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The Brief Case: *Loa loa* in a Patient from Nigeria

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CASE

An 18-year-old college student sought medical attention because she felt something moving in the sclera of her right eye and observed a worm when she looked in the mirror (Fig. 1A). She had similar symptoms 2 years ago but ignored it at that time because symptoms abated after about 2 h. Currently, she presented with painless swelling at the base of her right thumb and the dorsum of her right hand that lasted for a few days at a time and had waxed and waned over the past year. No contacts or family members had similar symptoms. She was born and raised in a large city in Nigeria but went to boarding school in a more rural area. She had traveled to the southeast region of Nigeria on vacation with her family shortly before moving to the United States 3 years ago to attend college. She had not returned to Nigeria since.

On physical exam, her sclera was clear and there was no evidence of a worm, but the clinical presentation, personal photos of the subconjunctival parasite, and history of residence in an area of endemicity prompted sending a specimen which was coincidentally collected at 13:32 for blood parasite examination. No organisms were seen on thin smear, but microfilariae were seen in a Giemsa-stained thick smear (Fig. 1B to D). The microfilariae were identified as *Loa loa* based on the size (average, 245 μm), presence of a short headspace, a dense nuclear column with the nuclei extending to the tip of the tail, and appropriate epidemiologic history. The microfilarial load was determined to be very low at 30 microfilariae/ml. Microfilarial loads are determined by calculating the number of microfilariae per milliliter using a measured quantity of blood (1). To obtain the microfilarial load, we prepared Giemsa-stained blood smears using 25 μl of EDTA-preserved blood for each smear. Our patient had 3 microfilariae in 4 smears, which equates to 30 microfilariae/ml. Serology to detect human IgG and IgG4 antibodies to *Onchocerca volvulus*-specific antigen Ov16 performed by the Laboratory of Parasitic Diseases, National Institutes of Health, Bethesda, MD, was negative. Our patient was treated with diethylcarbamazine (DEC) (9 mg/kg/day or 3 mg/kg of body weight every 8 h [q8h]) for 21 days, and her symptoms resolved.

DISCUSSION

Loa loa, commonly called the African eye worm, is a filarial parasite endemic to West-Central Africa south of the Sahara (2). As with all filarial nematodes, *L. loa* has a complex life cycle involving a vertebrate definitive host and an arthropod vector and intermediate host. *Loa loa* is transmitted by deer flies in the genus *Chrysops*, primarily *C. silaceus* and *C. dimidiata* (3). These *Chrysops* species are not found in the United States. Deer flies deposit L3 larvae at the bite site when taking a blood meal, and the larvae penetrate the wound. The L3 larvae molt twice to become adults in the subcutaneous tissues; occasionally, adult worms will migrate to the eye. Mated female worms release microfilariae which circulate in the blood during the day (diurnal

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For answers to the self-assessment questions and take-home points, see https://doi.org/10.1128/JCM.01589-20 in this issue.

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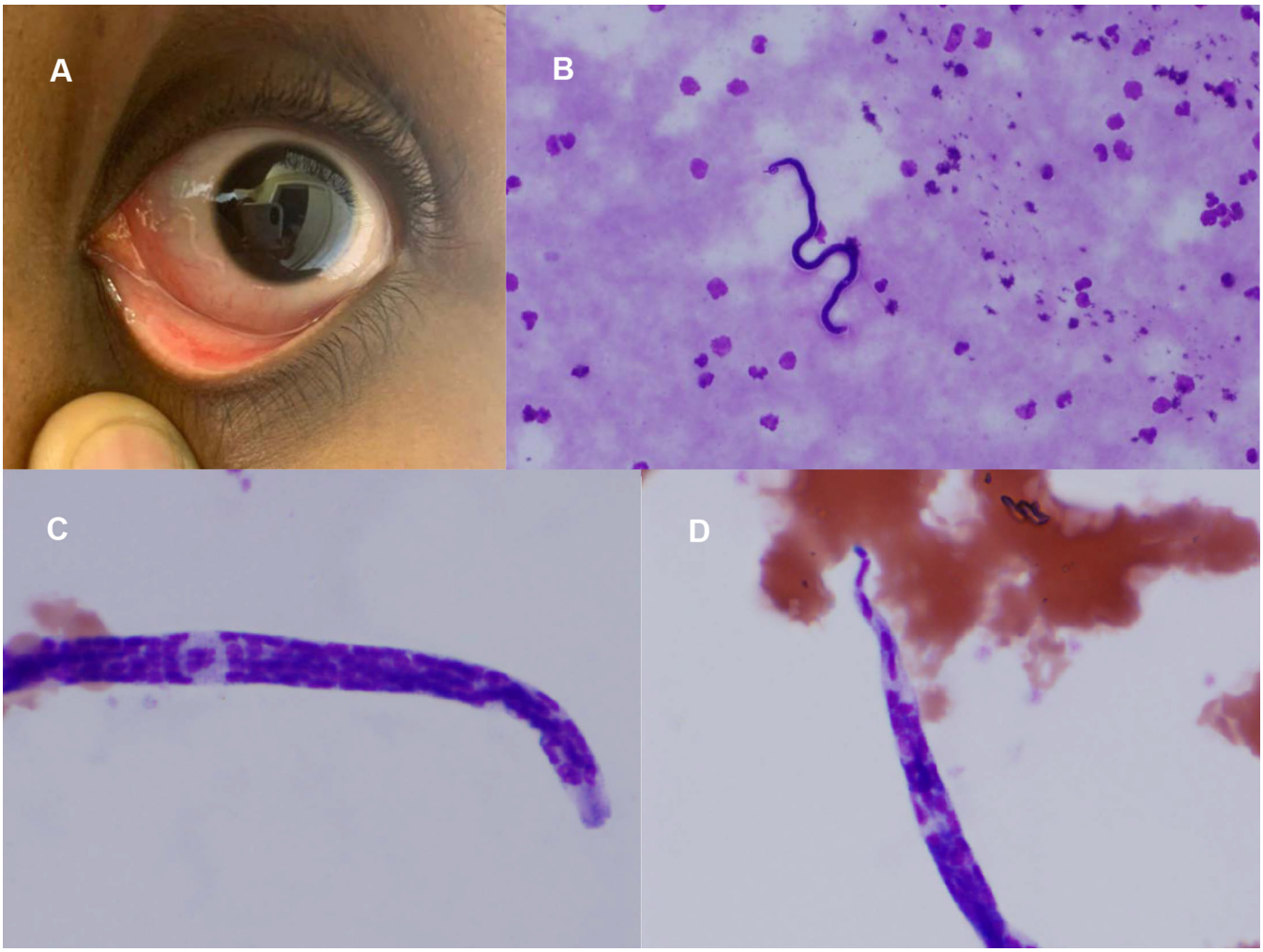

