MEFLOQUINE-INDUCED MANIA IN A 22-YEAR-OLD CHINESE MAN

Dear Sir,

A 22-year-old male Chinese undergraduate presented with manic and psychotic symptoms. One week earlier, he started having decreased sleep and social disinhibition, which later progressed to frank visual hallucinations of food transforming into other kinds of food. He exhibited an elevated mood and also developed delusions of grandeur, reference and persecution. He believed himself to be part of a special group with special powers and that everyone around him was putting on a façade to fool him. He also believed his phone was being tapped and that his mother was trying to harm him. He developed these symptoms three to four days after setting sail on a ship, and the doctor on board started him on olanzapine before evacuating him back to Singapore. He was continued on olanzapine by the psychiatrist at an outpatient clinic. However, he was admitted two days later due to worsening of symptoms.

He had a significant past psychiatric history of an episode of psychosis. This developed a week after he entered National Service (NS). At that time, he displayed delusions of persecution and believed his platoon mates were trying to harm him. He was admitted to a local psychiatric hospital for two weeks and treated successfully with risperidone. He was later followed-up uneventfully for two years. He completed his NS in a non-combat vocation. The patient had no other significant medical or surgical history of note and it was initially thought that he was not on any medication. The patient had just completed his first year in university with average grades and was interacting well with family and friends before setting sail. His parents claimed that there was no obvious stressor in his life. His physical examination and investigations (full blood count, renal and liver panel, thyroid function test) were normal.

The acute onset of symptoms prompted additional history taking from the family which revealed that the patient had started a course of melfoquine (250 mg a week) two weeks before embarking on the ship. They also recalled that the patient was also on antimalarials in NS before he developed his first psychotic episode. The patient was treated with low-dose risperidone and his symptoms slowly resolved over two weeks. He was followed-up in the outpatient clinic and he remained well four months after discharge.

Mefloquine is widely accepted as a safe and effective treatment and a prophylactic agent for cholorquine-resistant malaria[1]; it is prescribed over the counter in Singapore as Larium®. It is is a quinoline-methanol and has a slow onset of action, with a long half-life of three weeks. It acts by inhibiting the malaria parasite's haem polymerase. Neuropsychiatric sequelae of mefloquine can occur in up to 40% of patients[2]. Common sequelae include dizziness, confusion, sleep disturbances, anorexia, tremor, ataxia, and fatigue. Depression can occur in up to 1.2% of patients[3]. More disturbing symptoms (panic attacks, visual hallucinations) and serious adverse effects of psychosis, encephalopathy and convulsions and possibly suicidal ideation are much rarer[2,4-6]. The incidence of such sequelae ranges from 4-7 per 1,000 patients[4,5] (for patients taking mefloquine for malaria treatment) to 1 in 13,000 patients[4] (for patients taking mefloquine for malaria prophylaxis).

The causal mechanism for the side effects is not known. The typical picture for mefloquine-induced psychosis is paranoid (not manic) symptoms developing 11 days after the fourth dose of medication[6] but has been reported up to 120 days after the last dose[7]. The psychiatric symptoms usually resolve rapidly in response to anti-psychotics. To our knowledge, this is the second report of mefloquine-induced mania[8]. Locally, there are only two other reported cases of mefloquine-induced neuropsychiatric sequelae. The first was a 23-year-old woman who developed toxic confusional state requiring ten days admission and the second, a 55-year-old man who developed anxiety, confusion, depression, visual disturbances, and loss of coordination. They were also taking mefloquine for prophylaxis at the same dosage as this patient (250 mg per week). Unfortunately, we were unable to obtain further clinical details regarding these two cases.

The package insert for Larium® states that it is contraindicated in patients with active depression or with a history of psychosis or convulsions. In Singapore, it is sold as an over-the-counter medication and patients with a history of contraindicated conditions may inadvertently purchase such medication. It is pertinent for medical practitioners to be aware of the common side effects of prophylactic anti-malarials which patients may not consider as medication, and to exclude possible organic causes in patients presenting with a psychiatric condition without a typical prodrome.

Yours sincerely,

Tor Phern Chern
Department of Psychological Medicine,
National University Hospital,
5 Lower Kent Ridge Road,
Singapore 119074
Tel: (65) 6772 4511
Fax: (65) 6777 2191
Email: torphernchern@gmail.com

Lee Hon Yee
Department of Anaesthesia,
Alexandra Hospital,
378 Alexandra Road,
Singapore 159964

Tan Chay Hoon
Department of Pharmacology,
Yong Yoo Lin School of Medicine,
National University of Singapore,
MD2, 18 Medical Drive,
Singapore 117597

REFERENCES

1. Croft A, Garner P, Mefloquine to prevent malaria: a systematic review of trials. BMJ 1997; 315:1412-6.
2. White NJ. Mefloquine. BMJ 1994; 308:286-7.
3. Steffen R. Travel medicine - prevention based on epidemiological data. Trans R Soc Trop Med Hyg 1991; 85:156-62.
4. Larium (mefloquine). [product monograph] Compendium of Pharmaceuticals and Specialties. Ottawa: Canadian Pharmacists Associations, 2002: 876-7.
5. Barrett PJ, Emmins PD, Clarke PD, Bradley DJ. Comparison of adverse events associated with use of mefloquine and combination of chloroquine and proguanil as antimalarial prophylaxis: postal and telephone survey of travellers. BMJ 1996; 313:525-8. Comment in: BMJ 1996; 313:1552-4.
6. Piening RB, Young SA. Mefloquine-induced psychosis. Ann Emerg Med 1996; 27:792-3.
7. Bem JL, Kerr L, Stuerchler D. Mefloquine prophylaxis: an overview of spontaneous reports of severe psychiatric reactions and convulsions. J Trop Med Hyg 1992; 95:167-79.
8. Even C, Friedman S, Lanouar K. Bipolar disorder after mefloquine treatment. J Psychiatry Neurosci 2001; 26:252-3.