Walking unsteadily: a case of acute cerebellar ataxia

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SUMMARY

Acute cerebellar ataxia is an infrequent neurological syndrome in adults especially if complicated by additional neurological deficits. We report the case of a 69-year-old woman who presented with sudden onset of left facial droop, dizziness, slurred speech and impaired balance. Her medical history included paroxysmal atrial fibrillation and a sigmoid diverticular abscess treated with ciprofloxacin and metronidazole. Cranial computed tomographic angiography and MRI showed no signs of acute ischaemia or haemorrhage but demonstrated symmetrically distributed lesions in the cerebellar dentate nuclei. A diagnosis of metronidazole-induced encephalopathy was suspected. Metronidazole was stopped and the patient completely recovered. Metronidazole is a commonly prescribed medication. Clinicians should be aware of the clinical and radiological presentation of metronidazole-induced encephalopathy so that this serious but completely reversible condition can be promptly diagnosed.

BACKGROUND

Acute cerebellar ataxia is an infrequent neurological syndrome in adults especially if complicated by additional neurological deficits. However, the differential diagnosis of acute cerebellar ataxia is wide-ranging and requires an exhaustive diagnostic procedure. Neurotoxicity due to metronidazole is a well-known phenomenon. However, acute cerebellar ataxia during a standard treatment course of metronidazole is rarely reported.

CASE PRESENTATION

A 69-year-old woman presented with sudden onset of left facial droop, dizziness, slurred speech and impaired balance. Her medical history included a mixed anxiety-depressive disorder treated with fluoxetine, melitracen and alprazolam and recently diagnosed paroxysmal atrial fibrillation treated with aspirin. A sigmoid diverticular abscess was diagnosed shortly before presentation; current treatment included oral ciprofloxacin 500 mg twice a day (total cumulative dose at presentation of 11 g) and metronidazole 500 mg three times a day (total cumulative dose at presentation of 16 g).

INVESTIGATIONS

On admission, vital signs were normal. The patient was oriented to person, place and time. Neurological examination revealed unilateral facial paresis with light right-sided mouth asymmetry, spontaneous horizontal left-beating nystagmus, dysarthria and bilateral cerebellar ataxia that was more pronounced on the right side. There were no signs of meningeal irritation. Muscle strength, stretch reflexes and sensation were unremarkable.

Laboratory tests demonstrated leukocytosis (white blood cell count 18 900/mm³), while C-reactive protein, renal and liver function tests, electrolytes, serum levels of vitamin B1, B12, and thyroid-stimulating hormone were all normal. A 12-lead electrocardiogram demonstrated normal sinus rhythm. Cerebrospinal fluid (CSF) analysis showed normal protein and glucose levels, 1 nucleated cell/mm³ and no microorganisms on Gram stain. PCRs for HSV-1, HSV-2, Enterovirus and Mycobacterium tuberculosis were negative as were the results of CSF culture.

Cranial computed tomographic angiography, as well as cranial MRI, showed no signs of acute ischaemia or haemorrhage. However, T2-weighted MRI images demonstrated symmetrically distributed hyperintense lesions in the cerebellar dentate nuclei (figure 1).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of acute cerebellar ataxia is broad and includes ischaemic or haemorrhagic stroke, infection, trauma, primary or metastatic brain tumour, immunological and metabolic disorders, and toxic causes. In this case, specific MRI findings were critical for diagnosis. The differential diagnosis of T2 hyperintense lesions of the bilateral cerebellar dentate nuclei in patients with symptoms of acute encephalopathy includes methyl bromide intoxication,¹ maple syrup urine disease,² enteroviral encephalomyelitis,³ Wernicke encephalopathy⁴ and metronidazole-induced encephalopathy.^{5–7} Patient history and age of onset as well as serum and CSF analysis are critical for excluding other causes, while a temporal relationship between drug administration and symptom onset indicates a diagnosis of metronidazole-induced encephalopathy. Patients with metronidazole-induced encephalopathy typically show characteristic symmetrical dentate nuclei lesions on brain MRI^{5–7} occasionally associated with multiple symmetric lesions in the corpus callosum, midbrain, pons, white matter and basal ganglia.^{7–8}

TREATMENT

The patient was admitted to our hospital and metronidazole was stopped.

OUTCOME AND FOLLOW-UP

Dysarthria and ataxia improved progressively, and 1 month later the patient had recovered completely. A follow-up MRI performed 2 months after presentation confirmed the complete disappearance of cerebellar lesions (figure 2). The clinical and radiological response to withdrawal of the drug confirmed the definite diagnosis of metronidazole-induced encephalopathy.

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Figure 1 Axial T2-weighted cranial MR images at presentation show bilateral symmetric hyperintense lesions in the dentate nuclei of the cerebellum (white arrows).

DISCUSSION

Metronidazole is a nitroimidazole antimicrobial agent widely used to treat anaerobic infection and protozoal disease. Rare neurological adverse reactions to metronidazole therapy include seizures,⁹ peripheral neuropathy,¹⁰ acute mental status change¹¹

Figure 2 Axial T2-weighted cranial MR images at 2-month follow-up after drug discontinuation show complete disappearance of cerebellar lesions.

and cerebellar dysfunction.^{5 12} Metronidazole neurotoxicity is still incompletely understood. The suggested mechanisms leading to nervous tissue damage include the generation of semi-quinone and nitro anion radicals¹³ and vasogenic axonal oedema.¹⁴ A dose-related effect has been suggested as the vast majority of reported cases of metronidazole-induced encephalopathy involve patients on high cumulative doses of metronidazole.¹⁵ However, a few reports describe patients who have developed symptoms after receiving low cumulative doses of metronidazole¹⁶ (and including our report), leading to the supposition that a standard treatment course of metronidazole can trigger metronidazole-induced encephalopathy.

Learning points

- ▶ Metronidazole-induced encephalopathy is a rare adverse reaction to a widely prescribed medication.
- ▶ Consider drug toxicity in the differential diagnosis of adult-onset acute cerebellar ataxia.
- ▶ Metronidazole-induced encephalopathy is a completely reversible condition.

Competing interests None.

Patient consent Obtained.

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