FIG 1 (A) Adult *Loa loa* subconjunctival worm in patient's right eye. (B) Microfilaria in Giemsa-stained thick blood smear (original magnification, ×10). (C) Anterior end of microfilaria showing short headspace and nuclei that are coarse and densely packed throughout the length of the worm. A sheath is not present (original magnification, ×40). (D) Tapered tail with nuclei extending to the tip (original magnification, ×40).

periodicity); the optimal time for blood collection is between 10:00 and 14:00 (https://www.cdc.gov/dpdx/loiasis/index.html).

Loa loa is primarily diagnosed by the finding of microfilariae in thick and thin blood films stained with Giemsa, Wright, Wright-Giemsa, or hematoxylin stains. The microfilariae measure 231 to 250 μm long on stained blood films and possess a sheath that usually does not stain with Giemsa. Also, the sheath may be shed and not visible if there is a delay in processing the blood. Microfilariae of *L. loa* have a dense nuclear column with a short headspace and tail extending irregularly to the tip (2). Distinguishing characteristics of microfilariae affecting humans are presented in Table 1. *Loa loa* may also be diagnosed by the gross examination of adult worms removed from the eye or in histopathologic examination of skin biopsy specimens. In both instances, the adults need to be differentiated from zoonotic filarids in the genus *Dirofilaria* (2, 4). The adults of both worms are similar in size and macroscopic appearance. A distinguishing difference is that the adult *Loa loa* has small irregularly spaced bumps (bosses) on the surface of the cuticle, while the adult *Dirofilaria* has a thick cuticle with multiple longitudinal ridges (4). *Dirofilaria* microfilariae are rarely seen in human blood and are unsheathed, and nuclei do not extend to the tip of the tail.

Most patients with loiasis are asymptomatic. The classic clinical manifestation is the formation of Calabar swellings, which are transient subcutaneous nodules created by

TABLE 1 Characteristics of microfilariae affecting humans[a]

