A 56-year-old male Caucasian, who travelled to Thailand for a medical congress, and had planned to travel later also to Cambodia, was admitted to an ICU in Bangkok (Thailand) after the sudden appearance of fever, confusion, lethargy and blurred vision. His past medical history was unremarkable except for mild diastolic hypertension not requiring pharmacological treatment. He had been working as a biologist in a laboratory of immunological research at an Italian university. Two weeks before admission he had started taking mefloquine (1 tab. 250 mg/week) for malaria prophylaxis.

One week before admission he developed weakness, followed some days later by anorexia, myalgia and lethargy, and, finally, by fever, confusion and blurred vision. He denied drug allergy, the use of any medication other than mefloquine or other medicines containing quinine or quinine-like compounds. Physical examination was normal except for fever (38.6°C), leg petechiae and scleral icterus. Lung fields on X-ray were clear. Electrocardiogram, abdominal ecography and cerebral CT scan did not reveal any abnormality. Laboratory tests showed thrombocytopenia (26 000 platelets/mm³), leucocytosis (18 450 white blood cells/mm³), neutrophils 81%, anaemia (haemoglobin 10.1 g/L, haematocrit 29.6%) with anisocytosis and schistocytes, increased reticulocyte count (240 480 reticulocytes/mm³), and high lactate dehydrogenase (LDH) (22.40 µkat/L) and bilirubin levels (total bilirubin 54.7 µmol/L, indirect 42.7 µmol/L). Coagulation parameters were normal. Serum creatinine was 97.2 µmol/L; urine examination was normal except for microhaematuria. A central venous catheter was placed in the right jugular vein and two plasmapheresis sessions (12 units of fresh-frozen plasma) were performed in the first 24 h. Neurological status improved at the end of the first plasmapheresis; haematological abnormalities disappeared in the first few days of treatment (Figure 1). Plasmapheresis was continued daily for another 6 days (a total of eight sessions), until the patient was transferred back to Italy, then every other day for another week in a Nephrology Unit. We ruled out either infective or autoimmune processes. The former because the search for pathogens in blood, urine and faeces and imaging studies were negative; the latter, on the basis of extensive serology assessment for systemic lupus erythematosus, antiphospholipid syndrome and other immunological diseases. The patient was discharged home after 14 days.

To our knowledge this is the first report describing a case of TTP associated with the use of mefloquine, an antimalarial agent widely used for prophylaxis or treatment of malaria.

Palmer et al. reported eight cases of isolated thrombocytopenia following mefloquine administration, whereas Orlando et al. described a case of massive intravascular haemolysis, haemoglobinuria, oliguria and fever within 2 days of treatment with mefloquine and halofantrine for P. falciparum malaria. Finally, Palmer et al. reported five patients who developed haemolytic anaemia after taking doses of up to 1500 mg of mefloquine.

In our patient the presence of severe neurological symptoms together with fever, thrombocytopenia and microangiopathic anaemia suggests a more complex haematological abnormality, such as TTP. The causal relation between drug and disease is supported by the temporal relation of drug intake with the onset of the clinical symptoms and laboratory abnormalities, as well as by their prompt improvement after the apheresis treatment and drug withdrawal. Of note, the neurological abnormalities, which were the main clinical findings in our patient, appeared soon after the intake of the first dose of the drug, and worsened after each dose until the third dose. Lastly, the patient denied taking any other drug along with...
mefloquine, and other infectious or immunological diseases were ruled out.

Given the widespread use of mefloquine for malaria prophylaxis and therapy in Western countries, it is important to also include this drug among the assessment of previous drug exposure in any person manifesting acute neurological abnormalities associated with thrombocytopenia and microangiopathic haemolytic anaemia.

Correspondence

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Transparency declarations

None to declare.

References