

Cutaneous leishmaniosis: some aspects of epidemiology and a case report

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Abstract

Cutaneous leishmaniosis presents as unsightly wound, begins as an erythematous papule at the site of a sandfly bite on the exposed parts of the human and some mammalian body. The papule increases in size and becomes a nodule which eventually ulcerates and crusts over. The ulcer is typically large but painless unless there is secondary bacterial or fungal infection. The disease condition is associated with rural areas and poverty. The sandflies are found around human habitations and breed in specific organic wastes such as faeces, manure, rodent burrows and termitaria. This paper reviews the epidemiology of the sandflies and leishmania species and also considered a human case of cutaneous leishmaniosis in Sokoto, Sokoto state, Nigeria.

Keywords: Phlebotomine Sandflies, Leishmaniosis, Skin Lesions.

Introduction

Phlebotomine sandflies belong to the Family: Phlebotomidae, but more frequently regarded as Sub-family: Phlebotominae of the order: Psychodidae. They are brownish, hairy, long legged flies with narrow bodies and up to 5mm in length. They have lanceolate wings that are less than 3mm long and held erect above the body. The antennae are long, 16-segmented, filamentous and covered in fine setae. The mouth-parts are moderately long with functional mandibles in the female that are hematophagous. The mandible is absent in males that are non blood-suckers. There are about 700 species of the flies in five genera viz: Lutzomyia, Sergentomyia, Phlebotomus, Brumptomyia and Warileya (Kettle, 1993; Wall and Shearer, 2001).

Phlebotomus and Sergentomyia species are confined to the 'old world' (Europe, Africa and Asia) while Lutzomyia, Brumptomyia and Warileya species belong to the 'new world' (the Americas) (OIE Manual, 2004). Six species of Sergentomyia and two species of Phlebotomus were identified in an endemic area for leishmaniosis in Northern Nigeria (Agwale *et al.*, 1995).

The life cycle of sandflies is difficult to study as the larvae are tiny and do not live in well defined places like the mosquito larvae (Iziko museum of Cape Town, 2005). Females lay 50 – 100 eggs per egg batch and the eggs measure 300 – 400µm long by 90 – 150µm wide. The eggs are white when laid but in a few hours darken to various shades of brown to black. The eggs and larvae need contact with water to survive. They are usually unable to survive even in a saturated atmosphere. The manure larva is grayish white in colour with a dark head and no annulations of the body. The head of the larva bears chewing mouth-parts which it uses to feed on decaying organic matter, leaf mould, insect bodies, animal burrows and faeces. The larva passes through four instars before pupating. The pupa stands upright and secure to the substrate by the larval exuviae. It has short prothoracic respiratory horns that adapt it to aquatic environment.

Phlebotomine sandflies are found in arid savannah and desert areas in which they seek a favourable microclimate and are often found in the burrows of rodents and termitaria. Breeding takes place in these microhabitats and the females feed on their mammalian occupants or those in the close vicinity. This habit coupled with the short flight

range (100 – 200 meters, occasionally 1km or more) leads to the local concentrations of phlebotomines and the disease they transmit. Most species are exophilic, while some are becoming endophilic in human dwellings and anthropophilic in some instances.

Sandflies feed on exposed areas of human skin and these are the sites for the development of indolent ulcers of cutaneous leishmaniosis. Phlebotomines rest by day in dark, cool, humid niches where the microclimate is favourable for survival such as caves, tree holes and burrows (Kettle, 1993).

Leishmaniosis on the other hand is caused by several species of *Leishmania* and transmitted by sandflies (Cox, 2002). There are at least 16 species and subspecies of the organism. The clinical spectrum in humans ranges from asymptomatic infections to those with high mortality. There are three distinct forms being classically described: visceral (VL), cutaneous (CL) and mucocutaneous (MCL) (OIE Manual, 2004).

Leishmaniosis is endemic in 88 countries throughout Africa, Asia, Europe and North and South America. There are estimated 12 million cases with 1.5 to 2 million new cases each year. The disease is found among the world's poorest population in which about 80% earn less than \$2 a day (Davies *et al.*, 2003). A number of isolated cases of cutaneous leishmaniosis has been reported in Northern Nigeria by some workers and recent studies indicated that the disease is more widely spread and prevalent than previously anticipated (Fabiya, 2001; Jiya *et al.*, 2004).

