a spectrum of virulence determinants that may emerge in the right clinical circumstances.

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References


Neurotoxicity Due to Antimalarial Therapy Associated with Misdiagnosis of Malaria

Str—in support of recently published reports [1, 2], we present the case report of a patient who had neurotoxicity due to antimalarial therapy that was associated with misdiagnosis of malaria. A 39-year-old man sought medical attention at our clinic after returning to the United States from Sierra Leone. He reported tremors, a lack of coordination, an inability to concentrate, and severe anxiety after receiving five 10-day courses of artesunate therapy and one 10-day course of chloroquine therapy for the treatment of malaria during three separate episodes of fever, chills, and malaise. The patient received doxycycline therapy for malaria chemoprophylaxis and reported full adherence to treatment. A neurological examination demonstrated tremors, restlessness, hyperreflexia, and spasticity. The other findings of this examination were normal. The results of laboratory evaluations were also normal. The findings of a chest radiograph and an MRI of the brain were also reported to be normal. A serum specimen was analyzed by the indirect fluorescent antibody (IFA) method at the Centers for Disease Control and Prevention (Atlanta, GA) for detection of antibodies to all the human plasmodium species; all tests were reported to show a titer of <1:16 (consistent with no previous exposure to malaria). At subsequent evaluations after discontinuation of the antimalarial drugs, the patient’s symptoms had improved markedly.

The diagnosis of malaria for travelers and expatriates from developing areas may be a double-edged sword, in which failure to diagnose malaria may lead to fatal consequences, yet the use of inappropriate medications associated with misdiagnosis of malaria may result in unacceptable adverse effects. The IFA tests that were performed in the case we describe have a sensitivity of 95% and a specificity of 99% [3, 4]. Although we acknowledge that the patient had also experienced several self-limited infections, none of the more common viral or bacterial causes of relatively short-term fever should have caused his neurologic syndrome. Although reference laboratories were unable to measure serum levels of chloroquine and artesunate, the improvement of his condition several weeks after discontinuation of the medications suggests neurotoxicity due to multiple courses of artesunate therapy, perhaps compounded by chloroquine therapy.

ARTESUNATE AND ARTEMETHER ARE ANTIMALARIAL AGENTS DERIVED FROM SWEET WORMWOOD (ARTENISIA ANNUS) AND ARE WIDELY USED FOR THE TREATMENT OF MALARIA IN MANY COUNTRIES. THESE COMPOUNDS ARE CONSIDERED TO BE LESS TOXIC THAN QUINOLINE ANTIMALARIALS [5]. IN ANIMAL MODELS, HIGH DOSES OF ARTEMETHER PRODUCE NEUROTOXICITY CHARACTERIZED BY GIAT DISCOMFORT, LOSS OF SPINAL AND PAIN REFLEXES, RESTLESSNESS, TREMORS, AND INCOORDINATION [6]. THERE HAS BEEN NO EVIDENCE OF SIGNIFICANT TOXICITY IN THE >1 MILLION HUMAN PATIENTS WHO HAVE RECEIVED THE RESPECTIVE PREPARATIONS[7]. HOWEVER, THE COURSES OF TREATMENT USED FOR UNCOMPLICATED MALARIA ARE SHORTER THAN THE MULTIPLE COURSES RECEIVED BY OUR PATIENT. INDEED, CUMULATIVE NEUROLOGIC TOXICITY APPEARS TO BE THE MOST LIKELY CAUSE OF HIS SYMPTOMS. WE CANNOT RULE OUT A CONTRIBUTION BY CHLOROQUINE, SINCE ITS USE HAS BEEN ASSOCIATED WITH NEUROPSYCHIATRIC SYNDROMES AS WELL [7].

Travel-medicine practitioners should be aware of the potential toxicity associated with antimalarials in cases of a misdiagnosis of malaria. Providing pretravel advice about malaria prevention and self-treatment is critical, as is guidance on seeking adequate medical care when overseas. We encourage the establishment of communication protocols between individuals traveling to areas where malaria is endemic and health practitioners in their home countries, to reduce the risk of exposure to potentially unnecessary toxic medications.

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