Meropenem Associated Aseptic Meningitis - Muddying the Waters, and the CSF

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Background

Drug-induced aseptic meningitis is an uncommon hypersensitivity reaction. It is associated with many drugs including anti-rheumatic medications and non-steroidal anti-inflammatories[1]. It has been reported in the setting of antibiotic therapy, most frequently with amoxicillin and co-trimoxazole[2].

Clinical Case

A 22 year-old male presented with a penetrating injury through a rubber-soled sports shoe to his right foot through acquired on holiday in Germany. Initial empiric therapy consisted of flucloxacillin and clindamycin. Features at time of surgery were consistent with osteomyelitis of the right fourth metatarsal. *Pseudomonas aeruginosa* was subsequently isolated and he was commenced on Piperacillin-Tazobactam and discharged home on Outpatient Antimicrobial Therapy.

He presented again to hospital 6 days later with fever, rash, thrombocytopaenia and raised liver transaminases. Blood cultures were sterile and no infective cause was identified. Symptoms and lab abnormalities resolved following discontinuation of Piperacillin-Tazobactam. He was switched to ciprofloxacin, which was later discontinued due to the development of a rash, and meropenem was commenced.

Following 3 days of meropenem therapy, he developed a headache, increasing in intensity over a number of days. He developed a maculopapular rash and headache was non-resolving. Decision was made to stop meropenem on day 31 of effective therapy as a result. Soon after, he developed signs and symptoms of raised intracranial pressure, including vomiting and bilateral cranial nerve VI palsies. Neuroimaging identified no cause. Lumbar puncture was performed showing a raised opening pressure of greater than 40cmH_2O. CSF pleocytosis was present with a predominantly lymphocytic pattern. CSF glucose was 1.4mmol/L with a matched serum sample of 5.9 (table 1).

Investigations included infectious and autoimmune work-up, which were negative (table 2,3). Cytology was negative for malignancy and no cause identified on serial neuroimaging.

Serology
Anti-B. burgdorferi IgG/IgM not detected
Anti-Leptospira IgM not detected
Anti-treponema pallidum not detected
Hep B vaccinated Anti-hep C not detected
Anti-CMV IgG detected, IgM not detected Positive EBV IgG VZV IgG detected HIV not detected x 2
ANA, ANCA negative, normal C_3, C_4 Negative RF, Anti-CCP

Table 2

The decision was made to withhold all antimicrobial therapy at this point given clinical stability in conjunction with neurology and immunology services.

A diagnosis of drug-induced aseptic meningitis was made and symptoms resolved with cessation of antimicrobial therapy. Therapeutic lumbar punctures with were performed.

CSF Diagnostics
HSV 1 and 2 not detected on CSF PCR VZV, enterovirus not detected
No growth bacterial CSF culture
Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumoniae DNA not detected Meningococcal, pneumococcal, H. influenzae DNA not detected 16s not detected
MTB DNA not detected, AFB not seen No growth mycobacterial CSF culture
Cryptococcal antigen not detected Fungal culture negative 18s rDNA not detected
Cytology negative for malignancy Abundant T cells and eosinophils present

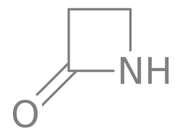
Table 3

	5/1/2022	7/1/2022	10/1/2022	17/1/2022
Opening pressure	>40cm H2O	41cmH2O	26cm H2O	8 cmH2O
CSF WCC count	210, 176, 210 75% mononuclear, 25% polymorphs	166 90% mononuclear, 10% polymorphs	630, 292, 276 90% mononuclear, 10% polymorphs	57,27 100% mononuclear
CSF Protein	0.95	0.91	0.53	0.34
CSF/Cap Glucose	1.4/5.9	1.3/5.1	1.1	2.7/5.2

Table 1: serial CSF results

Discussion

Aseptic meningitis has been reported with beta lactam antibiotic use. Neurotoxicity is a reported uncommon side-effect of carbapenem antibiotics, however drug-induced aseptic meningitis is not a documented side-effect. We propose this to be a manifestation of a severe beta-lactam allergy in a patient with hypersensitivity to other beta-lactam antibiotics. This case further highlights the diagnostic and therapeutic challenges of drug-induced aseptic meningitis and hypoglycorrhachia in a patient on antimicrobial therapy for other documented infection, with hypoglycorrhachia infrequently reported in chemical meningitis[3].



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