Cutaneous leishmaniosis is caused primarily in the 'old world' by *Leishmania tropica* (in urban areas) and *Leishmania major* (in dry desert areas). The incubation period is two to eight weeks, although longer periods have been noted. The disease begins as an erythematous papule at the site of the sandfly bite on exposed parts of the body. The papule increases in size and becomes nodules that eventually ulcerates and crust over. The border is usually raised and distinct. There may be multiple lesions especially when patient has encountered a nest of sandflies. The ulcer is typically large but painless unless there is secondary bacterial or fungal infection. The wound tends to heal spontaneously in months leaving a depressed scar that is usually round but can be irregular.

CL can become disseminated (diffuse CL) especially in immunosuppressed individuals. Patients with HIV infection are particularly susceptible.

Other unusual types of CL include 'leishmaniosis recidivans' in which small nodules develop around a healed scar and 'post-kala-azar leishmaniosis' in which widespread cutaneous lesions arise after a viscera infection (Markle and Makhoul, 2004).

Clinical signs in dogs include cachexia, splenomegaly and lymphadenopathy. Haematologically, there is moderate normochromic, normocytic anaemia with clinical chemistry of marked hypergammaglobinemia and hypoalbuminemia, reduction of lymphocytes in lymph nodes and tonsils (Nyindo, 1992).

CL can be diagnosed by any of the following procedures:

- (a) Cutaneous scraping test: administer local anaesthesia, clean ulcer of crust, and dry with gauze. Scrape margin and central area of ulcer of crust and prepare five slides.
- (b) Punch biopsy test: punch 2 to 3mm along active border; make tissue impression smears from a biopsy sample by rolling the cut portion on a slide after blotting excess blood
- (c) Needle aspirate test: this test is useful with nodular and popular lesions, using 0.1ml of preservative-free saline injected into the border through intact skin. The fluid is aspirated while the needle is moved back and forth under the skin; the fluid is useful for culture on blood agar Nicolle-Novy-MacNeal media.
- (d) Immunologic tests: antibodies are detected most consistently in mucosal disease. PCR test is highly sensitive but must be standardized. The test is species specific (Markle and Makhoul, 2004).

Morphologically, the amastigotes in human and other mammalian hosts are small intracellular, rounded or oval body, 1.5-3 x 2.5-6.5µm in size, and are found in vacuoles within the cytoplasm of the macrophages. There are no free flagella and the organism has relatively large nucleus and a kinetoplast consisting of a rod – like body and a dot – like basal body (OIE Manual, 2004). Differential diagnosis of CL includes: bacterial skin infections, blastomycosis, cutaneous anthrax, eczema, fungal skin infections, leprosy, *Mycobacterium marinum*, myiasis, sarcoidosis, skin cancer, sporothrichosis, syphilis, tuberculosis, yaws and verrucous lesions (Markle and Makhoul, 2004).

The drugs of choice in treatment of leishmaniosis include pentavalent antimony, pentamidine, amphotericin B, paromomycin, miltefosine and sitamaquine (Sundar, 2004). In some instances oral administration of rifampicin, dapsone, ketoconazole, itraconazole and allopurinol are indicated (El-On and Weinrauch, 2005). These drugs however have their individual attendant toxicity and side effects.

Over 90% of cases of CL heal spontaneously within 3 to 18 months and the rationale for drug use and determination of drug efficacy are different from those of visceral leishmaniosis (Davies *et al.*, 2003). Thus, World Health Organisation (WHO) recommended no treatment for uncomplicated CL, that is, those with fewer than five lesions with none more than 5cm in diameter and not nearer to vital organs (Asilian *et al.*, 2003).

In Iran, incorporation of 15% aminosidine (paromomycin) plus 10% urea in white paraffin in topical formulation was claimed to be effective in the treatment of CL, though local irritation developed in some cases (Asilian *et al.*, 2003).

Intervention strategies in leishmaniosis include vector control (through the use of insecticide spraying, genetic, biological and chemical control); control of animal reservoirs (both domestic and the wilds) and through the use of drugs and vaccine and personal protection (through vaccination and use of repellants) (Llanos-Cuentas, 2004). Insecticide impregnated fabrics is one of the most effective methods of reducing man vector contact and intra – and peri-domiciliary transmission of vector borne diseases including sandflies (Elnaiem, 2004).

