Answer to Photo Quiz: *Plasmodium falciparum* Infection with Hyperparasitemia

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Plasmodium falciparum can be differentiated from other *Plasmodium* species on blood smear by the absence of forms other than ring trophozoites and/or the presence of rarely observed banana-shaped gametocytes. However, morphologically, *P. falciparum* and *Babesia* ring forms may appear similar, leading to diagnostic uncertainty for patients, such as ours, with potential exposure in areas where both malaria (Haiti) (1) and *Babesia* (New England) are endemic. Notably, *Babesia* replicates by binary fission inside red blood cells (RBC), and therefore, observation of multiple ring forms in an individual RBC is quite common. In contrast, each *Plasmodium* ring in a single RBC represents a separate infection event. Therefore, the observation of more than two *Plasmodium* rings inside an RBC is vanishingly rare, and the presence of four rings in a single RBC is usually considered diagnostic for *Babesia* infection.

For our patient, the blood smear revealed not infrequent infection with up to three (see Fig. 1, upper left, in the photo quiz) and even four (see Fig. 1, darts, in the photo quiz) ring forms in a single RBC. However, despite polyinfection, several features taken together supported the diagnosis of *Plasmodium falciparum* infection. First, rings were mostly uniform in size and shape, in contrast to the pleomorphic ring forms more generally seen in *Babesia*. Second, large numbers of marginal rings (so-called appliqué/accolé forms) (see Fig. 1, long arrow, in the photo quiz) and rings with two chromatin dots (headphones) (see Fig. 1, short arrow, in the photo quiz), features of *P. falciparum*, were common. Third, extracellular ring forms, found not infrequently in *Babesia* infection, were absent. Finally, the Binax-NOW malaria antigen test (Alere Scarborough, Inc., Scarborough, ME) was *P. falciparum* positive. Presumably, this patient's very high parasitemia favored multiple infection of RBC and led to the highly uncharacteristic degree of polyinfection.

Of note, our patient was at particular risk for a complicated clinical course based on HIV-associated immunosuppression. Indeed, based on his high parasitemia alone, he met criteria for severe malaria (2). Severe *P. falciparum* infection is a medical emergency associated with significant mortality. The benefit of RBC exchange transfusion as an adjunctive therapy in severe malaria remains controversial, as the major organism disease burden lies trapped within capillary beds and therefore is not removable by exchange. A retrospective analysis in 2013 by the Centers for Disease Control and Prevention found no clear benefit for this therapeutic modality (3). However, the American Society for Apheresis continues to designate RBC exchange a category II indication (second-line therapy) with an 2B evidence grade (weak recommendation, moderate evidence) for high-level parasitemia (4). Notably, the parasite burden in our patient rapidly cleared with a combination of doxycycline-quinidine pharmacological therapy and apheresis-based exchange transfusion.

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See page 351 in this issue (<https://doi.org/10.1128/JCM.00193-15>) for photo quiz case presentation.

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