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Short Communications

Loiasis in a Japanese Traveler Returning from Central Africa

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Abstract: We encountered a probable case of loiasis in a returned traveler from Central Africa. A 52-year-old Japanese woman presented to our hospital complaining of discomfort in her eyes and skin. She reported having frequently visited Central Africa over many years and having been extensively exposed to the rainforest climate and ecosystem. Although no microfilariae were found in her blood, there was an elevated level of IgG antibodies against the crude antigens of *Brugia pahangi*, which have cross-reactivity with *Loa loa*. She was treated with albendazole for 21 days, after which the antigen-specific IgG level decreased and no relapse occurred.
Key words: filarial infection, loiasis, returned traveler

Introduction

Loiasis is a filarial infection endemic to Africa, particularly Central and West Africa [1]. Loiasis is transmitted though bites of deer flies or mango flies (*Chrysops*). Although the infection is most frequently seen in indigenous people living in the forest areas, there have been several imported cases in non-endemic countries due to increasing travel and migration of people to and from endemic regions [2]. The number of Japanese travelers visiting Africa exceeded 130,000 in 2012 [3]; however, reports of loiasis among travelers returning from Africa have been extremely limited [4]. It is important to have information pertaining to the appropriate diagnosis and management of loiasis in order to provide proper management and treatment of future suspected cases. We present a case of a returned traveler from Central Africa with suspected loiasis due to filaria-specific antibodies and clinical symptoms.

Case Report

A 52-year-old previously healthy Japanese woman presented to our hospital complaining of discomfort in her eyes and skin. Her medical history included malaria (5 years prior), and myiasis (5 weeks prior). She reported frequent visits to Africa, including trips within the last year to Gabon, Cameroon, Central African Republic, Malawi, and Democratic Republic of the Congo, the latest as recently as 7 weeks prior to her hospital visit. She spent several weeks in each visit. During her travel, she spent most of her time in a camping tent in rain forests in national parks. She had a pre-travel consultation and received appropriate vaccinations including tetanus toxoid booster, hepatitis A and B, rabies, and yellow fever.

Two weeks prior to the visit to our clinic, she noticed two localized nodules associated with redness and pruritus on the surface of her left forearm and upper arm. She could feel the nodules moving underneath her skin, but they disappeared the next day. They reappeared every 6–7 days, often on her left cheek or frontal chest, each time lasting for about a day at a time. One week prior to the visit to our clinic, the skin lesion reappeared for the third time on her left cheek, and it was then that she presented to our hospital. She also complained of discomfort in her eyes that had begun that morning.

Upon initial examination at the outpatient clinic, her

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physical examination was unremarkable except for a few reddish papules on the back of her neck, which our dermatologist determined to be a scar left by the removal of larvae during treatment the patient received for myiasis in Africa. Her blood test showed no abnormalities, and the eosinophil count was within the normal range. Although smeared samples of her blood taken at noon revealed no microfilaria, there was a slight elevation of IgG against filarial antigen (*Brugia pahangi* female crude antigens), compared to that of healthy individuals (Fig. 1). The serum was sent for screening for antibodies against the following parasites (SRL, Tokyo, Japan), which turned out to be negative: *Dirofilaria immitis*, *Toxocara canis*, *Ascaris suum*, *Anisakis* larvae, *Gnathostoma* spp., *Strongyloides stercoralis*, *Paragonimus westermani*, *Paragonimus miyazaki*, *Clonorchis sinensis*, *Fasciola hepatica*, *Cysticercus cellulosae*, and *Spirometra erinaceieuropaei*.

Two weeks after her initial visit to the outpatient clinic, the patient was admitted to our hospital for treatment of suspected loiasis. On admission, her left eyelid was swollen and found to be edematous. Her eye was reddened but no larval body was found upon examination. Treatment with albendazole (200 mg PO) twice daily was initiated upon admission. The eosinophil count remained between 3 and 5%, with white blood cell counts within the normal range throughout the course. The patient noticed linear erythematous cutaneous trail above her right knee on day 3 of albendazole treatment, which spontaneously disappeared within several hours. On day 5 of treatment, she noticed erythematous swelling over the dorsal surface of her left hand (Fig. 2), which disappeared in a few hours. On day 6 of treatment, her left arm became swollen (Fig. 3). The swelling gradually disappeared in 1 week, without any sequelae. She was discharged from our hospital on the 10th day of treatment, and oral administration of albendazole was continued at the outpatient clinic for a total of 21 days. No signs of relapse were observed at the time of follow-up, 5 months after the last day of oral treatment. The anti-filarial IgG antibody levels did not show change until day 3 of the albendazole treatment, but doubled on day 13, peaked on day 21, and decreased thereafter (Fig. 4). She received follow-up care at the outpatient clinic for 10 months after initial presentation, and no signs of relapse were observed.

