

A Confused State of Mind

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An 85-year-old man is brought to the ER by his wife and daughter. They are concerned by his increasingly confused state of mind.

He had two tooth extractions from the left, upper mandible with bridge sectioning two days prior to presenting at the ER. This was done in the same hospital where he had extractions done in 2004 and 2009. Both procedures were similarly complicated by fever and confusion.

Interestingly, in 2009, he underwent a lumbar puncture that showed 100 white cells, slightly elevated protein, and decreased glucose; however, his cultures never grew any organism. He badly deteriorated during his 2009 hospital visit to the point of requiring intensive care management, but a diagnosis was never reached. Of note, he was administered local anaesthetic with neuroleptic medication in 2010 for cataract surgery, and he did not have an adverse reaction on that occasion.

His past medical history is significant for previous right nephrectomy, oncocytoma, hypertension, transient ischemic attacks, dyslipidemia, essential tremor, early Parkinson's disease for which he is regularly followed by a neurologist, bilateral Dupuytren's contracture, and previous distant tonsillectomy.

He takes clopidogrel, 75 mg daily; enteric-coated ASA, 81 mg daily; tamsulosin, 0.4 mg daily; finasteride, 5 mg daily; rosuvastatin, 10 mg daily; fenofibrate, 160 mg daily; and vitamin D, 10,000 units daily, and he was started on amoxicillin, 500 mg t.i.d. before his dental procedure. He was also given amoxicillin for his previous dental extractions.

His examination reveals that he is not oriented of time or place, as he does not know where he is and does not recognize his wife or daughter. His



Figure 1: No Intracranial Hemorrhage or Active Infarction



Figure 2: Normal Ventricled with Moderate Age Related Atrophy



Figure 3: Normal P-A View Chest X-ray

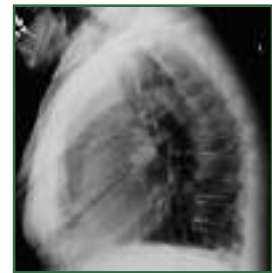


Figure 4: Lateral Chest X-ray

vital signs are stable apart from a temperature of 38.8°C and oxygen saturation is 94% on 3 L of oxygen by nasal prongs. There is decreased air entry to both bases, but no wheezes. Jugular venous pressure is borderline elevated, and heart sounds are normal with no murmurs; there is no stigmata of endocarditis. The abdominal examination is completely normal. He displays mild to moderate bilateral bipedal edema to the mid shins. He has full painless range of movement at his neck with no sign of meningism or jolt accentuation.

His brain CT scan is normal and the CT scan of his facial bones to rule out abscess is negative. Chest x-ray showed increased interstitial markings suggestive of possible heart failure, but recognizing also that there is poor inspiration. Lactate is

negative. TSH and CBC are normal with normal hemoglobin of 148 g/L and a normal white blood count of 7.5 with a normal differential count. Liver enzymes and coagulation parameters are also normal. Creatinine kinase is mildly elevated at 345, which has not changed since his previous admission in 2009.

ECG shows sinus bradycardia with a first-degree intraventricular block and a nonspecific intraventricular block with nonspecific T-wave abnormality. These changes do not appear new compared to the preoperative ECG.

There is no clinical evidence of meningitis, and the patient is admitted to ICU with a plan to do a lumbar puncture in a day or so, because the patient is on ASA and clopidogrel and there is no clear diagnosis.

He has a completely normal lumbar puncture after two days, and he gradually starts to improve by himself and is discharged home after five days with no concerns.

What is your Diagnosis?

The patient was reviewed by an infectious disease specialist and is found to be completely well, and a retrospective diagnosis of amoxicillin induced aseptic meningitis is reached.

Aseptic meningitis is a self-limiting, inflammatory disorder without any evidence of bacterial or fungal etiology. Viral infection is the usual cause, although chemical agents, including drugs, may produce similar symptoms. Other causes of aseptic meningitis include neoplastic diseases (e.g., brain tumours), systemic diseases (e.g., systemic lupus erythematosus sarcoidosis), and defects at the base of the skull (e.g., post-traumatic cerebrospinal fluid [CSF] fistula). Some criteria for diagnosis include an acute onset of signs and symptoms of meningeal involvement, such as headache, fever and stiff neck, changes in

CSF typical of meningitis, absence of bacteria in CSF, and a short and benign course of illness.

There have been several drugs that have been implicated as causes of aseptic meningitis, including NSAIDs (in particular ibuprofen), antimicrobials, (e.g., Trimethoprim-sulfamethoxazole, trimethoprim alone), intravenous immunoglobulins (IVIG), administration of intrathecal agents, vaccines (especially measles, mumps, and rubella), and other medications, such as carbamazepine and azathioprine.

The interval between drug use and the onset of symptoms of drug-induced aseptic meningitis may vary from several hours or days to some weeks. Symptoms appear earliest in individuals with a previous history of reaction to a given drug. The onset of drug-induced aseptic meningitis is usually acute with headache, delirium, fever, chills, nausea, and vomiting. Other symptoms include skin rashes, conjunctivitis, on a swelling of soft tissues of the face and joints accompanied by muscle pain.

Amoxicillin-induced aseptic meningitis

There are several documented cases of aseptic meningitis related to amoxicillin. Interestingly, in all cases, including this one, there were previous episodes of aseptic meningitis associated with amoxicillin. The onset of symptoms after initiation of amoxicillin was between two to seven days. Most patients present with fever and headache.

The patient was advised to wear a medic alert-type bracelet stating, "Aseptic meningitis due to amoxicillin."

Dr. Hayder Kubba graduated from the University of Baghdad where he initially trained as a Trauma Surgeon. He moved to Britain, where he received his FRCS and worked as an ER Physician before specializing in Family Medicine. He is currently a General Practitioner in Mississauga, Ontario.

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