Pathogen	Geographic distribution	Vector	Periodicity	Adult worm site of Infection	Clinical syndromes	Specimen	Microfilariae identifying characteristics		
							Sheath	Length (μm)	Nuclear column
Loa loa	Forested areas of Central and West Africa	*Tabanidae* (deer fly)	Diurnal	Subcutaneous tissues, ectopic migration to the eye	Skin swellings, allergic reactions, subconjunctival migration	Blood	+ (usually not stained using Giemsa)	231–250	Short headspace, dense nuclear column, continuous to tip of tail
Wuchereria bancrofti	Tropics and subtropics worldwide (Asia, Pacific, Africa, Americas)	*Culicidae* (mosquito)	Nocturnal, subperiodic	Lymphatic vessels and lymph nodes	Lymphangitis, fever, elephantiasis, hydrocoele, chyluria	Blood	+ (usually not stained using Giemsa)	244–296	Short headspace, loose nuclear column, no nuclei in tip of tail
Brugia malayi	Southeast Asia	*Culicidae* (mosquito)	Nocturnal, subperiodic	Lymphatic vessels and lymph nodes	Lymphangitis, fever, elephantiasis	Blood	+ (usually stains bright pink using Giemsa)	177–230	Long headspace, terminal and subterminal nuclei in tip of tail with large gap between
Brugia timori	Indonesia (Lesser Sunda Islands)	*Culicidae* (mosquito)	Nocturnal	Lymphatic vessels and lymph nodes	Acute fever, chronic lymphedema	Blood	+ (usually not stained using Giemsa)	290–325	Long headspace, terminal and subterminal nuclei in tip of tail with large gap in between
Mansonella perstans	Central and northern Africa, Central and South Americas, Caribbean	*Culicoides* (biting midge)	None	Peritoneal and pleural cavity	Angioedema, urticaria, pruritis	Blood	−	190–200	Compact, continuous to tip of tail; tail blunt
Mansonella ozzardi	Central and South Americas, some Caribbean islands	*Culicoides* (biting midge); *Simulium* (black fly)	None	Peritoneal cavity	Most are asymptomatic, but lymphadenopathy, urticarial, pruritis, and pulmonary symptoms have been described	Blood	−	163–203	Compact, no nuclei in tip of tail; tail tapered and pointed
Mansonella streptocerca	Central Africa	*Culicoides* (biting midge)	None	Subcutaneous tissue	Many are asymptomatic, but some develop inguinal lymphadenopathy and chronic dermatitis with pruritis	Skin snips	−	180–240	Single row to tip of tail; tail hooked
Onchocerca volvulus	Africa, Yemen, Central and South Americas	*Simulium* (black fly)	None	Subcutaneous tissue	Skin nodule, ocular complications (blindness)	Skin snips	−	304–315	No nuclei in tip of tail; tail tapered and often flexed

[a]Adapted from reference 2.

migrating adult worms. Calabar swellings can occur anywhere on the body but are most common on the trunk and arms. Occasionally, adult worms will migrate to the eye and can be observed grossly in the conjunctiva (5).

Diethylcarbamazine is the treatment of choice and is known to be effective at eradicating both microfilariae and adult worms but must be used with caution (6). There is significant risk of fatal encephalopathy in patients treated with DEC if the microfilarial load is high (>8,000 microfilariae per ml) in peripheral blood. (https://www.cdc.gov/parasites/loiasis/health_professionals/index.html#tx). As such, the microfilarial load should be calculated per milliliter. In patients with high microfilarial load, ivermectin can be used as initial treatment to reduce the microfilarial burden prior to treatment with diethylcarbamazine (6, 7). It is also important to rule out concomitant onchocerciasis, since DEC can cause blindness due to severe inflammation in patients who are coinfected. The incidence of coinfection is not well documented but was determined to be 15.3% of the individuals consenting for a study conducted in an area of central Cameroon known to be coendemic for loiasis and onchocerciasis (8). A similar study conducted in rain forest villages in southern Cameroon found an overall coinfection rate of only 5.57%; however, of individuals infected with *Loa loa*, 64.81% were also found to carry *O. volvulus* (9). A geographical information system mapping of the Bas Congo Province in the Democratic Republic of the Congo showed that areas where both onchocerciasis and loiasis prevalences were >20% were also associated with severe adverse events associated with mass distribution of ivermectin as part of national programs to control onchocerciasis (10). Exposure to *O. volvulus* is best determined using a serology assay that detects antibody of the IgG4 subtype against the Ov16 antigen (11). The Ov16 antigen is present in all stages of the *Onchocerca* life cycle, and IgG4 subtype response is considered the most specific (11). Assays of this nature are reported to have a sensitivity of 96% and specificity of 96% (11). Testing is available from the National Institutes of Health using an IgG4 anti-Ov16 assay with a normal range determined by values obtained from a large group of unexposed North American individuals. Because loiasis is rarely reported in the United States, DEC is no longer approved by the Food and Drug Administration and is not commercially available. Physicians can obtain the medication from the Centers for Disease Control and Prevention Drug Service for patients who meet eligibility criteria in the investigational new drug protocol. Albendazole has been useful in treating loiasis that does not respond to diethylcarbamazine. It slowly reduces microfilarial levels by its action on adult worms, and the risk of adverse reaction is low compared to that with diethylcarbamazine and ivermectin. However, a longer duration of treatment is required, and it does not sufficiently reduce high microfilarial levels to allow safe therapy with diethylcarbamazine in most cases (12).

SELF-ASSESSMENT QUESTIONS

1. What is the vector for transmission of the *Loa loa* parasite?
   a. Mosquitoes
   b. Biting midges
   c. Black flies
   d. Deer flies

2. *Loa loa* exhibits diurnal periodicity. What is the optimum time for blood collection?
   a. 10:00 to 14:00
   b. Any time
   c. 22:00 to 02:00
   d. 12:00 to 18:00

3. Which of the following morphologic features is consistent with *Loa loa* microfilariae?
   a. Less than 200 μm in length

b. Nuclei extend irregularly to the tip of the tail
c. Sheath usually stains bright pink with Giemsa
d. Long headspace

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