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Case Report

Cutaneous Leishmaniasis Case Report and Therapeutic Trial

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Abstract

A 13 Years old girl consulted our clinic in Asia Hospital complaining of painful twin ulcers. They were located in the right calf. The ulcers have reddish brown edges which are steep in nature. The floor is covered with dusky red eschar. Deferential diagnoses were put including cutaneous leishmaniasis which is confirm by smear. Cutaneous Leishmania's is caused by protozoa in addition to visceral mucocutaneous, recidivans types. They can be investigated by smear culture and PCR and LCR. Management is by pest control education mosquito net and secondary host control. Medications of different modalities play a role in treatment of the condition. Formula containing Pukka cream and Pantho-Eva-Emu gel helped in hastening healing of the ulcers. The mucocutaneous lesion healed promptly. Healing is without or with minimal scarring. This regime worth trial it is effective and without side effects.

Keywords: Leishmaniasis; Cutaneous, Mucocutaneous Visceral; Recedivan; PKDL; Amastigote; Sand Fly; Gerbil; Paromomycin; Antimony Compounds; Rifampicin; Low Level Laser (LLL); Cryo-Therapy; Pukka; Pantho-Eva Emu Gel

Introduction

Cutaneous leishmaniasis an important health problem. It conforms a challenge for control and treatment. Cutaneous leishmaniasis is a potentially severe and disfiguring disease. People with cutaneous leishmaniasis have one or several long-lasting lesions on the skin, usually poverty is important, since treatment is expensive and is therefore either unaffordable or involves a great loss of wages. The cost of treatment and implementation of prevention strategies needs sizeable financial and human resource investment. The disease burden in the Region is more than 50% of the cutaneous leishmaniasis burden worldwide. Cutaneous leishmaniasis due to *Leishmania tropica* and *L. major*.

History and Examination

On Jan 2014 a female aged 13 year accompanied by her mother consulted our clinic in Asia hospital. She walked in limping and anxious, she bared her right leg so by inspection the following was noticed: A twin of ulcers on her right calf were seen. They're about 2 cm in diameter and deep with sharp edges. The floor was covered by reddish brown escar. The edges were dusky red and sharply steep.

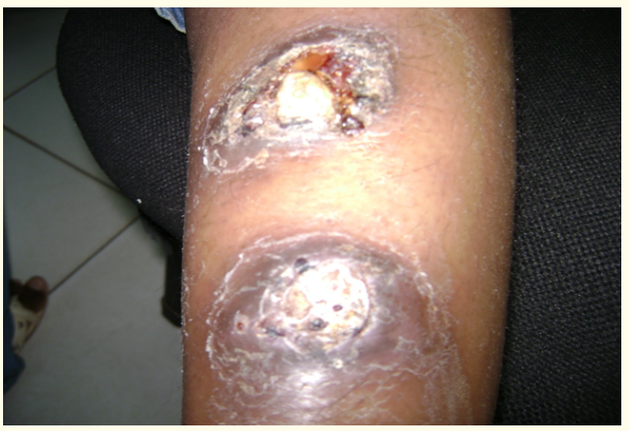

Figure 1: Cutaneous leishmaniasis on first visit.

Residence

The family lives in a mud house north of Omdurman city with electricity and water supply. The house is near the River Nile bank where bushes grow, and reservoir animals live.

On palpation: The lesion base was infiltrated and not tender, and on pressure no discharge was seen, also the lesion is not warm. The lymph nodes in the vicinity and catchment area are not enlarged or tender.

Differential diagnosis

The possibilities estimated are: cutaneous leishmaniasis – diphtheria – TB ulcer – tularemia – tropical ulcer – syphilitic gumma – deep fungal – ecthyma – Wegener's granulomatosis NB the history, the clinical examination, laboratory investigation including biopsy are helpful to differentiate between them.

Investigations

Stained smear has shown amastigote stage of leishmania and negative for other possibilities.

Profession

The patient is a pupil.

Family history

Her younger brother has similar ulcers on his arms.

Management

The lesion become ulcerated and phagedenic because the family used folklore medicine (a fruit of Acacia which is very sour and used for tanning of hides) that has led to this damage. So education was necessary to avoid this mistake.

