

## Paranoid psychosis related to mefloquine antimalarial prophylaxis

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### SUMMARY

**Mefloquine is an important antimalarial drug for treatment and prophylaxis of chloroquine-resistant malaria. Its use has been associated with neuropsychiatric side-effects. We report a case of paranoid psychosis associated with mefloquine occurring in a remote part of Papua New Guinea. Adverse reactions and contraindications are discussed. This case underlines the importance of awareness of neuropsychiatric side-effects with mefloquine use and of taking a careful psychiatric history before prescribing mefloquine.**

### Introduction

Extensive clinical and field trials have shown mefloquine to be one of the most effective drugs for treatment and prophylaxis of chloroquine-resistant falciparum malaria. It is used by Peace Corps workers and is popular as antimalarial prophylaxis in European and American visitors to malarious areas of South-East Asia and West Africa.

Psychotic reactions have been reported with prophylactic doses and treatment doses of mefloquine, alone and in combination with other antimalarial drugs (1). We report a case of serious adverse reaction to mefloquine admitted to Port Moresby General Hospital highlighting the need for a careful psychiatric history prior to prescribing mefloquine and the importance of early diagnosis of psychiatric reactions.

### Case report

A 39-year-old marine biologist from Catalonia, Spain was air-lifted from a remote island 200 kilometres north of Papua New Guinea to Port Moresby General Hospital with paranoid ideation and irrational behaviour.

He had started to take prophylactic doses of mefloquine 250 mg weekly two weeks earlier, with the last dose taken on the day of arrival in Papua New Guinea. He travelled to a remote island with a colleague to conduct research but after arrival he began to express an unreasonable fear of an imminent earthquake. He became paranoid that his colleague wanted to harm him and subsequently disappeared for 2 days, later to be found living with local villagers.

After his colleague had found him, he packed his luggage and walked into the ocean planning to return to Europe. His colleague subsequently arranged urgent medical transfer to Port Moresby General Hospital. Other past medical history was unavailable at the time of presentation. There was no history of illicit drug use before presentation and his companion was unaware of any use of prescribed medications other than mefloquine.

On admission he was disoriented in time and place. His speech was rambling and he was agitated and fearful of the medical staff. He was afebrile and there was no neck stiffness. There were no focal neurological signs. Cardiorespiratory examination was

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normal. The full blood count was normal and there were no malaria parasites on a thick blood film. Serum electrolytes were normal and renal and liver function tests were within normal limits. Thyroid function studies were normal.

A diagnosis of acute psychosis secondary to mefloquine was suspected. Mefloquine was ceased and changed to doxycycline 100 mg daily. The patient was treated with chlorpromazine 100 mg intramuscularly.

The psychosis resolved over the next 2 to 3 days. On further questioning after recovery the patient admitted that he had suffered from endogenous depression for 19 years. He had been taking phenelzine 15 mg orally daily and chlorthalidone, a benzodiazepine, as required.

### Discussion

Mefloquine has been considered to be a safe drug although some form of adverse effect may be seen in up to 40% of travellers taking the drug for malaria prophylaxis (2). Commonly recognized adverse effects are usually minor and include dizziness, nausea, vomiting and loose stools. The incidence of serious events ('serious' as defined by the Council for International Organisations of Medical Sciences as fatal, life-threatening, leading to or prolonging a stay in hospital or causing severe disability (3)) has been reported to be approximately 1 in 10,000 for chemoprophylaxis (4).

Neuropsychiatric reactions to mefloquine are well documented. These have included anxiety, nightmares, hallucinations, depression and, less commonly, psychotic episodes and seizures. The exact risk of neuropsychiatric adverse events has varied with the design of studies and diagnostic criteria used (5). The risk of all neuropsychiatric events may be as high as 27% and disabling events 0.7% (2). Reactions usually occur after the first or second dose (5) but may be delayed as long as 2-3 weeks after the last dose was taken.

The mechanism underlying adverse reactions to mefloquine is unknown. Neuropsychiatric adverse events do not appear

to be related to mefloquine metabolite concentrations or total mefloquine plasma levels (6). A recent review of all published cases suggests that reactions may be the result of primary hepatocellular injury, and in some individuals transient thyroid function abnormalities may appear (7).

Mefloquine is contraindicated for people with a known hypersensitivity to the drug. The World Health Organization recommends that travellers with a personal or family history of seizures or manic-depressive illnesses should not take mefloquine (8). Alcohol, recreational and hepatotoxic drugs should be avoided (7). In our case report the potential consequences of mental confusion and psychosis occurring in a remote area of Papua New Guinea cannot be overemphasized.

This case illustrates i) the importance of awareness of the psychiatric side-effects of mefloquine by health workers in malarious areas who may occasionally come into contact with such patients and ii) that mefloquine should not be prescribed if a psychiatric history exists.

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