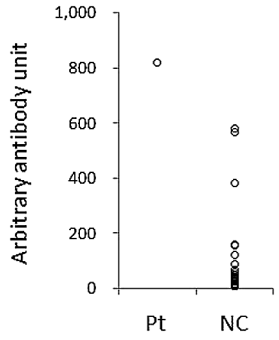

Fig. 1. Levels of IgG to *B. pahangi*. The patient's IgG level was higher than those of negative controls (n = 28). NC = negative controls; Pt = patient before treatment.

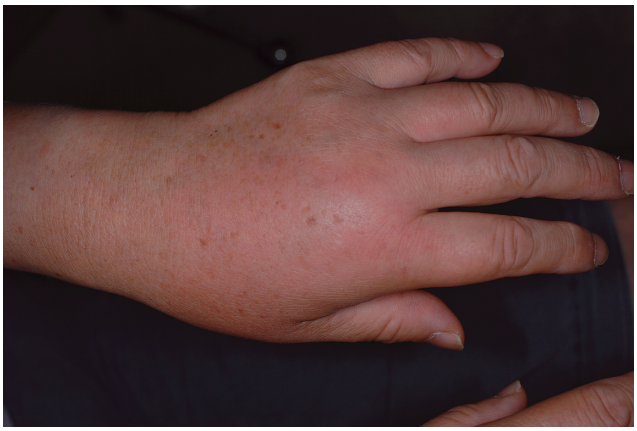

Fig. 2. Erythematous swelling over the dorsal surface of the left hand (Calabar swellings)

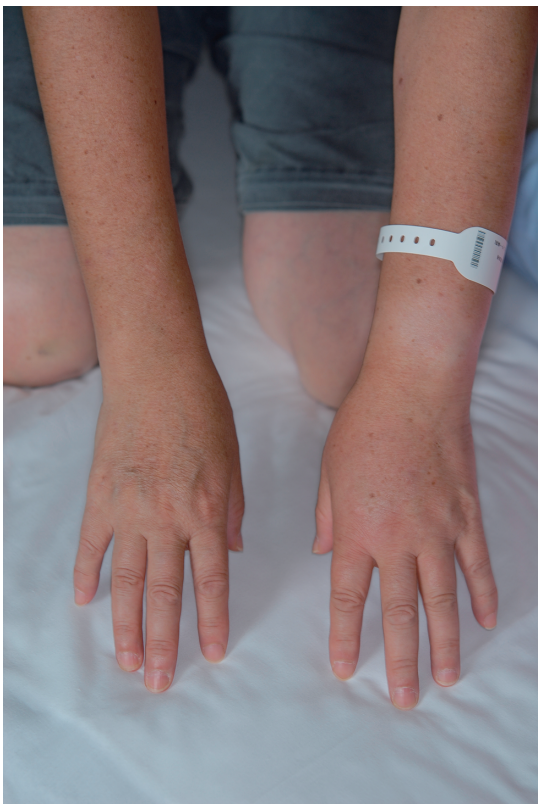

Fig. 3. Swelling of the left arm

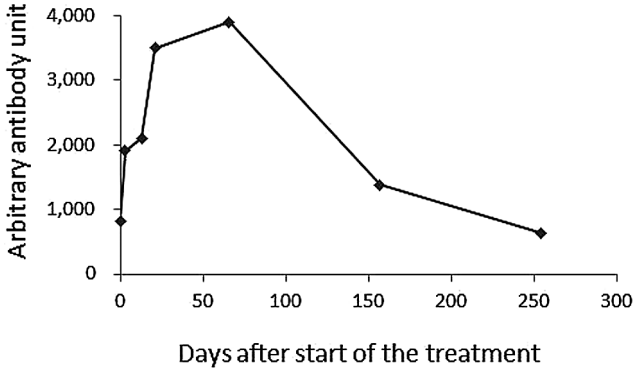

Fig. 4. Changes in anti-*B. pahangi* IgG levels after albendazole treatment. The anti-*B. pahangi* IgG level of the patient increased during albendazole treatment, showing a 2-fold increase after 13 days and a 4-fold increase after 21 days. Anti-*B. pahangi* IgG level decreased thereafter.

Discussion

Loiasis is a relatively rare disease seen in patients with previous histories of travel to endemic areas in Central Africa. Although a definitive diagnosis can be made by identifying the presence of a migrating adult worm in the subcutaneous tissue or eye, or by detecting microfilaria in a blood smear, these typical findings are not always present. A serologic test for anti-filarial IgG4 antibodies facilitates the diagnosis, as do the patient's signs and symptoms, which are consistent with loiasis [4].