So the treatment has included a formula to repair the ulcer (pukka cream® It is composed of Honey, propolis, St John wort extract, Aloe vera, Vit C, panthenol, Vit A, Zinc oxide, Tea Tree oil, Lanolin Glucose, Petroleum Jelly, Cetyl alcohol, methyl propane, Propyl Paraben, Liquid Paraffin.

Functions of Pukka

- It acts by Anti Septic, Accelerate Wound Healing, Anti-inflammatory and Analgesic, and Manipulate Necrotic Tissue) Pantho-Eva Emu-gel) (Acts by Repithelization of the wound) and cleansing solution.
- Support skin structures and Improves skin tone.
- Maintain moisture balance and elasticity of adjacent skin.
- Soften, smoothen, and reduce scar stiffness rapidly.
- Effectively eliminates inflammation.
- Supplies nutritional elements, needed for regeneration of tissue.
- Pantho-EVA- Emugel®
- ach 100 gm contains
- D-Pathenol 5 gm

Function

Panthenol promotes the acetylation of choline to acetylcholine, it has an important role in the formation of epithelial tissues. It is considered to have an important role in the normal function of all epithelial tissues.

NB: Both drugs are added equally or topical treatment of the giant ulcers and proves to be effective.

Medical treatments given are:

- Systemically: Rifampicin, Metronidazole, Itraconazole
- Topically: antiseptic solution plus Ketoconazole cream

The patient should come for follow-up.

NB: The patient came back to the clinic after two weeks Mild improvement was noticed. angular lesion of the mouth was observed (whitish sodden erosive in nature) mucocutaneous leishmaniasis was thought of but smear was negative.

Then she came after four weeks healing. By mild scaring.

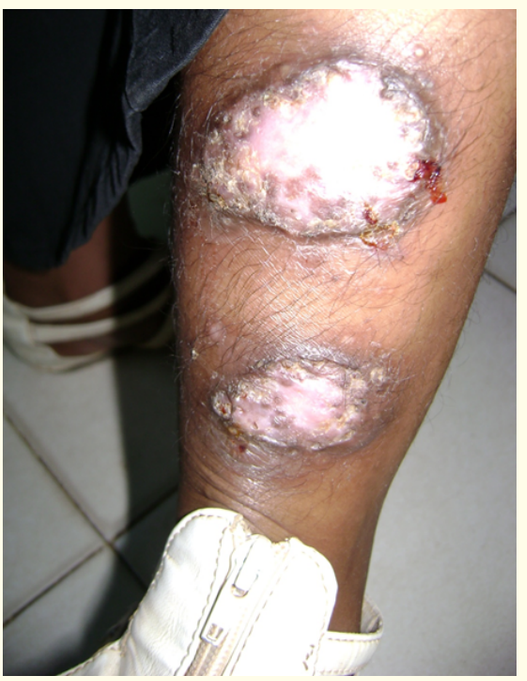

Figure 2: Signs of improvements after 2 weeks of treatment.

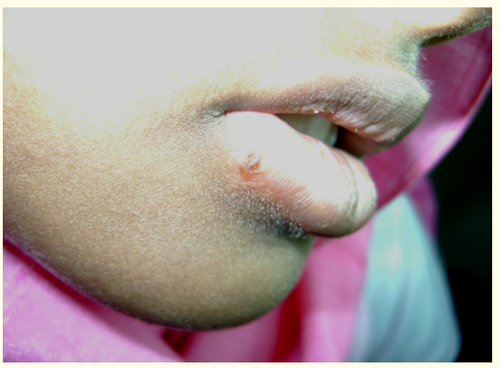

Figure 3: Mucocutaneous leishmaniasis? (Same patient).

Discussion

The case of concern is a female presented with double ulcers of cutaneous leishmaniasis. Her brother has a similar condition on his right arm. She lives in poor condition near the River Nile bank where bushes grow, and reservoir animals prevail. Investigations proved that the ulcers are to be cutaneous leishmaniasis. She responded slowly to topical a systemic treatment, noticed two weeks after the first visit.

Cutaneos leishmaniasis is limited to certain geographical areas, mainly the old-world e.g. Sudan, India, Middle East, Qandahar ext, but spreading fast because of improved travel and migration. It is spread by sand flies although human to human transmission is possible.

