A 48-year-old woman was seen at Mayo Clinic (Rochester, MN) with a 6-week history of worsening paresthesias, dysesthesias, and allodynia. Two months before presentation, she had traveled to Kenya, initiating mefloquine hydrochloride (250 mg) doses at approximately weekly intervals for malaria prophylaxis beginning 1 week before the 5-day trip (July 20) and concluding the medication 6 days after her return, for a total of 4 doses (July 20, July 27, August 3, and August 9). Five years before presentation, she had taken mefloquine malaria prophylaxis without incident. Her medical history was limited to chronic neck pain caused by cervical radiculopathy, gastroesophageal reflux, insomnia, and low vitamin B12, serum concentration (162 pg/mL; reference range, 193–982 pg/mL). Medications before the current illness included zolpidem tartrate (10 mg nightly), esomeprazole magnesium (40 mg daily), acetaminophen (325 mg)–ibuprofen sodium (550 mg 3 times daily) or naproxen sodium (550 mg twice daily).

Shortly after returning home and completing the third dose of mefloquine (August 3), the patient noted worsening of chronic cervical radicular pain and the onset of tingling, numbness, and “pins and needles” sensations involving the fingers of both hands and, to a lesser degree, both feet. She noted severe scalp burning, with marked sensitivity to light touch of the face, brow, and bridge of the nose. The sensitivity was clearly exacerbated by the cold. Three weeks before presentation, she had experienced 1 day of unexplained fever to 39°C. The sensory symptoms were intermittent and fluctuated significantly in severity. Because of the discomfort, she developed mild reactive depression and worsening of her preexisting sleep difficulties but exhibited no other cognitive or psychiatric features.

Except for allodynia, no abnormalities were noted on general or neurological examination of the patient. An extensive laboratory workup was unremarkable, including complete blood cell count, urinalysis, rapid plasma regain, serum chemical analyses, thyroid function tests, malaria serological analysis, tumor markers, urine heavy metal screen, and hepatitis A, B, and C serological evaluation. Antinuclear antibodies and other connective tissue disease markers were negative, as were a serum toxicologic screen and a chest radiograph. Her erythrocyte sedimentation rate was 12 mm/h, and her C-reactive protein level was 2.86 mg/dL (reference range, 0.00–4.00 mg/dL). The only serological abnormality noted was decreased C3 complement (510 μg/mL; reference range, 830–1170 μg/mL). Nerve conduction velocities, electromyogram, and magnetic resonance (MR) imaging of the brain were without significant abnormalities. An MR image of the spine documented the history of cervical disc disease. After irregularly administered oral vitamin B12, serum concentration in the past year and intramuscularly administered vitamin B12 given after the onset of the current illness, a serum vitamin B12 level of 664 pg/mL (reference range, 193–982 pg/mL) was reached, without changes in her symptoms.

We concluded that the patient was experiencing a hypersensitivity reaction to mefloquine manifesting as C-fiber irritation. The normal nerve conduction studies indicate intact large myelinated fibers. Thus, the patient suffered from either small fiber neuropathy or small fiber irritation. Gabapentin (300 mg) started shortly before presentation at Mayo Clinic was gradually increased to 600 mg 3 times daily, resulting in symptomatic improvement. Additional prescribed medications directed at symptomatic relief included oxycodone, ibuprofen sodium, and locally applied diclofenac sodium gel and amitriptyline hydrochloride–ketamine hydrochloride–lidocaine hydrochloride gel.

The patient experienced gradual improvement of all symptoms over 2 months. However, variable facial and extremity pain persisted 5 months after the last dose of mefloquine.

**DISCUSSION**

Neurotoxic effects of mefloquine are well described, particularly among individuals with low body mass index, but are generally limited to central nervous system symptoms, including neuropsychiatric events, insomnia, seizures, and ototoxic effects. To our knowledge, only three previous studies have documented mefloquine-induced peripheral polyneuropathy.

Jha and others have documented two patients with serious illness, including polyneuropathy, following a large dose of mefloquine (“front-loaded prevention”) administered immediately after treatment of acute malaria with other antimalarial agents. Watt-Smith and others reported a case of trigeminal sensory neuropathy limited to the lip following malaria prophylaxis with mefloquine.

In the third study, similar to the case reported herein, the patient at Week 3 of weekly mefloquine hydrochloride (250 mg) prophylaxis noted paresthesias and painful dysesthesias of the hands and feet, which resolved 3 weeks after mefloquine was discontinued. The authors also cite personal
communication from the manufacturer in which nocturnal extremity paresthesias are reported to be associated with the use of the drug.

Although our case does not prove causality, its similarity to the study by Olson and others, the coincidence of symptoms with mefloquine administration, and the gradual resolution of symptoms following discontinuation suggest that mefloquine prophylaxis was the cause of C-fiber irritation that resulted in the patient’s allodynia.

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