

CASE REPORT

Clarithromycin-induced akathisia: a class effect of macrolides?

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SUMMARY

Clarithromycin is an antibiotic of the macrolide family, which is commonly used in the treatment of respiratory tract infections. We report a woman aged 77 years with bronchiectasis who was prescribed oral clarithromycin for lower respiratory tract infection. She developed akathisia after 2 doses. On withdrawing the antibiotic, her symptoms resolved rapidly after 7 days.

BACKGROUND

While there are case reports of central nervous system (CNS) stimulation and retardation following clarithromycin ingestion and reports of akathisia following ingestion of azithromycin (another macrolide) in a paediatric population, this is the first time akathisia has been described with clarithromycin.

CASE PRESENTATION

A female patient aged 77 years was referred by her GP to the Ambulatory Assessment Unit (AAU) with a 4-day history of rapidly progressive generalised restless limb movements. She had a background of bronchiectasis, chronic obstructive pulmonary disease, rheumatoid arthritis and ischaemic heart disease. She lived with her husband and was normally independent.

She initially presented to her GP with lower respiratory tract infection symptoms and despite completing a 1-week course of oral amoxicillin and then a 1-week course of oral coamoxiclav, she continued to have productive cough and dyspnoea. Following 3 weeks of symptoms, she was subsequently started on oral clarithromycin 500 mg two times a day, prednisolone 30 mg once a day and carbocysteine 375 mg three times a day. Of note, she had previous exposure to prednisolone and carbocysteine but not to clarithromycin or any other macrolide.

Following the first dose of clarithromycin, she started to feel generally unwell. She continued taking the clarithromycin and the following day developed agitation and restlessness affecting her head and all four limbs. She found herself unable to remain still when sitting, repeatedly crossing and uncrossing her legs. When she concentrated, she was temporarily able to control the symptoms. At night, she was unable to sleep and felt compelled to get up and pace around. These symptoms became more pronounced, resulting in difficulty in mobilising and falls. In addition, she described visual hallucinations of animals crawling on the ceiling. She re-presented to her GP on day 4 of her

symptoms, who was perplexed and referred the patient for a same day review in the AAU. She reported to the ambulatory care physicians that her main concern was being so unsteady that she could not wear high heels (she is 4 ft 11 inches tall).

Clinical examination revealed a well-looking woman without features of sepsis who had generalised semipurposive movements of all four limbs as well as head tremor. She described a sensation of restlessness which on distraction could be controlled with a reduction in the observed limb movements. There were no abnormalities of tone, reflexes, sensation or muscle strength in the limbs. Systems examination was unremarkable with no evidence of respiratory distress or focal respiratory infection.

INVESTIGATIONS

Other than a white cell count of 16.88, routine blood tests (Hb, plts, U&Es, liver function tests, Ca, Mg, C reactive protein) were normal. ECG was normal and chest X-ray showed no new changes compared with previous imaging. An unenhanced CT head showed no acute infarct, haemorrhage or space-occupying lesion.

TREATMENT

Clarithromycin was immediately discontinued.

OUTCOME AND FOLLOW-UP

She was followed up in the AAU 1 week later. Her symptoms had entirely abated and she was able to mobilise normally with no further falls. She no longer had a feeling of inner restlessness or agitation. She was able to sit down without constantly fidgeting or crossing her legs. The insomnia she experienced and constant need to get up at night had resolved. In addition, she had no further visual hallucinations. A follow-up phone call a week after this confirmed that her symptoms had not recurred and she remained well. She reported that she was now able to wear high heels without postural dysequilibrium.

DISCUSSION

To the best of our knowledge, this is the first time that akathisia has been described in the literature following clarithromycin ingestion. Although cases of CNS stimulation and depression after clarithromycin ingestion have been described, these are rare. Geiderman¹ described three such cases; that of a man aged 46 years who developed euphoria, insomnia and giddiness, a boy aged 4 years who developed hyperactivity and a woman aged 39



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years who developed insomnia, agitation and emotional lability. In all three cases, symptoms abated promptly following cessation of clarithromycin. Other neuropsychiatric sequelae associated with clarithromycin use described in case reports include anxiety, delusions of grandeur, dizziness, light headedness and confusion.^{2 3}

Akathisia has been described in a case report following azithromycin ingestion.⁴ Other described neuropsychiatric side effects of azithromycin include choreiform movements, delirium, catatonia and hallucinations.

The exact pathophysiological mechanism of akathisia remains unknown. Evidence suggests it may be due to low activity of dopaminergic projections from the midbrain to the ventral striatum. This is because akathisia is primarily associated with antidopaminergic antipsychotic medications.⁵ Dopaminergic blockade is not part of clarithromycin's mechanism of action; hence, the mechanism in this case is unknown and likely to be idiosyncratic.

The serum concentration of prednisolone may be increased by clarithromycin. While agitation and sleeplessness are side effects of corticosteroids, to the best of our knowledge, akathisia has not been described with clarithromycin. This, in conjunction with the knowledge that our patient had previously tolerated prednisolone with no side effects but was clarithromycin naïve, means that clarithromycin was the likely cause of the akathisia.

Clinicians should be aware that akathisia is a rare side effect of this antibiotic and be vigilant for its occurrence. Furthermore, the symptoms can be effectively treated by prompt withdrawal of the drug.

Learning points

- ▶ Neuropsychiatric side effects following ingestion of macrolide antibiotics are rare.
- ▶ Akathisia is shown in this case to be a side effect of clarithromycin ingestion.
- ▶ Prompt discontinuation of clarithromycin should lead to complete resolution of symptoms.

Contributors Both authors have contributed substantially to this case report. The drafting of the article was undertaken by IIG. Further and final revision and identification of appropriate references was undertaken by DL.

Competing interests None declared.

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