The disease starts as an erythematous papule at the site of the bite, usually an exposed site, however in the black skin it starts as a hyperpigmented papule. The papule then becomes a nodule, which then ulcerated with raised distinct borders. Ulcers are typically large and painless unless there is secondary infection. There may be multiple lesions and lesions up to 200 have been described in a single patient. The skin lesions can be very disfiguring and may heal but recidivans is common. Treatment is with destructive methods and antimony compounds.

Cases of Leishmania/HIV co-infection has been reported. The case is diagnosed as cutaneous leishmaniasis with possible mucocutaneous leishmaniasis (Espundia).

Literature Review

Introduction

Three different diseases are caused by leishmania: Cutaneous leishmaniasis, caused by *L. tropica* or *L. mexicana*; mucocutaneus leishmaniasis, caused by *L. brasiliensis*; and visceral leishmaniasis or kala-azar, caused by *L. donovani* (Marsden). These four organisms cannot be differentiated morphologically, but they differ immunologically. A histologic spectrum similar to leprosy has been described, with well-defined tubercle formation at one end of the spectrum and diffuse parasite multiplication in her absence of cell-mediated immunity at the other. In contrast to leprosy, The great majority of cases occupy the middle of the spectrum. In cutaneous leishmaniasis, as in leprosy, there is an inverse relationship between the cellular immune response of the host and the parasite load of patient. Therefore, if the leishmania, or Montenegro, test is negative, parasite will be generally found in a biopsy specimen or a direct smear of the lesion [1,2].

Old World cutaneous leishmaniasis, or oriental sore, has been described in texts dating back to 1500 - 2500 BC. Arab physicians provided more detailed descriptions in the 10th century. James Homer Wright (186-1928), American pathologist, who is also remembered for his eponymous blood stain, and Homer Wright pseudorosettes of neuroblastoma, is generally credited with identification of the parasite.

Sir Williams Leishman (1865 - 1926), Director General of the Royal Army Medical Corps, was a Glaswegain, and was more famous at the time for his work on an antityphoid vaccine, which successfully protected troops in World War I. He also developed his eponymous stain for the staining of malaria, trypanosomes, and other blood parasites. It was in his honour renamed leishmaniasis. Chales Dnovan was professor of physiology at Madras University.

The identification of the vector involved took much longer, and it was not until 1921 that proof of transmission by sandflies was made. This was followed by proof of infection via the bite of sand fly in 1941 [3].

Epidemiology

Incidence

Each year there are about 1.5million new cases of cutaneous disease and 0.5 million new cases of visceral disease [1]. There are 2 cases annually seen in the UK which usually result from travel to the Mediterranean.

Prevalence

More than 12 million people in 88 countries are known to be infected but many cases are asymptomatic. Furthermore, reporting is far from complete in many areas and true numbers are almost certainly very much higher [1]. It causes 70.000 deaths a year worldwide. The male to female ratio is about 2:1, probably due to greater exposure to places where there is a risk of sand fly bites.

Risk factors

Usually transmission is by the bite of the female sand fly. In some areas there are animal reservoirs but in others humans are the only mammalian source. It is a disease associated with poverty.

Other risk factors include:

- Malnutrition
- Poor housing
- HIV infection [2]
- Rarely-through sharing of needles, sexual intercourse, transpla cental infection, organ transplantation [3,4].

Life cycle [1-3]

Leishmania is dimorphic. In mammalian host: amastigote (leishmanial) form 2 to 3 Mm in length, oval/round, aflagellate; lives intracellularly in cells of reticuloendothelial system. In GI tract of sand fly in culture: promastigote (leptomonad) form-10 to15 Mm in length, spindle-shaped, flagellated; extracellular speciation: isoenzyme patterns, kinetoplast DNA buoyant densities, specific phlebotomine vectors, monoclonal antibodies, DNA hybridization, DNA restriction endonuclease Fragment analysis [2,5].