In this case, the patient exhibited Calabar swellings typical of loiasis, which comprise episodic angioedema potentially due to hypersensitive reactions to migrating adult parasites and/or microfilaria [5]. We did not observe any other clinical manifestations of loiasis such as eosinophilia, peripheral blood microfilariae, and eye worm migration, which have been previously reported to occur in 82.1%, 61.4%, and 53.5% of described cases, respectively [2]. Furthermore, the filaria-specific IgG4 test was negative in this patient. However, amicrofilaremic loiasis is a common occurrence, as microfilariae were previously reported to be absent in 1 of 3 cases of loiasis in people indigenous to the endemic area [6]. In another previously reported case, a traveler in Japan who had returned from Cameroon was also amicrofilaremic and was only diagnosed through the identification of increased anti-filarial IgG4 antibodies [4].

There have been reported cases of amicrofilaremic loiasis with concomitant increases in the IgG4 titer [4, 7], a highly specific indicator of loiasis [8]. Although the filaria-specific IgG4 test in this case was negative, we reached a final diagnosis of loiasis based on a positive anti-*B. pahangi* IgG level that dramatically increased over the 3-week clinical course, in addition to the patient's history of frequent travel to endemic regions and symptoms suggestive of loiasis [2]. These signs disappeared after completion of a 3-week therapy course, indicating along with the clinical course before treatment that *L. loa* was the causal pathogen.

We treated the patient for suspected loiasis because of the adverse outcomes that might have appeared without treatment, such as encephalitis, neurological disorders and, less frequently, endomyocardial fibrosis and renal failure [9–11]. Several available drugs have described for the treatment of loiasis, including diethylcarbamazine, ivermectin, and albendazole. In general, diethylcarbamazine is recommended for the treatment of loiasis based on its activity against both microfilariae and adult worms [10, 12]. However, adverse events have been reported following diethylcarbamazine treatment as a result of rapid microfilariae killing, especially in patients with high microfilariae burdens [10]. As the patient in the present case did not show evidence of microfilaremia, diethylcarbamazine was a potential treatment option. However, we decided to treat the patient with albendazole, which does not have significant microfilaricidal activity, because fewer adverse effects were expected and it would be possible to follow up clinically with the patient if albendazole treatment was insufficiently effective. The skin reactions (e.g., erythematous changes, swelling) that appeared after initiating albendazole treatment were thought to be Calabar swellings due to immune reactions to degenerated worms.

Limitations of this report include the lack of observed eye worm migration and peripheral blood microfilariae in this patient, although these findings have not been reported in all patients with loiasis. Additionally, the anti-filarial IgG antibody used in this study is not specific for loiasis, as it cannot differentiate loiasis from other filarial nematode infections; furthermore, the anti-filarial IgG4 antibody test was negative. A polymerase chain reaction (PCR) analysis based on sequences of the repeat 3 region (15r3) of the gene encoding the *L. loa* 15-kD protein was developed and reported to have a loiasis detection sensitivity rate of 95% [13]. In this study, however, PCR was not available. Therefore, even though the clinical course and changes in the anti-filarial IgG antibody titer strongly suggested a diagnosis of loiasis, the evidence to support this diagnosis in the current case is incomplete.

The case reported herein should be considered a probable case of loiasis. Patients with loiasis, notably non-African travelers and expatriates, might present clinically with isolated migratory edema. In this context, such cases are probable cases with diagnoses suspected on the basis of

a clear history of Calabar swellings following a stay in an endemic area, positive serology assay results, and treatment efficacy, but are not confirmed definitely via microfilariae detection in the blood using a concentration method along with additional smears performed near midday or PCR assays. Eosinophilia may be lacking in such cases [14–16].

Given the diagnosis of probable loiasis according to circumstantial evidence and an elevated anti-*B. pahangi* IgG titer, it remains possible that *Onchocerca volvulus*, another type of microfilaria, was the causal pathogen in this patient. Onchocercosis is widely distributed throughout sub-Saharan Africa and overlaps the endemic area of loiasis. We evaluated this patient as more likely to be afflicted with loiasis than onchocerciasis because she did not exhibit typical onchocercomata over typical body sites, such as bony prominences including the pelvic girdle, or onchocercal skin disease [17, 18]. In addition, in the African forest areas where the patient stayed, ocular lesions are rare and usually involve the posterior eye segment, which did not correspond with the patient's eye symptoms [19]. Furthermore, the appearance of Calabar swelling after treatment has previously been documented in cases of loiasis [20].

However, cases of loiasis with *O. volvulus* co-infection have been reported [21]. As we could not perform a skin snip test to detect *O. volvulus* microfilariae, the possibility of onchocercosis in this case cannot be denied.

It is important to advise anyone traveling to loiasis-endemic areas to avoid insect bites, especially from deer flies, by wearing long-sleeved clothing and using insect repellant. In addition, a prophylactic regimen of diethylcarbamazine (300 mg weekly) may be proposed for high-risk patients [22].

In conclusion, we encountered a rare case of loiasis in a returned traveler from Central Africa; this patient was amicrofilaremic but was successfully diagnosed based on anti-*B. pahangi* IgG antibody seropositivity and treated accordingly.

Conflicts of Interest

The authors state that they have no Conflict of Interest (COI).

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