A Case of Loaisis

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The prevalence of Loa loa infections in non-endemic areas such as Korea is very low, even though it is quite common in the endemic regions of West and Central Africa. We describe a patient who presented with temporary localized edema (classical Calabar swellings) after travelling to Cameroon and in whom the diagnosis of loiasis was made by ELISA. This is the second reported case of loiasis in Korea. As international travel is becoming more frequent, Loa loa infection should be considered in the differential diagnosis for patients with eosinophilia and Calabar swellings in Korea.

Key Words: Loiasis, calabar swellings, eosinophilia

The prevalence of Loa loa infections in the endemic regions of West and Central Africa is high. Infection is most commonly seen in residents of endemicity where more than 20% of the residents are microfilaremic and probably more than twice as many have amicrofilaremic infections (Fain, 1981). Also, the risk of infection to temporary residents is considerable (Nutman et al. 1988). With the increased frequency of travel, infection in expatriates is becoming more common.

Infections in humans are associated with two common clinical manifestations—Calabar swellings and African eyeworm. Calabar swellings are areas of angioedema associated with the migration of adult worms through the subcutaneous tissues and they are often found at the extremities, especially around joints (Duke, 1991). Patients who complain of seeing worms migrate through the eye are said to have African eyeworm.

Since the first report of suspected loiasis in Korea in 1987 (Min et al. 1987), there have been no further cases. We report a case of loiasis occurring in a male patient who travelled to Cameroon and in whom the diagnosis was made by the typical Calabar swellings and ELISA.

CASE REPORT

A 37-year-old man presented with a 5-day duration of right arm swelling on March 31, 1997. He was a producer working for the Korean Broadcasting System and had stayed in Cameroon in Central Africa from October 20 to November 11, 1996 to prepare a documentary film on the life of a Pigmy tribe. After returning to Korea on November 13, 1996, he developed insect-bite-like lesions on his whole body with severe itching. He was treated at a private clinic with antihistamines and topical steroids, but without any remarkable effects. The lesions disappeared after two weeks in late November 1996, but the itching persisted for three months until
February 1997. Then he developed urticarial wheal-like lesions, especially at night. Concomitantly, he developed acute hepatitis with jaundice and was admitted to another hospital. His liver enzymes, SGOT and SGPT, were elevated to more than 1000 IU/ml at that time, but HBsAg was negative. After being admitted for one week, he was discharged and 2 weeks later on March 1997, he developed swelling of the right arm and hand (Fig. 1). There was no itching sensation or tenderness of the affected area but he had difficulty in moving and grasping due to swelling of the hand. Physical examination revealed a somewhat hard, ill-defined erythema of the right lower arm. The patient complained that the swelling waxed and waned and also that it sometimes occurred on the other hand and both lower legs. Furthermore, he recalled having intermittent fever, chilling, and arthralgia. Under the impression of an endemic African disease, probably African sleeping sickness, we performed various blood tests and a skin biopsy. The patient had blood eosinophilia (29%) with an eosinophil count of 2640/μL, but other blood tests including complete blood counts, liver function tests, renal function tests, HBsAg, HBs antibody, T and B cell count, and urinalysis were all normal or within normal limits. Skin biopsy of the erythematous swelling showed focal degeneration of collagen with many eosinophils in the dermis. Stool examination showed eggs of Clonorchis sinensis and he was treated with praziquantel for two weeks, but follow-up tests still showed eosinophilia (37.6%) with 5430/μL. We tried 3 times to detect microfilaria in the blood by the Knott procedure (Gillespie and Hawkey, 1995) but were unsuccessful. As we lacked the technology to perform a diagnostic assay, we sent three samples of the patient’s blood to Dr. Tom Moore, who is a specialist in the field of filariasis at the National Institute of Allergy and Infectious Diseases (NIAID) at the National Institute of Health (NIH) in the United States. All three samples showed a positive reaction to loiasis by ELISA with the level of antibodies greater than 380.5 μg/ml (normal value is less than 13.5 μg/ml). Consequently, we looked for an appropriate medication but all the diethylcarbamazine (DEC), reported to be effective in loiasis, available in Korea was past the expiration date. Therefore, the patient volunteered to go to France to receive Mectizan (Ivermectin), a new drug. He took two tablets (12 mg) of Ivermectin once on the first day and the swelling promptly started to disappear. However, after 7 days, an ill-defined swelling of the wrist recurred and 1 month later he was given a second dose of Ivermectin and a blood test showed the eosinophil count was down to 5.7%. One year later, the patient has not yet shown any evidence of recurrence.

**DISCUSSION**

Human filariasis due to *Loa loa* is endemic in West and Central Africa. It was first described by Mongin in 1770 and received its present name in 1913 (Grove, 1990). Transmission occurs through the bite of flies of the genus chrysops and the infected larvae penetrate the skin and develop into adult worms over the next several months (Ottesen, 1990). These worms live primarily in the subcutaneous tissues and can sometimes be seen migrating through the subconjunctiva. Each adult female worm produces thousands of microfilariae that appear in the blood at their highest concentrations around noon (Manson-Bahr and Bell, 1987). The clinical manifestations of loiasis in endemic and non-endemic subjects differ in presentation. The most common symptoms of loiasis in endemic areas are pruritus with secondary dermal lesions, hypereosinophilia, temporary localized edema (Calabar swellings), subconjunctival eye passage of the adult worm and fatigue (Pinder, 1988; Carme et al. 1989; Noireau
et al. 1990). Non-endemic subjects tend to have more severe symptoms and are of the allergic type (Nutman et al. 1986; Klion et al. 1991). Such expatriates are much more likely to have Calabar swellings (95% vs 16%) and much less likely to have detectable microfilariaemia (10% vs 90%) than are natives of West Africa. In the series conducted by the National Institute of Health, all expatriates had an elevated eosinophil count, while one-half of the patients from endemic areas had eosinophil counts that were normal (Klion et al. 1991). These findings lead to the hypothesis that a suppression of immune response is caused by infections due to endemic loiasis. This hypo-resistantiveness is partly attributed to active suppression by T cells, adherent cells, or serum factors (King and Nutman, 1991).

The pathology of loiasis varies and is not very helpful in the diagnosis. The typical pathological features of Calabar swellings have not been well studied but there have been reports of adult worms found in the subcutaneous tissue associated with a variable inflammatory infiltrate consisting mainly of eosinophils (Gutierrez, 1990), microfilaria in dermal capillaries (Connor et al. 1976), and leukocytoclastic vasculitis (Portilla et al. 1991; Rakita et al. 1993). Our case showed focal degeneration of collagen with many eosinophils in the dermis.

Loiasis is very different from other filarial infections in that as many as two-thirds of the infected patients present permanently with no peripheral microfilariae (Dupont et al. 1988). The mechanisms of the suppression of microfilariaemia have not yet been identified but epidemiological studies suggest either immunologic, genetically determined, or external factors such as the mating success of adult worms and the release of microfilariae from the female, etc. (Wahl and Georges, 1995).

Accurate diagnosis of loiasis is not easy and only rarely can microfilariae be found in the peripheral blood or are adult worms seen in Calabar swellings. In the past, several attempts have been made to detect Loa loa by detecting elevated antibody titers using heterologous filarial antigen (Noireau and Pichon, 1992), homologous total antigen (Van Hoergarden et al. 1987), or homologous excretory-secreting antigen (Goussard et al. 1984). A recent study showed that IgG4 directed against homologous total antigen were detected in 85% of microfilariaemia and occult loiasis patients, but only in 6% of patients solely infected with Mansonella perstans (Akue et al. 1996).

However, the specificity of these tests, in particular with regard to Mansonella perstans, has not been clearly identified and some cross-reaction can be anticipated.

Many new tests are being tried for the purpose of specifically demonstrating Loa loa. A polymerase chain reaction (PCR)-based novel method to detect Loa loa DNA in the blood lysates of infected individuals was designed, and by using the DNA 396-bp sequence, species-specific diagnosis of occult loiasis was possible with no cross-reactions with Mansonella perstans and Onchocerca volvulus (Touré et al. 1997b). Although this assay claims to have a sensitivity of 95% in detecting occult loiasis, further trials and evaluations are needed for it to be recognized as the diagnostic tool of choice.

The standard treatment for loiasis has been DEC, given daily at 8–10 mg/kg for 3 weeks. This lowers the microfilariaemia to 2–12% of its initial level for up to 6 months (Duke and Moore, 1961) and kills about 30% of the adult worms in experimentally-infected primates (Nutman et al. 1986; Klion et al. 1992). In comparison, other studies claim that DEC treatment is not very effective, with 24–45% of cases relapsing (Hovette et al. 1994). DEC is not well tolerated because of adverse reactions such as pruritus, subcutaneous nodules, hematuria, arthralgia (Nutman et al. 1986), and the most dangerous complication, encephalopathy (Ottesen, 1990).

Recently, ivermectin, a semi-synthetic macrolide, has been recognized as a promising drug for the control of loiasis with less systemic side effects compared with DEC. Ivermectin given at doses of 200 ug/kg reduces microfilariaemia of Loa loa by 70% for up to 3 months (Richard-Lenoble et al. 1988; Chippaux et al. 1992), and by 88% for up to one year at 400 ug/kg (Martin-Prevé et al. 1993). Furthermore, a single dose of 200 ug/kg reduces the clinical symptoms in occult loiasis patients for up to 1 year (Hovette et al. 1994). The possibility of a permanent effect of ivermectin on adult Loa loa worms at high and repeated doses has been suggested (Martin-Prevé et al. 1993).

Our patient presented with classical Calabar swellings after visiting Cameroon and a diagnosis of loia-
sis was made by ELISA. Although this method is known to cross-react with other filariae, it is the only assay readily available and other novel assays still need further clinical trials for specificity and sensitivity. We advised the patient to take Ivermectin since it is effective in loiasis, onchocerciasis, and lymphatic filariasis. The patient showed prompt resolution after taking the medication and showed no evidence of recurrence for 1 year after taking two doses. As international travel is becoming more frequent, Loa loa infection should be considered in the differential diagnosis for patients with eosinophilia and Calabar swellings in non-endemic areas such as Korea.

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