Correspondence

Dysgeusia and auditory hallucination associated with linezolid therapy

Linezolid is an extensively used antibiotic against Gram-positive infections. Several adverse reactions have been reported with this antibiotic. Dysgeusia is a rare side-effect of the drug. We report an elderly patient with dysgeusia and auditory hallucination during the second exposure of the drug.

A 61-year-old man was admitted for permanent pacemaker implantation due to complete heart block. He had no past history of any major illness. He had no past history of any allergy or any hypersensitivity reaction to any drugs. His family history was unremarkable except for heart block, essential hypertension and type 2 diabetes in first-degree relatives. Clinical examination was essentially normal except features of complete atrioventricular (AV) dissociation.

Detailed work-up before pacemaker implantation including routine haematological and biochemical tests, chest X-ray and CT scan of the brain showed no abnormality. The CT scan of the brain was done to rule out any head injury as he fell down during a Stokes–Adams attack.

Electrocardiography (ECG) showed complete AV dissociation with a pulse rate of 48.

He was started on linezolid 600 mg twice daily along with amoxycillin and clavulanic acid and paracetamol, and a dual-chamber sensing and pacing pacemaker was implanted without any complication. All medications were given orally.

He started having headache within a few hours of starting linezolid, though his blood pressure was normal (130/85 mmHg). The headache was not associated with hypertension but was poorly controlled on paracetamol. The headache lasted for 72 hours followed by auditory hallucination of clicking sounds which lasted for 3–4 days and stopped after linezolid therapy was stopped. He also developed dysgeusia with burning sensation in the tongue within 48 hours of linezolid therapy. This was not associated with any fungal infection or black hairy tongue. The patient explained this sensation as numbness with burning sensation even with bland food, and taste for sweet and salty material was altered and appeared bitter. This sensation persisted for 2 weeks after stopping the therapy and slowly returned to normal. Detailed clinical examination including neurological examination done several times during this period revealed no abnormality except altered taste sensation and auditory hallucination as described.

This was the second time the patient had received linezolid. He had taken linezolid 2 weeks ago for 6 days following a fall on the street. At that time, he had no untoward effect.

Our patient was unique in terms of adverse reaction from several aspects; he developed headache, auditory hallucinations and dysgeusia only during the second episode of drug therapy. On the Naranjo Probability Scale of adverse reaction, his reaction fell between 6 and 7, making this reaction a probable adverse reaction. This argues in favour of a hypersensitivity/immunological reaction.

Linezolid is a newer class of oxazolidinedione antibiotic having a morpholino side chain. This drug has considerable activity against Gram-positive organisms. Side-effects such as peripheral neuropathy, Bell's palsy, hearing loss, optic neuropathy, haematological toxicity in the form of thrombocytopenia, anaemia and reversible myelosuppression have been described. Some other side-effects such as black hairy tongue, monoamine oxidase (MAO) inhibitor-like effect, serotonin withdrawal syndrome, hyponatraemia, syndrome of inappropriate antidiuretic hormone secretion, bradycardia and convulsion have also been reported in the literature. Lactic acidosis due to its mitochondrial toxicity has also been reported.[1–4] A small proportion of patients also complain of abnormal taste or loss of taste with this drug. How uncomfortable this dysgeusia could be has not been highlighted in any publication till date.

Adverse events in the literature were found to be common following prolonged administration of linezolid (34.3%); treatment discontinuation was needed in 12.8%. The most common event was anaemia (13.4%) followed by gastrointestinal symptoms (11.1%).[4] Reversible myelosuppression was seen in 2% of the patients on prolonged therapy.[2]

Neurological and neuropsychiatric adverse reactions including optic neuropathy and peripheral neuropathy were found to be common and they were mostly reversible. Moreover, as linezolid is known to cause bradycardia,[5] it is tempting to suggest that there could be some interactions of these medications in this patient with bifascular block, which led to complete heart block during a previous course of linezolid medication. Hence, this antibiotic should be used with caution in patients with heart block. Auditory hallucination has not been reported with linezolid before in the English literature, hence represents a novel adverse reaction.

Dysgeusia is an extremely rare manifestation of adverse drug reaction due to linezolid therapy and has been reported mostly in persons above 60 years of age. Of the more than 8438 adverse events reported to the US Food and Drug Administration till 26 April 2021, only 16 patients (0.19%) presented with dysgeusia.[6] Hence, dysgeusia, though extremely rare with linezolid therapy, can be unpleasant but eventually reversible and may have hypersensitivity reaction as its basis. However, its ability to cause MAO inhibitor-like effect and serotonin withdrawal syndrome-type reaction suggests that this mechanism of action might be operative for dysgeusia, but continuing dysgeusia for 2 weeks after stopping the drug will be an argument against this mechanism. Peripheral neuropathy involving the nerve carrying taste sensation could be plausible. We could not get an electroencephalogram/MRI done in the patient during the episode which might have been instructive in ruling out focal electrical discharge or an anatomical lesion as a cause of this type of symptom.

Conflicts of interest. None declared

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