Tafenoquine: Treatment for relapsing Babesia

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A 36-year-old man was hospitalized in 2019 due to unexplained fevers he had been having for two weeks. He was later diagnosed with *Babesia* with 8.5% of his blood showing the parasite.

He had been diagnosed with granulomatosis with polyangiitis in 2001 and was considered immunocompromised related to treatment 2 years earlier with rituximab, a monoclonal antibody used for immunotherapy. The man had also been treated with methotrexate, cyclophosphamide and steroids.

The man's initial treatment for Babesia included atovaquone and azithromycin for 10 days. The atovaquone was 750 mg once daily instead of twice daily. Two months later he relapsed. His blood smear was again positive. He was treated with azithromycin plus atovaquone for 12 weeks with clearing of the parasite.

Two months later he had his second relapse. Atovaquone plus azithromycin were again prescribed for an additional 45 days. Clindamycin was added for two weeks because of a persistent positive blood smear for *Babesia*.

Two months later he had a third relapse. "A blood sample was tested for genetic evidence of drug resistance to either azithromycin or atovaquone, and at least partial resistance to both azithromycin and atovaquone was found, although this was not known until August 2020," the authors wrote.

Babesia treatment: 4 drug combination

The doctors then switched treatment to include a four drug combination. "Therefore, on 1/29/20 the patient was started on a malarone®-based 4 drug regimen that included high dose azithromycin at 1000 mg per day, plus clindamycin orally at 450 mg three times per day, plus a 750 mg dose of atovaquone (in addition to the 1000 mg/day of atovaquone received as part of the malarone® drug therapy) for 41 days," according to the authors. Tafenoquine is marketed under the name Krintafel in the US.

The patient, however, remained ill and was started on a 6-week regimen of tafenoquine alone.

"Tafenoquine is an 8-aminoquinoline primaquine analogue that received United States Food and Drug Administration approval in 2018 for two indications: prophylaxis of malaria for up to 6 months in total duration and prevention of relapse of Plasmodium vivax malaria," the authors wrote. *Note: In animal models, tafenoquin was able to rapidly clear Babesia microti parasites.*

It was determined that the patient did not have a psychiatric history, a glucose-6-phosphate dehydrogenase deficiency, or QT interval changes before prescribing tafenoquine.

The patient responded well to the Babesia treatment. However, investigators were not able to determine if

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the success was from tafenoquine or the weeks of therapy leading up to tafenoquine.

"Experimental data from 3 different studies conducted using hamsters or mice, including highly immunocompromised mice (severe combined immunodeficiency [SCID] mice) have demonstrated that tafenoquine can rapidly clear *Babesia microti* parasites."

They concluded, "Therefore, this single drug regimen may be of potential clinical importance, especially for treating highly immunocompromised patients with babesiosis, who require a minimum of at least 6 weeks of treatment, often extending into many months."

<u>Editor's note:</u> The authors did not address the possibility that the patient might have *Babesia duncani*, which was originally identified on the West Coast of the U.S. but is now found in the East, as well. *Babesia duncani* has at times been difficult to treat.

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References:

1. Marcos LA, Leung A, Kirkman L, Wormser GP. Use of tafenoquine to treat a patient with relapsing babesiosis with clinical and molecular evidence of resistance to azithromycin and atovaquone. IDCases. 2022;27:e01460. doi:10.1016/j.idcr.2022.e01460

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