aspirate grew *Candida albicans*. A sputum smear tested for acid-fast bacilli (AFB) and a polymerase chain reaction were negative. He was commenced on a combination of intravenous amikacin, klacid, Tienam (MSD, Elkton, US), and fluconazole. His condition improved clinically, fever subsided and he was successfully weaned off the ventilator. He was transferred to the geriatric ward but developed fever again 2 days later and his level of consciousness deteriorated. A repeated sepsis workup was performed and enterococcus was grown from his urine. His fever persisted despite intravenous vancomycin and Tazocin (Wyeth, Puerto Rico), and further investigations were performed.

Seven weeks following admission, a lumbar puncture revealed turbid cerebrospinal fluid (CSF).

A laboratory analysis revealed a red blood cell count of 2.109×10^{12} /L; a white cell count of 1.12×10^{12} /L with 72% polymorphs and 28% lymphocytes; a smear for AFB was negative. The CSF protein level was 4.25 g/L and the glucose level was 2.9 mmol/L. The CSF opening pressure was 9.6 mm Hg. He was treated as having partially treated bacterial meningitis or tuberculous meningitis. Resolution of fever and a rapid improvement followed prescription of anti-tuberculous drugs, intravenous ampicillin, Rocephin (Roche, Kaiseraugst, Switzerland), and dexamethasone. Brain magnetic resonance imaging (MRI) 4 days later revealed features of meningitis with communicating hydrocephalus. A neurologist and microbiologist were consulted but differed in their opinions on whether anti-tuberculous treatment should be continued. Clinically, the patient responded to the multi-antibiotic regimen and steroid treatment and could obey simple commands. Anti-tuberculous treatment was continued with the addition of intravenous metronidazole.

A second and third lumbar puncture were performed to determine progress but revealed microbiological deterioration (TABLE). An urgent follow-up MRI brain scan was performed to detect any new lesion, microabscess, or complication of hydrocephalus. The results demonstrated ventriculomegaly and a fluid level with heterogeneous signal layering in the lateral ventricles (FIGURES 1 and 2). This had a low signal on T1 and a high signal on T2 and fluid attenuated inversion recovery (FLAIR) sequences. Also evident were diffused ependymal and meningeal enhancement. These find-

TABLE
Progress of lumbar puncture results

Results*	9 Mar 2005	16 Mar 2005	23 Mar 2005
CSF cell count			
RBC ($\times 10^{12}/L$)	2.109	-	0.648
WBC ($\times 10^{12}/L$)	1.120	1.574	9.266
Polymorph	72%	94%	98%
Lymphocyte	28%	6%	2%
CSF biochemistry			
Protein (g/L)	4.25	-	29.3
Glucose (mmol/L)	2.9	-	3.4
Opening pressure (mm Hg)	9.6	11.0	10.3