Reservoir [1,2,4]

Varies with geography and leishmanial species. Zoonosis involves rodents/canines. Mediterranean littoral-dogs. south ern Russia-gerbils. Vector female sandflies of genus phlebotomus (old

world) and lutzomyia and psychodopygus (new world). breed in cracks in buildings, rubbish, rubble, rodent burrows, termite hills, rotting vegetation. weak fliers remain close to ground near breeding site ingest amastigotes while feeding on infected mammals, converting to promastigotes in the gut of the sand fly replicate in gut. Transmission promastigotes deposited on skin of host into a small pool of blood drawn by probing sand fly. Season OWC L.t. major-summer through autumn epidemics; OWCL L.t. minor-year round; ACL-rainy season [2,5,6].

Incubation period

Inversely proportional to size of inoculums; shorter in visitors to endemic area. OWCL: l.t. major, 1 to 4 weeks; l.t. minor, 2 to 8 months; ACL: 2 to 8 weeks or more [4,6].

Etiology

Leishmaniasis is caused by intracellular protozoa belonging to genus leishmania spread by sand fly. Old world cutaneous leishmaniasis (OWCL). *L. tropic*a major causes wet (rural). l.t. minor causes dry(urban) [4,7,8].

Presentation

Presentation will vary significantly according to the species of infection and the location in the world. The following are generalisation.

Cutaneous leishmaniasis (CL)

Lesions tend to occur on exposed parts which are easily bitten by sandflies. In the New World they are usually solitary lesions but in the old world they are often multiple.

They start as erythematous patches but change to plaques or ulcers that are usually painless unless there is secondary bacterial infection. These lesions often heal spontaneously from 2 to 15 months, depending largely upon the species involved. They may leave pigmentation and scars. New world disease may progress to mucocutaneous leishmaniasis

Diffuse cutaneous leishmaniasis

Occurs with a poor immune response. There is a primary lesion which spreads to involve multiple areas of the skin. Plaques, ulcers and nodules may form over the entire body. It may look similar to lepromatous leprosy but there is no involvement of nerves and there is no systemic invasion. Infection is chronic and may recur despite of treatment.

Leishmaniasis recidivans

Can occur years after a cutaneous lesion has healed and is of then on the face. New ulcers and papules form over the edge of the old scar. Dormant parasites or new infection may be the cause, but these infections tend to be resistant to treatment [1-3,13].

Less toxic requires only 5 to 10 days of treatment or even as a one-off stat dose. In India it is 90% effective.

Ketoconazole, itraconazole, fluconazole, allopurinol, and dapsone are all less effective than the previously mentioned drugs. Miltefosine is the first oral treatment, and lacks the serious reactions associated with other drugs. Experience is still limited but results are promising. One advantage appears to be that it is safe to use in an outpatient setting. In mucocutaneous disease, plastic surgery may be required [2,3,9].

Investigations

Clinical suspicion is confirmed [5] by diagnosis is based on identification of the organism in tissue samples (Smear) [5] or culture. The specimen should show parasites at the stage of amastigotes in the form of Leishman-Donovan bodies.

PCR LCR new advent in diagnosis of leishmaniasis [13]

Various serological tests are available, but most cutaneous cases do not develop a significant antibody response. They are attractive as they require less resources than tissue diagnosis. There are 2 serological tests- direct – agglutination (DAT) and Ks30 dipstick, currently under investigation. Both appear to perform well in a meta-analysis. However, their main downside is that they remain positive for years after successful therapy. Other tests are also under design. In CL most usual blood parameters will be normal [10,12].

Pathophysiology

Course determined by host's cellular immunity and species of Leishmania. MCL: destructiveness of metastatic lesions due to hypersensitivity to parasite antigens. DCL: Leishmania reaction negative, i.e. selective energy [5]

Cutaneous leishmaniasis requires a punch or wedge biopsy from the raised edge of an active lesion where the parasites are most likely to be present. The necrotic centre is unlikely to yield results. Saline aspiration, scalpel scrapings, or slit incisions can also provide sample. Microscopy and culture are about 85% sensitive [10].

Histopathology

In acute leishmaniasis, during the first few months, the dermal infiltrate consists predominantly of large macrophages filled with great numbers of leishmania organisms. In addition, lymphoid cells and a few plasma cells are present. When ulceration sets in, secondary infiltration with neutrophils occurs. The leishmania organism are present exclusively within macrophages.

