Acute encephalopathy associated with metronidazole therapy

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Summary

A forty-eight year-old male with amoebic liver abscess became encephalopathic 3 days following oral metronidazole. Withdrawal of the drug led to prompt resolution of all encephalopathic sympthoms.

Résumé

Un homme âgé de quarante-huit ans presentant un abscès du fois dû à l'amibiase est devenut ancephalopatique 3 jours après le debut d'un traitement à la metronidazole. L'arrèt du traitement a aboutit à la disparition rapide de tous les symptomes ancephalopatiques.

Introduction

Metronidazole is a nitroimidazole anti-microbial compound used in treating infections and infestations caused by anaerobic bacteria and susceptible protozoa. Neurologic side effects previously attributed to metronidazole include sensory polyneuropathy [1-3], ataxia [4], cerebellar injury [5] and convulsion [6]. We describe here acute encephalopathy associated with metronidazole therapy in a patient with amoebic hepatic abscess.

Case presentation

A 48 year-old man who was diagnosed hypertensive and whose blood pressure was satisfactorily controlled on a daily tablet of (amiloride/thiazide combination), presented in hospital with fever, rigors, malaise, right upper quadrant abdominal pain, profound anorexia and progressive weight loss of 4 weeks duration. He also had a 10-day antecedent history of foul-smelling, watery, non-blood, and non-mucoid stools which responded initially to oral tetracycline therapy. He did not take alcohol.

On clinical examination, he was chronically ill-looking, wasted, and febrile (Temp. 38.6°C). There was a tender and smooth, but firm hepatomegaly with no bruit on auscultation. Digital rectal examination was normal. Blood pressure was 130/80 mmHg. There was cardiomegaly and a loud aortic component of the second heart sound.

Stool microscopy revealed trophozoites of *E. histolytica*. The packed cell volume (PCV) was 36% and total white cell count was 10 x 10^9/L with neutrophil of 89%, lymphocytes 10%, and oesinophils 1%. The electrolytes and renal function tests were normal. The liver function test showed an alkaline phosphatase level of 35 i.u/L (20-91), ALT of 29 i.u/L (0-15), and AST of 58 i.u/L (0-20). The serum albumin was 39 g/L (35-58). The chest X-ray showed significant elevation of the right dome of the diaphragm.

The ultrasonograph showed a large cavity in the postero-superior part of the right lobe of the liver. The diagnosis of amoebic liver abscess was made and the patient was placed on oral metronidazole 400 mg 8 hourly. He became restless, confused, and disoriented on the 4th day of initiating therapy. There were no other predisposing conditions for the observed neurologic findings. He was not taking other medication. A computerized tomography (CT) of the brain and cerebro-spinal fluid analysis were normal. However, CT of liver corroborated the ultrasongraphic finding.

Metronidazole was withdrawn and the encephalopathy cleared within 4 days. He was, however, re-challenged with metronidazole 2 days after complete recovery from the encephalopathy. He re-developed another episode of the acute confused state. Metronidazole was then stopped completely with the encephalopathy clearing again within 3 days. The patient was eventually treated with chloroquine for 3 weeks and was discharged from hospital 2 weeks after stopping metronidazole therapy. The follow-up examination 4 weeks after discharge revealed no abnormality.

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Discussion

Metronidazole has been proved to be an effective drug in amoebiasis even though occasional resistance to the drug has been reported [7-10]. This patient recovered completely from the acute encephalopathy after the metronidazole was withdrawn, thus supporting the diagnosis of metronidazole-induced acute encephalopathy.

Acute neurotoxicity associated with metronidazole therapy in anaerobic infections has previously been described [5]. However, acute encephalopathy associated with metronidazole therapy in amoebiasis in this environment is uncommon. It is known that the drug crosses the blood brain barrier in humans. The CNS effects do not seems to be related to hepatic or renal dysfunction or to the level of metronidazole in the blood or cerebro-spinal fliud [6]. Frytak *et al.* [11] did not find any correlation between metronidazole and seizure disorders.

The mechanism of neurotoxicity of metronidazole is not precisely known. It is postulated to be related to binding of metronidazole or its metabolite to neuronal RNA inhibiting protein synthesis and, hence, causing axonal degeneration [2,12]. Cerebellar damage has also been found [13,14]. Whatever the mechanism of effects on the CNS, fibre regeneration is the rule [2] when therapy is stopped. It is concluded, therefore, that metronidazole can cause an acute confused state in some patients taking the drug and this report is meant to stimulate awareness to this rather rarely reported effect.

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