* CSF denotes cerebrospinal fluid, RBC red blood cell, and WBC white blood cell

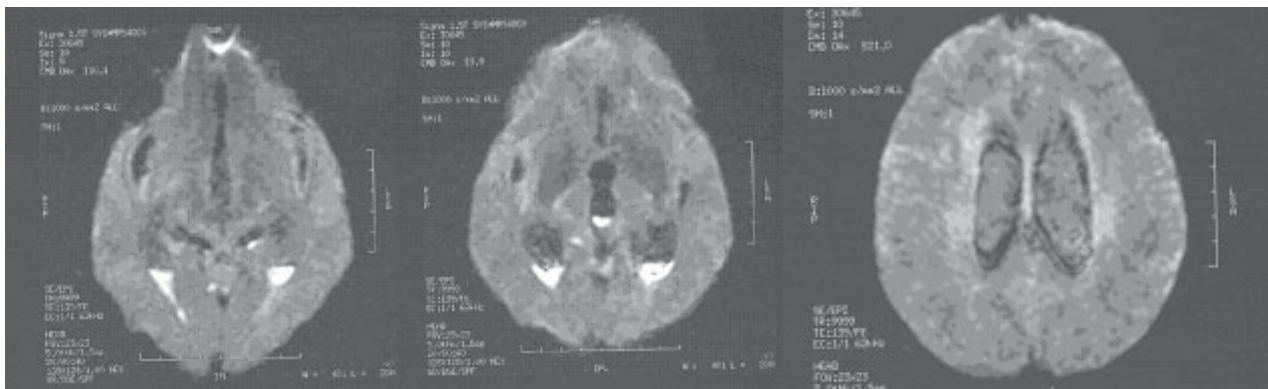


FIGURE 1. T-2 weighted MRI shows fluid level as high signal

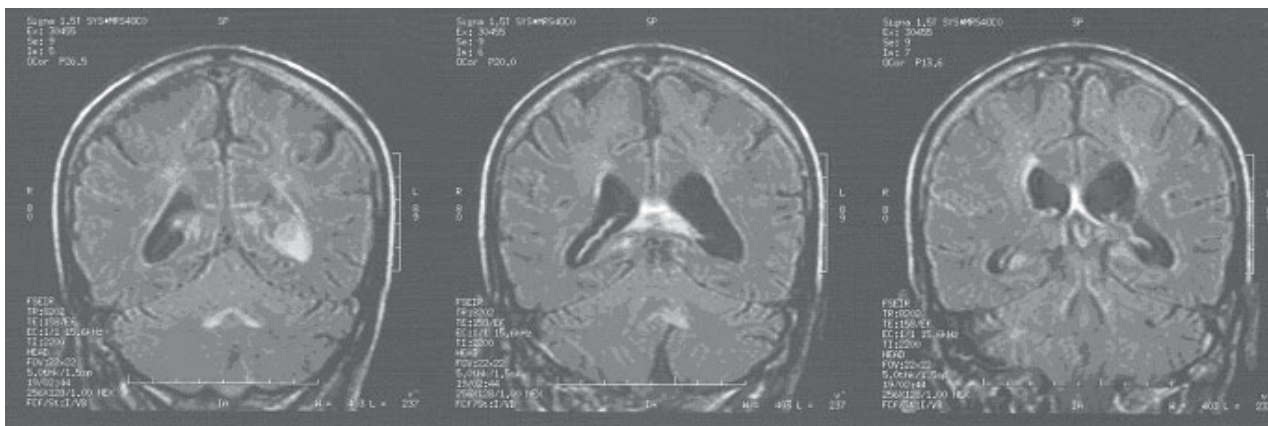


FIGURE 2. MRI FLAIR sequence shows fluid in the lateral ventricle and diffused meningeal high signal

ings were consistent with pus in the ventricle and a diagnosis of ventriculitis was made.

In view of the new MRI brain findings, intravenous meropenem was commenced empirically and a neurosurgeon was consulted for surgical drainage and intra-ventricular antibiotics. The neurosurgical opinion was that surgery was not indicated. In addition, the patient's relatives were reluctant to proceed to surgical intervention. The patient

responded well to the antibiotic regimen and his CSF white cell count rapidly reduced ($0.85, 0.34, 0.004 \times 10^{12} /L$) over a 2-week period. The patient became more interactive and could obey simple commands. Intravenous meropenem was prescribed for a total of 8 weeks and then stopped; anti-tuberculous treatment was continued. Three days later the patient again developed a swinging fever with respiratory distress and died after a further week, due to hospital-acquired methicillin-

resistant *Staphylococcus aureus* pneumonia. Autopsy findings revealed features of chronic meningitis and mild ventriculitis. Staining for AFB and fungi remained negative.

DISCUSSION

Pyogenic ventriculitis refers to inflammation of the ventricular ependymal lining accompanied by pus in the ventricular system. The condition is difficult to characterise because it is synonymous with pyocephalus, ventricular empyema, and ependymitis.¹⁻⁵ All these terms are associated with varying definitions and monitoring practices. Pyogenic ventriculitis is uncommonly reported in adults and is almost exclusively seen in patients who have undergone cranial surgery, placement of a drain or shunt, or sustained head trauma. Nonetheless, pyogenic ventriculitis can complicate central nervous system (CNS) infections such as meningitis or brain abscesses and may even occur as a spontaneous infection in significantly immunocompromised patients.

There is little information in the literature about the incidence and prevalence of pyogenic ventriculitis but estimates range from approximately 1 to 2% of patients who undergo neurosurgery to 5 to 50% of patients following placement of an intraventricular catheter. It may account for nearly 17% of CNS infections in patients with head trauma.⁶ There are few reports on the prevalence of pyogenic ventriculitis as a complication of bacterial meningitis as seen in this patient.

Ventriculitis is associated with a high mortality, from 30 to 70%.⁷ Various known predisposing factors include a recent neurosurgical procedure, head injury with CSF leakage, meningitis, and brain abscess. Ventriculitis associated with ventricular drains is the form most often discussed in the literature. The most common organisms isolated from patients who have undergone neurosurgical procedures (including shunt placement) include coagulase-negative *Staphylococcus* and *S aureus*.⁸ Nonetheless gram-negative species, such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, and *Enterobacter aerogenes* are becoming increasingly common. This is especially true for nosocomial infections.⁹ Common organisms in immunocompromised patients include cytomegalovirus,

Nocardia, and *Coccidioides*.⁶ Ventriculitis is a frequent complication of meningitis in infants.¹⁰

The presentation of a patient with pyogenic ventriculitis varies and depends on the associated risk factors. The onset can be insidious with slow progression of cognitive decline, especially in the elderly and immunocompromised patients. Patients may present with meningismus, encephalopathy, or multiple cranial neuropathies secondary to abscess rupture and may have focal neurological deficits. They may also present with acute hydrocephalus and rapid loss of consciousness.

Because of the associated high rate of morbidity and mortality, early diagnosis of ventriculitis is crucial. It should be considered in any patients with known risk factors, namely meningitis that is not responding to appropriate antibiotic therapy, recent neurosurgery, presence of a ventricular shunt or drain, or a severely immunocompromised state.

Diagnosis of pyogenic ventriculitis is difficult and relies on a high degree of clinical suspicion. Presentation of the condition varies, depending on the underlying patient risk factors. Culture of CSF is commonly sterile because of prior administration of broad-spectrum antibiotics for suspected CNS infection or for prophylaxis after a neurosurgical procedure.

Serum procalcitonin may help differentiate bacterial ventriculitis from aseptic meningitis or ventriculitis in patients with external ventricular drains.¹¹ Similarly, CSF lysozyme reaches a higher concentration in bacterial meningitis than aseptic meningitis.¹² The concentration of CSF lysozyme appears to correlate with the degree of disease activity. To date, CSF tests have been found unreliable for the diagnosis and progress monitoring of ventriculitis. Brain imaging is more useful and accurate. The most common computed tomography (CT) and MRI imaging features of pyogenic ventriculitis include irregular ventricular debris, hydrocephalus, and ependymal enhancement with contrast.¹³ Magnetic resonance imaging is both more specific and more sensitive than CT because blood, post-neurosurgical debris, and pus cannot be reliably differentiated by CT. Also, MRI can offer several sequences (T1, T2, FLAIR, diffusion, and gradient echo) and allows a more detailed assessment of the ventricular content. Ventricular pus will

appear hyperintense compared with CSF on T1-weighted images and hypointense compared with CSF on T2-weighted images.

Treatment should begin promptly for any suspected intracranial infection. Empiric antibiotics should be selected according to the particular patient risk factors and initiated at a maximum dose, then adjusted according to microbiological results. The use of intra-ventricular antibiotics for pyogenic ventriculitis remains a subject of significant debate. Advantages of their use include the ability to achieve a high concentration in the CNS, thus ensuring bactericidal activity.¹⁴ Nonetheless, they have been associated with significant morbidity such as aseptic meningitis, eosinophilic granulocytosis, polyradiculopathy, cerebritis, and seizures. The optimal duration of antibiotic treatment remains controversial.

Conclusion

Infection of the CNS should be considered high on the list of differential diagnoses in an elderly patient with pyrexia of unknown origin. Ventriculitis can be indolent and lethal, even when meningitis is treated. Early diagnosis is essential to enable appropriate treatment. The finding of irregular ventricular debris and pus is characteristic and, in an appropriate clinical setting, should prompt aggressive and prolonged antibiotic therapy including intra-ventricular administration.

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