The parasitized macrophages measure 20 to 30 μm in diameter. After several months duration, primary lesions show a gradual reduction in the number of organisms, so that the diagnosis can be made only by means of culture or skin testing.

In chronic leishmaniasis, one finds a granulomatous infiltrate intermingled with lymphocytes and histocytes. It is often indistinguishable from that of lupus vulgaris. The lack of caseation necrosis may help in the distinction. A few leishmania organisms can be found occasionally on careful searching. In leishmaniasis recidivans, the histologic changes combine features of both the acute and the chronic forms. The dermis shows an infiltrate of macrophages, lymphoid cells, and some plasma cells as well as tuberculoid granulomas.

The leishmania organisms, which represent protozoa, appear in sections as round to oval bodies from 2 to 4 µm in diameter. They have deeply basophilic nuclei. Although visible in routine stains, leishmania organisms are seen best when a Giemsa, Wright are stain is used. With this stain, the nucleus and the kinetoplast appear bright red [1].

Smear

A hypodermic needle is inserted into the normal skin and to the edge of the ulcer base. The needle is rotated to work loose some material and serum, which is then aspirate and spread on glass slide and stained with Giemsa's or Wright's stain.

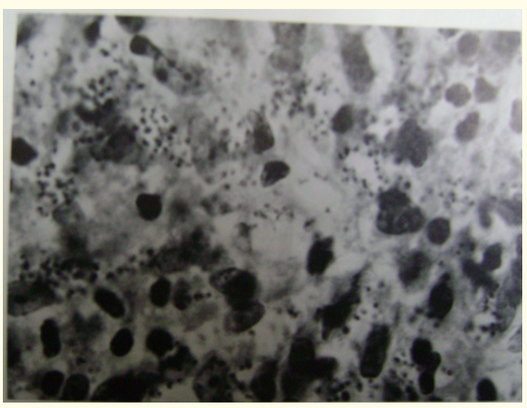

Figure 4: Smear from cutaneous leishmania ulcer.

Culture

Nicole-Novy-MacNeal (NNN) media at 22 to 35°C is recommended to demonstrate the leptomonds [4]. Leishmanin (Montenegro) Skin Test of no use in endemic areas. Negative in DCL. Serology Lacks specify

Dermatopathology

Large macrophages filled with 2 to 4 organisms

Transmission

Human to human transmission takes place through bite of infected sand flies.

Clinical features

The different manifestation include

- Cutaneous leishmaniasis.
    - Incubation period varies from weeks to months.
- Acute cutaneous leishmaniasis:
    - Frequently occurs on face and hands.
    - Asymptomatic, solitary edematous and erythematous nodule which ulcerates and ultimately heals with a depressed scar.
- Chronic leishmaniasis.
    - Lesions last longer than 2 years
    - Do not usually ulcerate [2,5,7].
    - Diffuse cutaneous leishmaniasis
- Mucocutaneous leishmaniasis:
    - Seen in Brazil.
    - Starts on the skin as edematous, erythematous plaques which secondarily involve nasal mucosa after several years.
    - The cutaneous lesions heal with scarring while the mucosal lesions show no tendency to spontaneous healing and may extend into the nasopharynx causing multilation [11,14].
- Post Kala-azar Dermal Leishmaniasis (PKDL).

Diagnosis

Diagnosis of cutaneous leishmaniasis is based on:

- Presence of solitary edematous nodule often with crateri form ulcer which heals spontaneously with scaring
- Lesions on exposed parts (bite-prone areas) [13-15].

Differential Diagnosis

Acute CL insect bite reaction, impetigo, furuncle, carbuncle, ecthyma, anthrax, orf milkers, nodule, tularaemia, swimming pool granuloma, tuberculosis cutis, syphilitic gumma, yaws, sporotrichosis, blastomycosis kerion, myiasis, dracunculiasis, molluscum, warts, pyogenic granuloma, keratoacanthoma, basal cell carcinoma, squamous cell carcinoma, metastases, lymphoma, leukaemia.

Chronic CL and Relapsing CL

Lupus vulgaris, leprosy, sarcoidosis, granuloma faciale, Jessner's lymphocytic in infiltrate, lymphocytoma cutis, discoid lupus erythematosus, psoriasis, acne, rosacea, cellulitis, erysipelas, keloids, Wegener's granulomatosis, syphilitic gumma [4,11].

Management

Prevention

Control of reservoir hosts and sandfly vectors involves spraying with insecticides, including indoors.

Avoid being bitten by sandflies using repellents, long sleeves and trousers and mosquito nets. Nets impregnated with insecticides are best. The creature is very small and so a small mesh net is required. This may reduce the circulation of air and be uncomfortable at night in hot climates.

No vaccine is yet available but there are hopes for the fairly near future [4,14].

Treatment

Systemic treatment

Since the 1930s the mainstay of treatment has been pentavalent antimony compounds. The main one is sodium stibogluconate.

For selected CL, MCL, DCL. Sodium antimony gluconate (Pentostam) IV or IM in single daily dose of 10 mg/kg for adults and 20 mg/kg for patients < 18 years of age for 10 days. Meglumine antimoniate (Glucantime) 20 mg/kg daily for 10 days. ECG control.

Amphotericin B or pentamidine or sodium antimony gluconate plus interferon gamma for resistant cases.

Combined immunotherapy: Leishmanial antigen in BCG [4,12].

Miltefosine: Oral anti-leishmania drug.

Others: Ketoconazole, rifampicin [15].

In the cutaneous leishmaniasis (CL) types that heal spontaneously the question is whether any treatment should be offered, especially as it can be quite toxic.

Old world CL may be left alone or treated if lesions are slow to heal or disfiguring.

Other systemic treatments are: Itraconazole, Dapsone, Allopurinol, Trimethoprim-Sulfamethoxazole, Metronidazole, Rifampicin [16].

Topical treatment:

- Antiseptic wash
- Topical 15% paromomycin sulfate in vegetable oil
- 12% methylbenzethonium chloride in white paraffin twice daily for 10 days [4,13]
- Gentamicin

Intralesional therapy

In CL may progress to mucocutaneous disease and so should be adequately treated. Old world CL may left alone or treated if lesions are slow to heal or disfiguring.

Topical treatment is more desirable for local disease and options include injection of anti-monials into the border of the lesion, cryosurgery, ultrasound-induced local hyperthermia, excision.

Also intralesional bleomycin may be tried as well as low level laser (LLL) [2,4-13].

Course and Prognosis

- CL Whether caused by *L. tropica* or *L. Mexicana*, CL is self-limited. Scarring is increased by secondary bacterial infection.
- MCL May extend to secondary sites. Secondary infection common. Mortality is from pneumonia.
- DCL is Progressive and refractory to treatment; cure is rare.
- Secondarily infected Leishmania ulcer may need 6 months to heal by fibrosis and may followed after years by Leishmania Recidivans.
- Malignant change is not recorded [2,4]
- Modern approach to diagnoses can be used e.g. PCR,LCR plus conventional manoeuvres.
- Cutaneous leishmaniasis and mucocutaneus leishmaniasis are still prevalent in the Three-Towns capital of the Sudan.

Conclusion

- The formula of Pukka and Pantho-Eva-Emu gel shortens, the course of the Cutaneous Leishmaniasis and other skin ulcers.
- Healing is without or with minimal scarring.
- This regime worth trial it is effective and without side effects.
- The mucocutaneous lesion healed promptly.

Recommendations

- Produce a regional manual for diagnosis and treatment of cutaneous leishmaniasis
- Develop national guidelines on case management, with regular updates.
- Improve awareness and knowledge among vulnerable populations to encourage early diagnosis and treatment

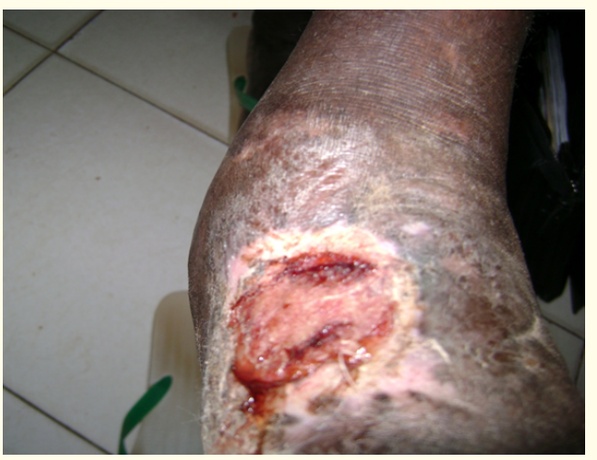

Figure 5: Pyoderma Gangoronosum-First visit.

