Cutaneous leishmaniasis: a case report

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Abstract
Cutaneous Leishmaniasis (CL) is a vector-borne protozoal infection of the skin. It is endemic in the tropics and neotropics. Several species of Leishmania cause this disease in the Old World. It is manifested as chronic nodular to ulcerative lesions of the skin, which last for many months and may be disfiguring. Despite its increasing worldwide incidence, it is infrequently reported from Nepal. We are reporting a case of CL in a man who acquired the disease while working in Saudi Arabia and who was successfully treated with Sodium Stibogluconate injections.

Introduction
Leishmaniasis is the result of infection with intracellular protozoa Leishmania donovani which are transmitted by infected female sandfly. There are about 1.5 million new cases of CL each year, of which more than 90% occur in middle east countries like Afganistan, Algeria, Iran, Iraq, Saudi Arabia in the old world, and Brazil and Peru in the new world. It is often referred to as a group of diseases because of the varied spectrum of clinical manifestations, which range from small cutaneous nodules to gross mucosal tissue destruction. It is manifested as chronic nodular to ulcerative lesions of the skin, which last for many months and may be disfiguring. Despite its increasing worldwide incidence, but because it is rarely fatal, CL has become one of the so-called neglected diseases, with little interest by financial donors, public-health authorities, and professionals to implement activities to research, prevent, or control the disease.

Case Report
A 27 years-old road-painter from Sunsari district of Nepal, working in Saudi Arabia for the past 4 years presented to the outpatient department of Dermatology and Venereology of Bir Hospital with the history of a progressively growing erythematous rough plaque on back of right hand for 2 months and multiple, deep seated nodules on extensor aspect of the right forearm for 15 days. He gave the history of probable bite by an unknown insect while sleeping outdoors in Saudi Arabia. On the next day he developed red papules on back of right hand which were 4 in number that soon ulcerated and were covered with crusts in the center of the lesions in 3 weeks (Figure 1 and 2). After sometime the three crusted lesions became confluent. It then enlarged for about 6 weeks then became stationary. The lesions were asymptomatic. There was no history of overt trauma or accidental spillage of paint or any sexual contact. He disclosed that even his other friends who were working there in Saudi Arabia had similar kind of eruptions and were being treated with injections. There were no systemic complaints. The lesions had failed to heal spontaneously. While returning from abroad and before going to his native home he had come directly to the hospital seeking treatment.

On examination there was a single well-defined faintly violaceous rough plaque on the ulnar side of the back of right hand (size- 5x5 cm) with central crusting and stellate fissuring which was exuding serosanguinous discharge. A smaller but similar lesion was also present (size-2.5x2 cm) adjacent to the confluent lesion near the wrist (Figure 1).

Figure 1. Violaceous plaque with central crusting & stellate fissures on back of hand
Fig. 2. Deep seated nodules on right forearm
A smaller but similar lesion was also present (size-2.5x2cm). Multiple non-tender firm subcutaneous nodules, about 5 in number, were palpable along the draining lymphatics on extensor aspect of the right forearm Figure 2). Regional lymph nodes were not enlarged.

Complete blood count and biochemical tests (liver function test, renal function test, sugar and electrolytes) were within normal limits. Mantoux test was negative. The smear of the scrapings taken from beneath the crusts as well as from the aspirates of the subcutaneous nodules was treated with Giemsa stain. Leishman-Donovan (LD) bodies were detected on the smear made from subcutaneous nodules.

Fig. 3 CL after 1 week of Sodium Stibogluconate
The patient was admitted in the hospital and treatment was started with daily intramuscular injections of Sodium Stibogluconate (20mg/kg) for 21 days. Routine blood tests, liver function tests and ECG were done on weekly basis. There was a significant improvement of the lesion after 1 week of treatment (Figure 3). The lesions flattened, became less indurated and the crusts fell off. The patient happily returned home. Currently he is back at his work abroad with out any complaints. This case is presented here for its rarity in Nepal.

Discussion
Cutaneous Leishmaniasis (CL) is a vector-borne protozoal infection of the skin. Several species of Leishmania cause this disease in the Old World. It is transmitted by the bite of a female sandfly. The bite of one infected sand fly is sufficient to cause the disease, since a sand fly can egest more than 1000 parasites per bite. The typical lesions of CL were described as early as 900 BC and have been referred to as the "Balkan sore" in the Balkans, the "Delhi boil" in India, the "Baghdad boil" in Iraq, and "saldana" in Afghanistan.

