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Case report

Vancomycin-resistant enterococcal meningitis treated with intrathecal streptomycin

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Abstract

Enterococcal meningitis is a rare complication of neurosurgical procedures. We present a patient who developed vancomycin-resistant enterococcal ventriculitis – meningitis after a brain tumor resection and ventriculoperitoneal shunt placement, treated successfully with intrathecal streptomycin through bilateral cerebrospinal fluid drainage catheters in addition to systemic antibiotics. This is the first report of such treatment for this resistant organism.

Keywords: *Enterococcus*; Vancomycin; Resistant; Streptomycin; Intraventricular; Shunt; Meningitis

1. Introduction

The aminoglycoside streptomycin is still being used for the treatment of tuberculosis, plague, tularemia and infrequently for resistant infections caused by Gram-negative bacilli such as *E. coli*, *Proteus*, *A. aerogenes*, *K. pneumoniae*. It has also been used in urinary tract infections by *Enterococcus faecalis* and in endocardial infections by *S. viridans* and *E. faecalis* –concomitantly with penicillin – but there has been no documented case of intrathecal streptomycin for resistant Gram-positive infection of the central nervous system [1].

2. Case report

A 64-year-old man was admitted to the Neurosciences Intensive Care Unit at Henry Ford Hospital for resection of a single right frontal lobe melanoma brain metastasis. He was diagnosed with melanoma of his ankle in 2001 and had resection of the lesion and inguinal lymph nodes, radiation and chemotherapy. In the summer of 2006 he developed seizures, was diagnosed with brain metastasis and received radiosurgery treatment as well as systemic high-dose dexamethasone for 3 months prior to the index admission. In addition, a left ventriculoperitoneal shunt was placed for obstructive hydrocephalus. He was re-admitted for decreased mental status and pneumonia in October of 2006, and was treated with a 10-day course of cefepime, vancomycin and tobramycin IV with clinical improvement. One month later he had microsurgical excision of the brain metastasis. The left shunt was also changed to an external ventricular drainage device (EVD), when the cerebrospinal fluid (CSF) from the reservoir was found infected with Gram-positive cocci the next day. The patient was started on empiric antibiotic treatment with vancomycin, ampicillin and gentamicin IV. Vancomycin was stopped and gentamicin was switched to streptomycin IV on post-operative day (POD) 5, as cultures grew *Enterococcus feacalis* resistant to vancomycin [(VRE), with minimum inhibitory concentration (MIC) > 32] and gentamicin (synergy screening) and sensitive to ampicillin

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(MIC < 2), linezolid (MIC < 1.5) and streptomycin (synergy screening). Intravenous streptomycin was also changed to intrathecal dose via the EVD (4 mg initial dose followed by 2 mg every 12 h) and linezolid IV was added on POD 6. Despite the resection of the metastatic mass and partial relief of the midline shift, the patient remained comatose. Therefore, the surgical cavity was re-explored on POD 9. Because of purulent fluid-containing cavities, after debridement a surgical bed drainage catheter (SBD) was placed in the right fronto-temporal region and the left EVD was changed to a new catheter via the same Burr hole. Both catheters were impregnated with antibiotics against Gram-positive organisms (BACTISEAL®, Codman, Raynham, MA). Both surgical tissue cultures and CSF obtained from the EVD and SBD post-operatively grew *Enterococcus faecalis* resistant to vancomycin. After the second surgery, in addition to the systemic antibiotics, the central nervous system infection was treated initially with 1 mg (in 1 ml preservative-free saline) intrathecal streptomycin, being injected through the EVD and 3 mg through the SBD under sterile conditions every 12 h. Before the injection, 5–8 ml of CSF was withdrawn from the two drains. The antibiotic was flushed with 4 ml preservative-free normal saline and the drains were clamped for 1 h before reopening at a fluid column resistance ("pop-off height") of 10 cm for the EVD and 5 cm for the SBD. The CSF collected before the injection was sent once/day for biochemical and microbiological studies. On POD 8 the CSF from the EVD had decreased white blood counts (WBC) and no growth of any organisms (Fig. 1). CSF from the SBD, however, continued to have elevated WBC, elevated protein levels and moderate to rare *Enterococcus faecalis*. Because of no significant improvement in these counts, on POD 12 the dose of intrathecal streptomycin through the SBD was increased to 9 mg every 12 h. The dose through the EVD remained the same. Since the CSF studies after POD 13 showed no growth of organisms and those from the EVD had low WBC counts, the linezolid was stopped on POD 16 and the intrathecal streptomycin injections via this catheter were discontinued the next day. Because the CSF from the SBD revealed continued elevated WBC and protein levels, however, the intrathecal injections were continued via the SBD at an increased dose of 10 mg every 12 h until POD 27. Although for several days, the CSF from both drains showed persistent negative cultures and subsequently normalization of WBC and protein levels, the IV ampicillin was continued for a total of 6 weeks. The level of consciousness of the patient showed significant improvement. There was no clinical sign of hearing loss. Both catheters were removed on POD 33 with no subsequent complications. Approximately one month later, the family made a decision to withdraw care after a new neuroimaging study of his brain revealed multiple new distant melanoma metastases and the patient expired soon after.