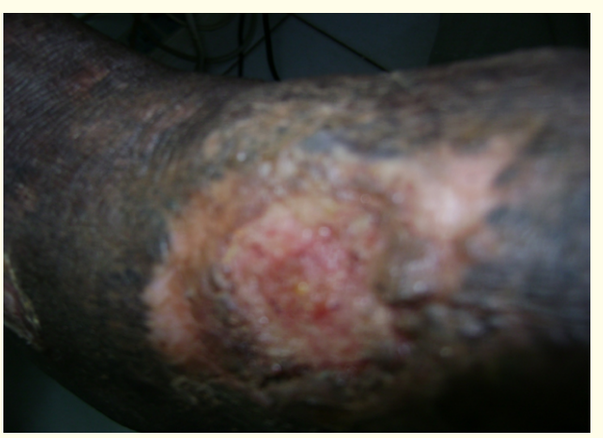

Figure 6: Pyoderma Gangoronosum-Second visit (after one month)

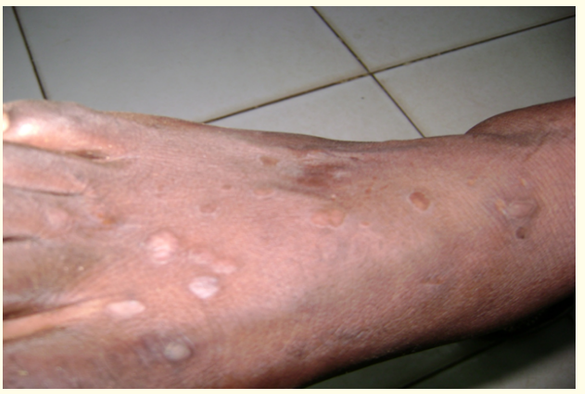

Figure 7: Pyoderma Gangoronosum-Third visit (After two months-complete healing).

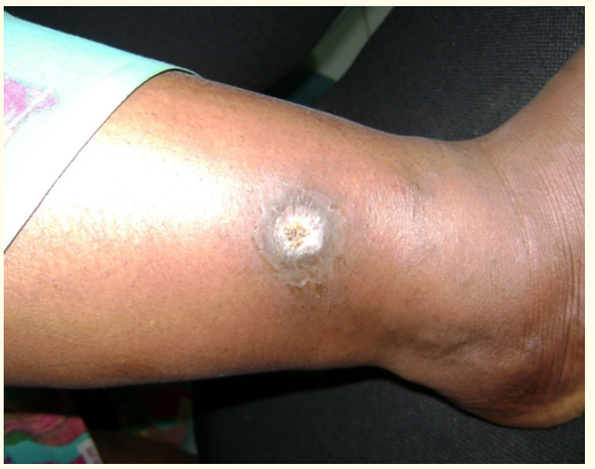

Figure 8: Echthyma (Right lower leg).

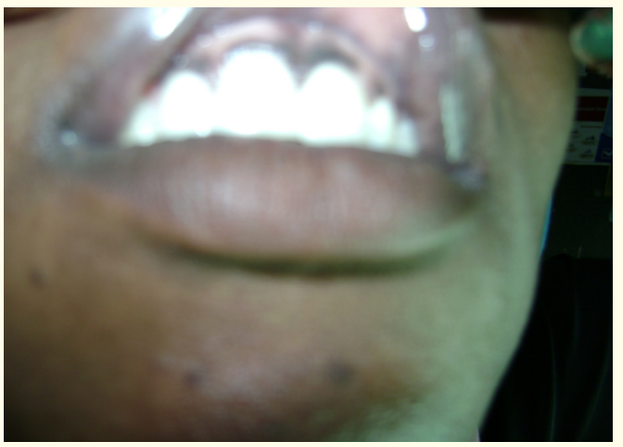

Figure 9: Mucocutaneous Leishmaniasis-First Visit.

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