Most of the cases found in the United States are acquired elsewhere such as in travelers to Latin America. More recently, more than 500 cases of leishmaniasis were diagnosed over an 18-month period in soldiers returning to the United States from the Middle East, especially from Iraq. A large portion of these was identified as CL. The Centers for Disease Control and Prevention (CDC) estimates that approximately 1.5 million new cases of CL occur worldwide each year. Incidence is highest in tropical and subtropical regions where conditions are favorable for sandflies. Most cases of CL are seen in Afghanistan, Brazil, Iran, Iraq, Peru, and Saudi Arabia, while visceral leishmaniasis is most common in Bangladesh, Brazil, India, Nepal, and Sudan. In a study of CL in Riyadh region of Saudi Arabia, non-Saudis represented 67% of the total number of patients and 65% of them had 3 or more lesions compared with 10% in Saudis. Males are more commonly infected than females, most likely because of their increased exposure to sandflies. Children are at greater risk than adults in endemic areas. Malnutrition has been shown to contribute to the development of disease. CL of Americas are caused by L. tropica mexicana, L. braziliensis, and L. amazonensis, where as CL of Old World are produced by L. tropica, L. major, L. infantum, and L. aethiopica.

Cutaneous leishmaniasis can be simple or diffuse. Different species, as well as host factors, can also affect the clinical picture, where some species cause "wet" ulcers and others "dry" ulcers. The broad spectrum of clinical manifestations of CL is often compared with that of leprosy. After the bite of an infected sand fly, the incubation period is usually several weeks after inoculation, but this incubation period is variable. Initial lesions can appear immediately after a bite, or the incubation period may last for several months. These lesions are usually painless. Over a period of weeks to
years, some lesions may resolve spontaneously without pharmacotherapy. Skin trauma can result in activation of seemingly latent cutaneous infection long after the initial bite. Initially, the lesion is a small, red papule up to 2 cm in diameter. Over several weeks, the papule becomes darker and will crust in the center, eventually ulcerating to present a typical appearance of an ulcer with raised edges and surrounding dusky red skin. The ulcers can be moist or open with seropurulent exudate or dry with a crusted scab. After about 3-6 months, the ulcers heal, leaving a raised border. Sores usually are found on exposed areas of skin, especially the extremities and face, varying in size from 0.5 to 3 cm. Regional adenopathy, satellite lesions, and subcutaneous nodules can be present. Systemic signs usually are absent in CL. Untreated sores can leave depigmented, retracted scars. A rare and unusual presentation of CL is the erysipeloid type which has been reported by Salmanpour et al. Untreated CL can progress to disseminated mucocutaneous leishmaniasis, and death can occur from secondary infection. leishmaniasis in certain areas. Incomplete therapy of initial disease is a risk factor for recurrence of leishmaniasis. Expanded differential diagnosis for cutaneous leishmaniasis includes syphilis and leprosy as well as sporotrichosis, blastomycosis, chromomycosis, lobomycosis, cutaneous tuberculosis, atypical mycobacterial infection, sarcoidosis, lupus vulgaris, yaws, and neoplasms.

Diagnosis usually is based on the appearance of the lesion. In more than 70% of CL cases, microscopy of the parasite in Giemsa stains or histological section can reveal the parasite and should be attempted first. Culture of the organisms is an option but is unreliable because organisms are difficult to isolate from the lesion, especially as the lesion becomes older. The organism grows on Schneider Drosophila medium (positive results in 1 wk) and Novy-MacNeal-Nicolle (NNN) medium (media available from the CDC). Cultures can produce positive results in 1-3 weeks. The leishmaniasis skin test (Montenegro test) produces positive results 3 months after the appearance of lesions. The Montenegro test is performed by injecting killed promastigotes intradermally and examining the skin 48 hours later to see if a delayed-type hypersensitivity response has formed. A positive result is defined as induration of 5 mm or more. The two main drawbacks are that acute infections cannot be identified (in endemic regions, more than 70% of the population will test positive) since it remains positive for life and those who are immunosuppressed may not mount a response. Serologic tests such as isoenzyme or monoclonal antibody analysis are not well established. However, polymerase chain reaction (PCR) is being used more frequently and is more accurate in determining new-onset leishmaniasis than serum tests. Of note, very few of these diagnostic tests are available in developing countries, where most diagnoses is made clinically. Monoclonal antibodies (MoAb) or hybridization of tissue touch blots with labeled kinetoplast DNA probes are used for identification of different strains of Leishmania. An immuno-chromatographic strip test exists for rapid detection of antibodies to Leishmania antigen K39.