Presently there is no effective vaccine against the infection in dogs and humans as Leishmanin (first generation vaccine) is no longer available commercially due to the need for further standardization (OIE Manual, 2004). The second generation vaccine currently being developed is a recombinant vaccine (Reed, 2004).

The case report

An undergraduate student of Usmanu Danfodiyo University, Sokoto was bitten by an insect while reading in preparation for the first semester examination (2004/2004 session). He noticed a small pustule-like lesion without pruritus or pain on his right arm. The lesion kept on increasing in size with open wound noticed between June 13th and 23rd, 2005. He visited a physician on 8th July, 2005 (at this time crater-like indolent ulcers with satellite nodules were observed). The following prescription was given after examination: Nizard® (ketoconazole) 1 tab. for 10 days, Ketrax® (Levamisole) 1x1x15 days, Pavidine Iodine solution for topical application.

On the 18th July, 2005, it was observed that the satellite lesions had began to disappear and another set of prescription was given: Nizard® 1 tab x 10 days, KetraxR 1x1x 10days. It was observed that most of the nodules had regressed but the open wound remained.

On the 27th July, 2005, the authors with the permission of the patient made smears from the satellite nodules' aspirate, stained with Giema stain and examined under microscope for the presence of amastigotes. Due to the slow process of healing, the patient decided to visit another physician on the 4th

of August, 2005. The wound was dressed with savlon®, methylated spirit and cicatrine powder. Ivermectin was to be taken as 4 tablets at the commencement of therapy, 2 tablets each for 3 days and 1 tablet each for another 4 days. Patient was advised to dress the wound on daily basis.

On the 12th August, 2005, the seemly healed wound becomes suppurative and the patient was advised by the physician to start another regime of treatment using Ketoconazole. By late August 2005, the wound had closed up with few satellite nodules remaining.

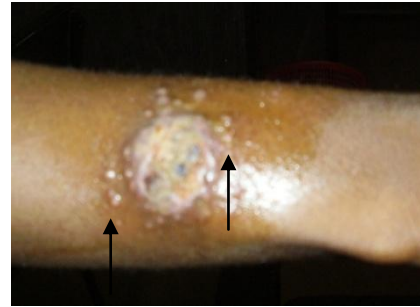


Plate I
Gross lesions; note the ulcer and satellite nodules shown by the arrows.

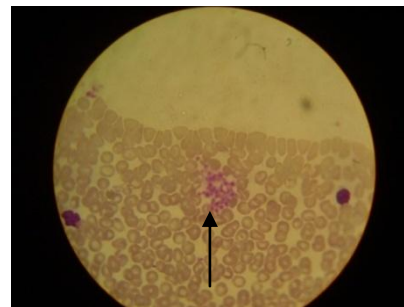


Plate II
Amastigote from satellite nodule as shown by the arrow.

Discussion

The crater-like ulcer observed with the satellite nodules (Plate I) are typical of cutaneous leishmaniosis and the presence of the amastigotes in the smear prepared from the nodules lesions (Plate II) confirmed this.

The use of ketoconazole is indicated in the treatment of leishmaniosis but it is primarily an antifungal agent. The drug has to be taken for several weeks or months without breaking the regime to ensure that the infection does not recur (Medline Plus, 2005). The major side effect of prolonged use of ketoconazole is liver damage.

The patient's wound relapsed early September, 2005 which may be as a result of discontinuation in the use of prescribed ketoconazole. Cutaneous leishmaniosis is sometimes self-limiting and may heal up spontaneously after some weeks (Davies, *et*

al., 2003), but the danger here is recrudescence. The patient sought further treatment outside Sokoto thereafter.

Due to the attendant side effects and toxicity of the drugs in use against the infection, a new innovative, simple, cheap and effective ointment comprising of 15% paromomycin sulphate and 12% methyl-benzethonium chloride in soft white paraffin has been developed and marketed as 'Leshcutan', presently manufactured by Teva Pharmaceutical Industries, Israel. The ointment has proved effect against a variety of leishmanial strains both in human and animal models (El-On and Weinrauch, 2005).

There are many termitaria scattered around the suburbs of Sokoto and this is characteristics of most parts of Northern Nigeria. Coupled with this is the indiscriminate dumping of refuse and animal wastes that are favoured sites for sandflies breeding. Human activities around these places may predispose to infection especially as men are fond of staying outdoor in the evening during which the vectors are most active (Lindgren *et al.*, 2004).

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