

CASE REPORT

New World Cutaneous Leishmaniasis Treated with Intralesional Injection of Pentavalent Antimony

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Cutaneous leishmaniasis is a skin infection caused by the *Leishmania* species, an intracellular protozoan parasite that is transmitted by various species of female sandflies. According to the geographic distribution and vectors, leishmaniasis is classified as Old World or New World cutaneous leishmaniasis. In Korea, 24 cases of Old World cutaneous leishmaniasis have been reported, but New World cutaneous leishmaniasis has not been reported as yet. A 37-year-old man presented with a 3-month history of a painful and erythematous nodule with two satellite papules on the left postauricular area and a papule on the left arm after traveling to the Amazon region in Brazil. After we performed skin biopsies of the lesions, diagnosis of cutaneous leishmaniasis was made by the histopathological findings. After intralesional injection of sodium stibogluconate (Pentostam[®], GlaxoSmithKline) twice a week for 4 weeks, the lesions improved with scarring. Herein, we discuss this case of New World cutaneous leishmaniasis that was successfully treated with intralesional injection of sodium stibogluconate (Pentostam[®]) in Korea. (*Ann Dermatol* 25(1) 80~83, 2013)

-Keywords-

Cutaneous leishmaniasis, Leishmaniasis, Sodium stibogluconate (Pentostam[®])

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INTRODUCTION

Leishmaniasis is a vector-borne disease caused by the parasite *Leishmania* species and transmitted by various species of sandflies^{1,2}. Cutaneous leishmaniasis is typically divided into two forms: Old World and New World cutaneous leishmaniasis. Since the first case of cutaneous leishmaniasis was reported in 1978, 25 cases of cutaneous leishmaniasis have been reported in Korea. Most cases were reported after patients had traveled to Middle East Asia and Africa except one case. In this case, a patient had no history of a trip abroad³. While most patients were treated with oral antibiotics and antifungal agents, such as Bactrim, metronidazole, and itraconazole, only one patient was treated with intralesional injection of meglumine antimoniate in Korea. Recently, we encountered a patient who traveled to the Amazon region in Brazil and presented with cutaneous lesions on the left arm and left postauricular area. We diagnosed it New World cutaneous



Fig. 1. (A) A solitary, painful, and erythematous nodule with two satellite papules on the left postauricular area and (B) a papule on the left upper arm.

leishmaniasis based on clinical and histopathological findings. We subsequently treated the patient with intraleisional injection of sodium stibogluconate (Pentostam[®], GlaxoSmithKline, Brentford, UK).

CASE REPORT

A 37-year-old man presented with a 3-month history of cutaneous lesions on the left postauricular area and left arm. The patient had experienced several insect bites while traveling to the Amazon region in Brazil five months

ago. On physical examination, a painful and erythematous nodule with two satellite papules on the left postauricular area and a papule on the left arm were observed (Fig. 1). Initially, we suspected cutaneous leishmaniasis because of the appearance of the lesions and history of insect bites when he traveled to the endemic area. Then, we performed skin biopsies of the lesions. Histopathological examination revealed numerous Leishman-Donovan bodies in the cytoplasm of macrophages (Fig. 2). After confirming the diagnosis of New World cutaneous leishmaniasis, the patient was treated with itraconazole 200

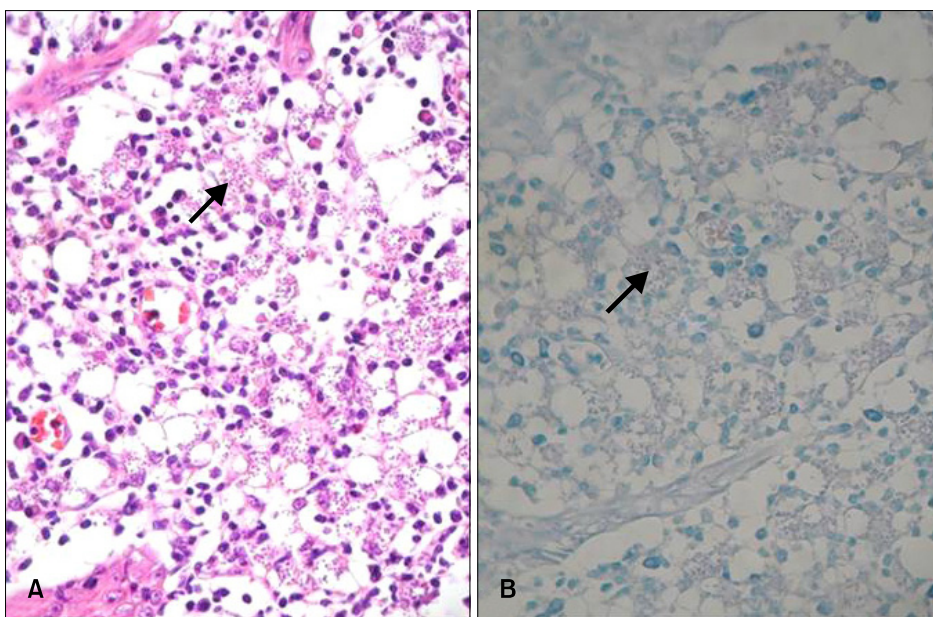


Fig. 2. Histopathological findings show numerous Leishman-Donovan bodies (arrows) in the cytoplasm of macrophages (A: H&E stain, $\times 400$; B: Giemsa stain, $\times 400$).

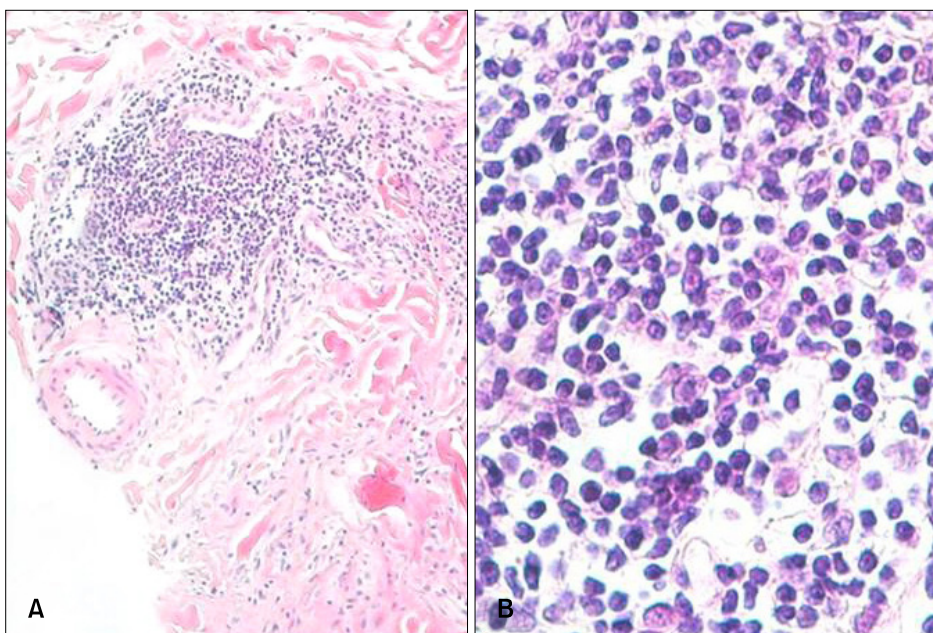


Fig. 3. Histopathological findings show chronic granulomatous inflammation and no evidence of Leishman-Donovan bodies (A: H&E stain, $\times 100$; B: H&E stain, $\times 400$).



Fig. 4. Skin lesions at 3 months after treatment (A) on left postauricular area and (B) left arm.

mg/day for 7 weeks and metronidazole 1,500 mg/day for 5 weeks; however, there was no improvement. After the patient received intralesional injection of 0.1 ml of sodium stibogluconate (Pentostam[®]) twice a week for 4 weeks, the lesions were improved with minimal scarring. During treatment, several subcutaneous nodules developed around the lesion on the left arm. Histopathological examination of the new lesions showed chronic granulomatous inflammation and no evidence of Leishman-Donovan bodies (Fig. 3). After 3 months, the newly developed lesions were resolved without further treatment (Fig. 4), and no recurrence of the lesions has been observed to the present.

DISCUSSION

Cutaneous leishmaniasis is usually classified as either Old World or New World cutaneous leishmaniasis. The Old World cutaneous leishmaniasis occurs in Southern Europe, the Middle East Asia, and Africa and is primarily caused by *L. tropica* and *L. major*^{1,3}. The New World cutaneous leishmaniasis occurs in Central and South America and is caused by *L. mexicana* complex and *L. braziliensis* complex subgenus. The former is transmitted by the *Phlebotomus* species, and the latter is transmitted by the *Lutzomyia* species^{1,4}.

There are various clinical manifestations of cutaneous leishmaniasis. A skin lesion develops at the site of a sand fly bite after an incubation period of 1~4 months that may sometimes last from 2 weeks to a year. Lesions begin as small, erythematous papules (5~10 mm initially), and over 1~3 months, they can progress into erythematous nodules, indurated plaques, and then ulcers^{5,6}. A typical lesion is a painless ulcer with a raised, indurated margin

and a necrotic base. Like the case presented here, satellite lesions may sometimes occur. Most lesions heal over the course of several months or years, leaving depigmented retracted scars. Spontaneous resolution may occur, depending on species of the parasite and the immunity of the host. While most Old World species cause benign cutaneous disease, New World species cause a broad spectrum of conditions from benign cutaneous disease (if caused by species such as *L. Mexicana*) to severe mucosal lesions (if caused by species such as *L. amazonensis* or *L. braziliensis*). The lesions caused by these species can persist much longer and spread to mucocutaneous leishmaniasis. Mucosal lesions usually appear within 6 months following cutaneous lesions.

The diagnosis of leishmaniasis is based on direct visualization of the amastigote parasite under the microscope in Giemsa-stained smears or biopsy specimens⁷. Culturing aspirates or biopsy material in Novy-MacNeal-Nicolle medium is another method for diagnosis. The sensitivity of these methods is variable: 19~77% for direct visualization of parasite and 58~62% for cultures⁸⁻¹⁰. The Leishman skin test is also available, but it is not routinely used in most industrialized countries. Recently, polymerase chain reaction (PCR) has been regarded to be the diagnostic method of choice. It has high sensitivity (89~100%)⁸ and can determine *Leishmania* species¹¹. However, we could not determine the *Leishmania* species that cause cutaneous leishmaniasis of our patient, because we were unable to perform the PCR.

As previously mentioned, there are 25 cases of cutaneous leishmaniasis reported in Korea. Although most cases were reported after traveling to the Old World regions, there is a case of cutaneous leishmaniasis without history of a trip abroad³. For this reason, they could not conclude its species according to the geographic distribution, and it is thought that ours is the first case of New World cutaneous leishmaniasis.

There are a wide range of treatment modalities for leishmaniasis including systemic and topical therapies. Systemic treatment is recommended if there are multiple (> 5~10) or large (4~5 cm) lesions, if the lesions are located in a cosmetically sensitive area, or if the lesions are over joints¹². Pentavalent antimonials are the mainstays of systemic therapy. Two preparations are currently available: meglumine antimoniate (Glucantime[®], Sanofi-aventis, Paris, France) and sodium stibogluconate (Pentostam[®]). These drugs can be used for both systemic and topical therapy¹³. The mechanism for their effectiveness is not well understood, but may involve inhibition of adenosine triphosphate synthesis. In addition, there are several alternative treatment options available. Systemic

therapy, such as pentamidine, miltefosine, paromomycin, and itraconazole, or topical therapies such as surgical excision and cryotherapy have been used successfully for leishmaniasis¹⁴.

There are also differences in treatment between Old World and New World cutaneous leishmaniasis. For Old World cutaneous leishmaniasis, patients usually have benign cutaneous disease which often heals spontaneously, leaving depigmented retracted scars. Therefore, these patients require only topical or no treatment at all. However, with New World cutaneous leishmaniasis, spontaneous healing is less common, and systemic treatment is usually required depending on the species¹. For example, *L. mexicana* requires topical treatment or no treatment at all; however, *L. braziliensis* requires systemic treatment. Since it is difficult to differentiate the New World cutaneous leishmaniasis species by PCR in clinical practice, in nonendemic areas, systemic pentavalent antimonials are generally used as the first choice of treatment. Our patient was treated initially with itraconazole and metronidazole. However, the skin lesion was not improved. Although systemic treatment was required for our patient, the patient refused this treatment because of his work. Intralesional injection of pentavalent antimonials for the treatment of New World cutaneous leishmaniasis was reported to have a cure rate as high as 79.7%, in 1997¹⁵. Therefore, we decided that intralesional injection of pentavalent antimonial should be used for treatment. Treatment with intralesional injections of sodium stibogluconate was followed by improvement of the skin lesions. However, during treatment, several subcutaneous nodules developed around a papule on the left arm. Skin biopsy showed chronic granulomatous inflammation and no evidence of Leishman-Donovan bodies. It is known that over time, there is a gradual decrease in the number of amastigotes and macrophages, leaving a granulomatous infiltrate consisting of lymphocytes, epithelioid cells, and multinucleate giant cells in leishmaniasis. Therefore, it is likely the newly developed subcutaneous nodules were a part of the natural course of the disease.

In conclusion, we documented the first case of New World cutaneous leishmaniasis successfully treated with intralesional injections of sodium stibogluconate. New World cutaneous leishmaniasis will be more frequently observed due to the increasing number of travelers to the New World regions. Therefore, physicians should keep in mind the characteristic features of cutaneous leishmaniasis and consider intralesional injections of pentavalent antimonials for the treatment of New World cutaneous leishmaniasis.

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