Treatment of CL differs according to the etiology and geographic location of the infection. Although cutaneous leishmaniasis can heal on its own, early lesions can also be treated with physical measures, such as local cryotherapy, electrocoagulation, or surgical removal. Nonspecific measures, such as local heat and cleanliness, contribute to the spontaneous healing of the ulcers. For certain types of CL where the potential for mucosal spread is low, topical paromycin can be used. For more invasive lesions (eg, those failing to respond to topical treatment; metastatic spread to the lymph nodes; or large, disfiguring, and multiple skin lesions, especially those on the face, near mucosal surfaces, or near joints), sodium stibogluconate, meglumine antimonate, or pentamidine are the mainstays of therapy.

Sodium antimony gluconate (known as Pentostam in the United States) is the drug of choice for treatment of CL in the United States any many other countries of the world. Children often tolerate therapy better than adults. They are given intravenously (i.v.), intramuscularly (i.m.), or intrasallaneously. For all forms of the disease, treatment should be started with a 200-mg test dose and then followed by daily injections of 20 mg/kg IV (preferably) or IM for for 20 days; Meglumine antimonate is dosed exactly the same and is equivalent in efficacy and toxicity to sodium stibogluconate. Sodium antimony gluconate may cause myalgias and arthralgias (50%), fever, phlebitis, rash, and GI symptoms, including nausea, vomiting, anorexia, and abdominal pain; adverse effects of hepatotoxicity, hemolytic anemia, cardiac dysrhythmias, and renal damage are rare. During the treatment with these compounds the patient has to be monitored weekly for 3 weeks after beginning treatment and then twice per week with serum chemistries, complete blood counts, and electrocardiography; The therapy has to be discontinued if the following occur: aminotransferase levels increase 3-4 times normal levels, significant arrhythmias, corrected QT intervals are greater than 0.50 seconds, or concave ST segments.

Pentamidine (Pentam-300) Inhibits growth of protozoa by interacting with trypanosomal
kinetoplast DNA and interferes with polyamine synthesis by a decrease in the activity of ornithine decarboxylase. Pentamidine also works by inhibiting incorporation of nucleic acids into RNA and DNA, causing inhibition of protein and phospholipid synthesis.

Fluconazole has also been shown to have some effect against CL in a dose of 200 mg daily for six weeks. Miltefosine treatment against CL has not been well studied.

Local care of the lesion and treatment of secondary bacterial infection with antistaphylococcal antibiotic may be needed.

Disease prevention and control are difficult because of the complexity of cutaneous leishmaniasis epizoolgy, and the few options available for effective vector control. Following points can help prevent the transmission of CL:

- Deliberate scarification (ie, making numerous superficial incisions) of the extremities with material from human lesions was once practiced to prevent facial scarring that might result from a later natural infection.
- The treatment of infected persons and elimination of diseased reservoir vertebrates can reduce the source of infection.
- Sandfly control (fine-mesh bed netting must be used, because sand flies are small enough to pass through ordinary mosquito netting) impregnated with an insecticide such as permethrin or deltamethrin, and use of insect repellent can prevent disease.
- General precautions, such as protective clothing, and minimizing outdoor exposures at peak times (e.g., dusk) should also be used.
- Some studies have shown protection against cutaneous leishmaniasis with vaccination of killed *Leishmania* promastigotes and live *bacillus Calmette-Guérin* (BCG).
- Current efforts are being made by organizations such as the Tropical Disease Research branch of the World Health Organization and other vaccine initiatives to develop second-generation vaccines against leishmaniasis.

Prognosis depends on nutritional and overall immune status of the host and on the precise species of infection. With early treatment, the cure rate is higher than 90%. The success of treatment should be assessed 6 weeks after its completion and patients should be followed up for 6 months.

References: