

CORRESPONDENCE



Reduction of *Loa loa* Microfilaremia with Imatinib — A Case Report

TO THE EDITOR: Efforts to eradicate lymphatic filariasis and onchocerciasis (“river blindness”) through mass drug administration have been hindered in Central Africa in areas where *Loa loa* is coendemic, because patients with very high levels of *L. loa* microfilariae in the blood are at risk for serious adverse events (including encephalopathy and death) after the administration of ivermectin-based therapy.¹ The pathogenesis of these serious adverse events after ivermectin treatment (or after diethylcarbamazine treatment) is believed to involve an inflammatory response to the massive release of parasite antigens that occurs with the rapid death of *L. loa* microfilariae.² Recently, elimination efforts have begun to focus on screening potential recipients of ivermectin and excluding from drug treatment those who have high levels of *L. loa* microfilariae to avoid these adverse effects — a strategy that is termed “test and not treat.”³ We have previously reported in the *L. loa* genome the presence of a homologue of the human c-Abl tyrosine kinase.⁴ The inhibition of this *L. loa* c-Abl-like tyrosine kinase with imatinib led to the slow death of microfilariae in vitro,⁴ probably because imatinib targets the tyrosine kinase expression in the nuclei of the microfilariae.⁵

We report a case of *L. loa* infection in a 29-year-old woman who presented with eyeworm, limb angioedema (Calabar swelling), rashes, and pruritus after she had traveled to the Democratic Republic of Congo and Central African Republic. She was referred for treatment under an institutional review board–approved protocol and was found to have an *L. loa* microfilarial level of 2250 microfilariae (mf) per milliliter. After the patient was administered a single 600-mg

dose of imatinib, repeated concentrated peripheral blood smears showed a slow decline in microfilarial levels to a nadir of 150 mf per milliliter over a 6-day period (Fig. 1). Aside from a mild, transient headache that occurred after imatinib administration, the patient reported no new symptoms but noted a decrease in pruritus over the ensuing days. A blood smear obtained on day 11 showed that the microfilarial level had started to increase again (392 mf per milliliter), and she was given definitive treatment for *L. loa* infection with diethylcarbamazine.

A previous study showed that a single dose of diethylcarbamazine cleared microfilariae from the bloodstream within 24 hours and ivermectin resulted in a 1- \log_{10} decrease in the microfilariae count within the first 1 to 3 days after treatment.² The current case suggests that it may be possible to lower *L. loa* microfilarial levels in the blood safely and slowly with a single oral dose of imatinib so that definitive diethylcarbamazine treat-

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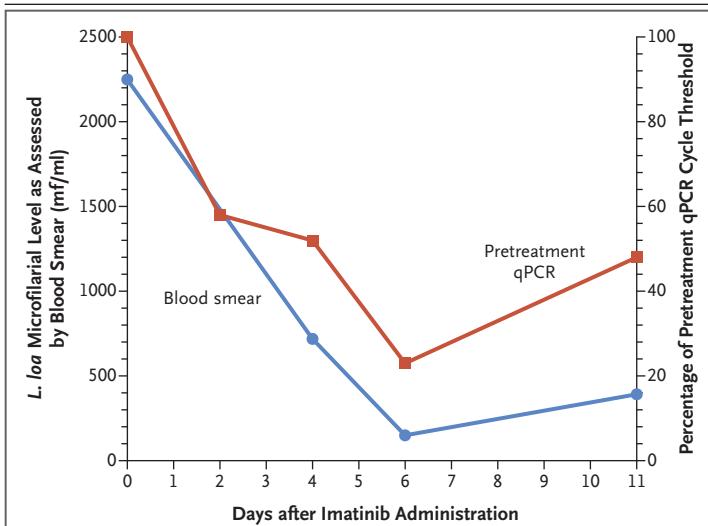


Figure 1. Microfilarial Response to a 600-mg Dose of Imatinib in a Patient with *Loa loa* Infection.

Loa loa counts are expressed as absolute microfilariae (mf) per milliliter and percentage of the pretreatment quantitative polymerase chain reaction (qPCR) cycle threshold. Day 0 represents the pretreatment microfilarial level in the blood (2250 mf per milliliter; 100% of the pretreatment qPCR cycle threshold of 26.5) in a patient with *L. loa* infection. Day 1 was the first day after the patient received treatment with imatinib. By day 4, a 1-log_{10} decrease in microfilarial level still had not occurred (719 mf per milliliter). The nadir microfilarial level (150 mf per milliliter) was attained on day 6, before the level started to rise again (392 mf per milliliter on day 11).

ment or ivermectin treatment as part of a mass administration program can be given to persons with previously unsafe levels of *L. loa* micro-

filariae. A larger prospective trial is planned (ClinicalTrials.gov number, NCT02644525) so that more definitive conclusions can be drawn regarding the use of imatinib in the treatment of *L. loa* infection. This case report serves as a proof of concept to further these efforts.

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Intensive Blood-Pressure Treatment and Patient-Reported Outcomes

TO THE EDITOR: Berlowitz et al. (Aug. 24 issue)¹ reported scores on the Patient Health Questionnaire 9-item depression scale (PHQ-9) and the Veterans RAND 12-Item Health Survey (VR-12) that were similar between patients who received standard blood-pressure treatment and those who received intensive blood-pressure treatment, although they found significant differences in clinical outcomes.² These findings could be due to poor sensitivity of the patient-reported outcome instruments used. In their trial, summary scoring was used in a population with a considerable ceiling effect for satisfaction with blood-

pressure care, satisfaction with medication, and PHQ-9 and VR-12 scores at baseline.¹ The ceiling effect further exacerbates the noise level in the measurement of patient-reported outcomes.

The sensitivity of an instrument for the measurement of patient-reported outcomes is lowest when summary scoring — the simple addition of ordinal values representing response categories — is used. Summary scoring assumes that response categories are equidistant from one another on a scale and that all items have the same worth. Item-response theory proves that neither assumption is valid. Therefore, these as-