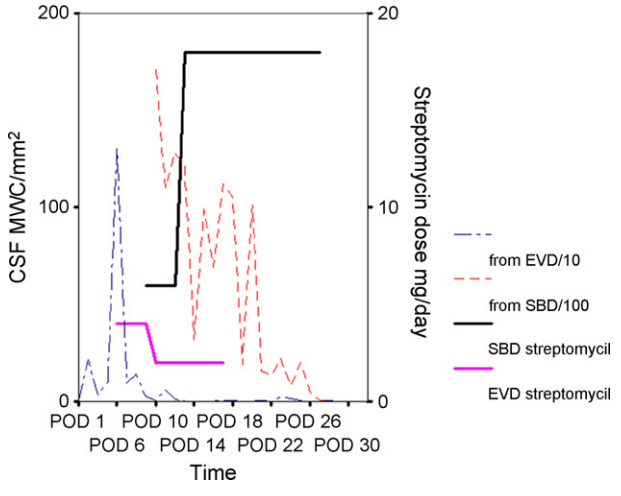

Fig. 1. Cerebrospinal fluid white blood cell count and antibiotic dose and duration EVD = external ventricular drain, SBD = surgical bed drain, POD = post-operative day.

3. Discussion

Intrathecal antibiotics have been used for a long time to treat meningitis, ventriculitis or shunt infection from Gram-positive [2,3], Gram-negative [4–9], mycobacterial [10–12] and fungal [13,14] organisms. Because of the need for an invasive administration route and the significant side effects, including vestibular and auditory toxicity, encephalopathy, seizures, parkinsonism, arachnoiditis and local tissue irritation and necrosis [13,15,16], intrathecal administration is usually reserved for the most hopeless cases. Although the specific indications are not well-defined, intraventricular administration may be necessary in cases of shunt infections that are difficult to eradicate or cannot undergo the appropriate surgical treatment [17].

Our patient demonstrated symptoms and signs of meningitis and *E. faecalis* grew from both the wound and CSF. Enterococcal meningitis is uncommon, accounting for 0.3–4% of bacterial meningitides cases and has usually been reported as a complication of gastrointestinal disorders [18]. In a study from Spain, 39 cases of enterococcal meningitis were identified over 25 years. The vast majority occurred in the postoperative period (85%) and the rest spontaneously. *E. faecalis* accounted for 90% of isolates and *E. faecium* and *E. durans* for 10% each. Regarding antibiotic sensitivities, only one case had VRE. In a literature review of 101 additional cases between 1956 and 2003, the most common predisposing factors for postoperative enterococcal meningitis were CSF devices, neurosurgical procedures, CSF leak and head trauma. Only 16/140 (11%) were VRE, and they were treated more often with intrathecal antibiotics compared to non-VRE stains (47% vs. 14%, $p < 0.05$) [18]. In another series, 20 neurosurgical patients with enterococcal meningitis were identified over a period of 9 years. The most frequent underlying diseases were intracerebral haemorrhage (55%), brain neoplasms (25%), head trauma (15%) and hydrocephalus (5%). The isolates identified were in the vast majority *E. faecalis* ($n = 18$), with *E. faecium*