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Severe imported falciparum malaria – Clinical and drug supply challenges

Dear Editor,

We read with interest a case series on a cohort of Italian patients with severe Plasmodium falciparum malaria treated in the intensive care unit with predominantly positive outcomes [1]. In light of lengthy processes of approval from the Food and Drug Administration (FDA) for drugs which are already routinely prescribed around the world, it has come to our attention that patients may not be receiving potentially life-saving antimalarial agents quickly enough to prevent rapid dissemination of parasite burden and eventual progression of disease.

In December 2017, we saw a 50-year old man who had recently returned from a trip to Africa with one week of progressive fever and altered mental status. Peripheral blood smear (Fig. 1) confirmed a diagnosis of malaria with high parasite load (20%). The patient had been started on doxycycline and quinidine (the FDA-approved therapy within the U.S.) before being transferred from a hospital in rural Georgia to Grady Memorial Hospital in downtown Atlanta. Due to complications of Quinidine therapy in the form of QT interval prolongation and ventricular arrhythmias, efforts were made to obtain artesunate (an investigational drug recommended by the World Health Organization and used broadly in Europe) through FDA waiver. Despite rapid administration of artesenate acquired from the Center for Disease Control (CDC) located a few miles from Grady Memorial Hospital, the patient rapidly developed shock, liver dysfunction, kidney failure, and peripheral ischemia. The patient was maintained on four vasopressor agents before being started on angiotensin II to decrease vasopressor burden. After five days of continuous vasopressor support to maintain circulation and continuous renal replacement therapy to manage acute kidney injury and refractory metabolic acidosis, the patient eventually succumbed to the disease due to multiorgan failure.

A recent acknowledgement by the CDC in 2016 states that “intravenous quinidine gluconate is the only parenteral drug available in the United States (US) for the treatment of severe malaria. This situation is, to our knowledge, unique to the US and is problematic.” The CDC has made the drug available at 18 designated Quarantine Stations nation wide. A recent report determined that artesunate was safe for use in the US and was more effective in treatment of severe malaria than traditional quinidine [2]. That said, it is obvious that there will be delays in obtaining IV artesunate for immediate use given that it will not be held on formulary at hospital pharmacies, but instead will be available at only 18 locations across the country. In the case of our patient, it is entirely possible that the outcome may have been different if IV artesunate had been initiated at the rural hospital in Georgia instead of quinidine. The CDC, in attempting to correct this issue has

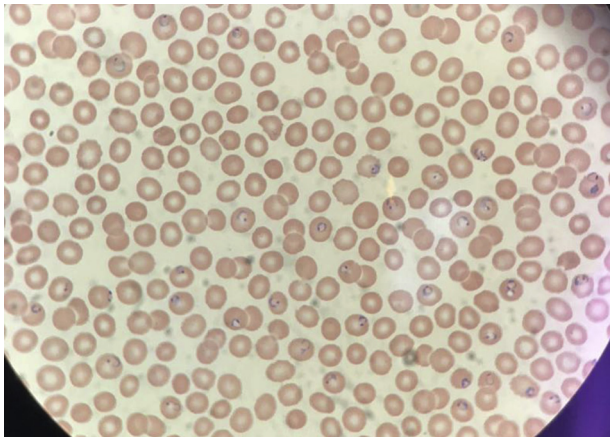

Fig. 1. Plasmodium falciparum malaria in ring-form (20% parasite load).

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issued a “protocol for compassionate use of IV artesunate.” [3].

In conclusion, cerebral malaria is a condition that is rarely encountered in the U.S., but is treatable when proper anti-parasitic medications are administered within an appropriate time frame. The U.S. lags behind European countries in wide-spread adoption of artemisinin antimalarial agents due to lengthy FDA approval processes.

References

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