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RESEARCH ARTICLE

CUTANEOUS LEISHMANIASIS: A CASE STUDY

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Abstract

Introduction : Leishmaniasis is a parasitic disease found in parts of the tropics, subtropics, and southern Europe. Leishmaniasis has several different forms. In this article, we will discuss a case of cutaneous leishmaniasis (CL), the most common form.

Case presentation: Our case is a 36-year-old lady, presented with a large disfiguring lesion on her left arm expanding during the last three months. Systemic examination was unremarkable. Examination of her arm showed a 6x6cm erythematous crusted plaque covering her medial aspect of the distal forearm.

Management and outcome:A biopsy was done and was suggestive of Leishmaniasis. She was diagnosed as CL and started on a course of systemic itraconazole along with cryotherapy. She was satisfied with the result after 4 sessions of cryotherapy and lost follow up.

Discussion and Conclusions: We had a chance to see a full-blown lesion in our patient that was treated with systemic azole and cryotherapy as according to the guidelines and had a satisfying result for the patient. Although it is rare to have a full recovery, we were hoping to have a better result.

Introduction:-

Leishmaniasis is a group of syndromes caused by an intracellular protozoan parasite, *Leishmaniadonovani*., that transmitted to humans by the bite of a blood-sucking female sandfly, mainly *Phlebotomies*. It occurs mostly in tropical and subtropical regions [1].

Leishmaniasis has three forms: cutaneous, visceral, and muco-cutaneous [2,3]. In this article, we focus on cutaneous leishmaniasis (CL) that is our case. It is the most common form of leishmaniasis [1]. CL is considered as a mild dermal condition, usually self-limited but can leave disfiguring scars, which is a part of the disease burden [1]. It has an incubation period of 1 to 4 weeks and up to several years [3]. Manifestations and severity of the skin lesions depend on species of *Leishmania* and the immune response of the host. It occurs in areas of the body that exposed to sandfly bites. Ears, nose, upper lip, and cheeks are the most involved areas and to a lesser extent, legs, hands, forearms, and ankles [3]. However, a study in Kuwait (1980) showed that the lesions in cases happened in Kuwait were mainly distributed on the upper and lower limbs [4].

There are no recent studies of the prevalence of leishmaniasis in Kuwait. However, currently, a patient with CL is not a regular case to present to our clinic.It was the purely interesting case to deal with and follow up the whole

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course of the disease and its management.It is a typical textbook case regarding the course of the disease. However, regarding the etiology and the transmission, our patient denied any history of insect bite, any recent travel, and any contact with animals.

Case Presentation

Our case is Miss B., a 36-year-old Filipino housemaid lady in Kuwait, previously healthy, presented to our clinic with a large disfiguring lesion on her left wrist.She noticed it three months back.According to the patient, it started as a small painless pimple. It was non-itchy, red in color, and less than one cm in diameter. Then, it increased size and became more prominent and ugly looking throughout the following three months before her presentation. The patient has no history of fever or weight loss.The systemic review was unremarkable. The patient also denied the history of travel or trauma and any history of insect bite in the last five years. Her past medical history is unremarkable. She is not on any medication and has no medical allergies. She is not married and her family live in the Philippines.

On examination, Miss B. was generally well. The general systemic examination was unremarkable. Dermatological examination showed; raised dull erythematous crusted plaque with three small ulcers (less than 1 cm in diameter). The whole lesion is covering the medial aspect of the distal forearm in an area of around 6x6 cm (Figure 1).

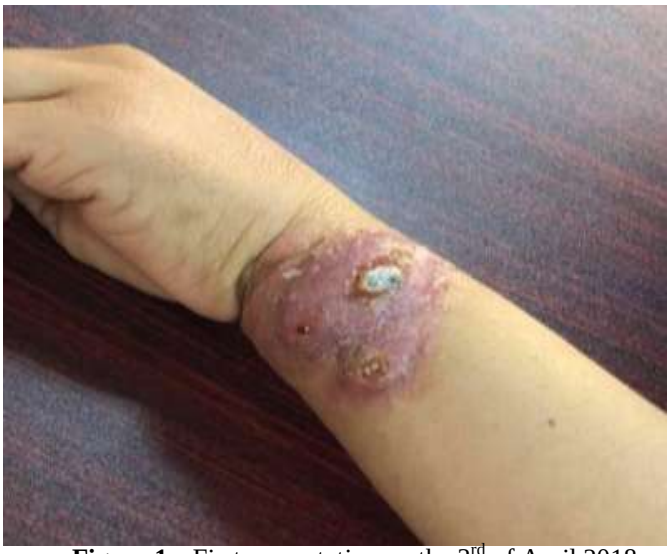

Figure 1:- First presentation on the 3rd of April 2018.
Dull erythmatosis

Management and outcome:

Our differential diagnoses were as follows:
- Lupus vulgaris
- Deep fungal infection
- Leishmaniasis (Cutaneous Leishmaniasis)
- Atypical mycobacteria

Routine lab investigations were unremarkable. A skin biopsy was taken from the lesion and sent for histopathology lab. The patient was advised to follow the results as soon as possible. Miss B. presented to our clinic after one month to follow the results of the biopsy. The lesion increased in size and became more dry and had a hyperkeratosis verrucous surface. (Figure 2).

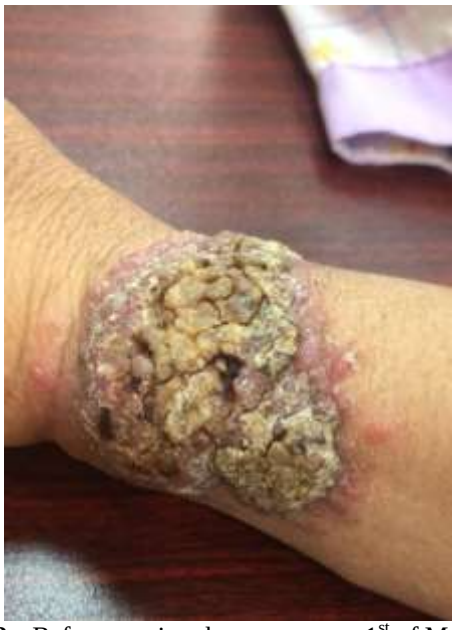

Figure 2:- Before starting the treatment – 1st of May 2018.
Hyperkeratosis verrucous plaques

Histopathology report revealed that skin punch biopsy taken from the lesionshowed dermal granulomatous inflammation with prominent lymphocytes.Histiocytescontaining oval-shaped, small organisms with bar-shaped paranuclear kinetoplast where noticed. Features are suggestive of Leishmaniasis (Figures 3; A-H).

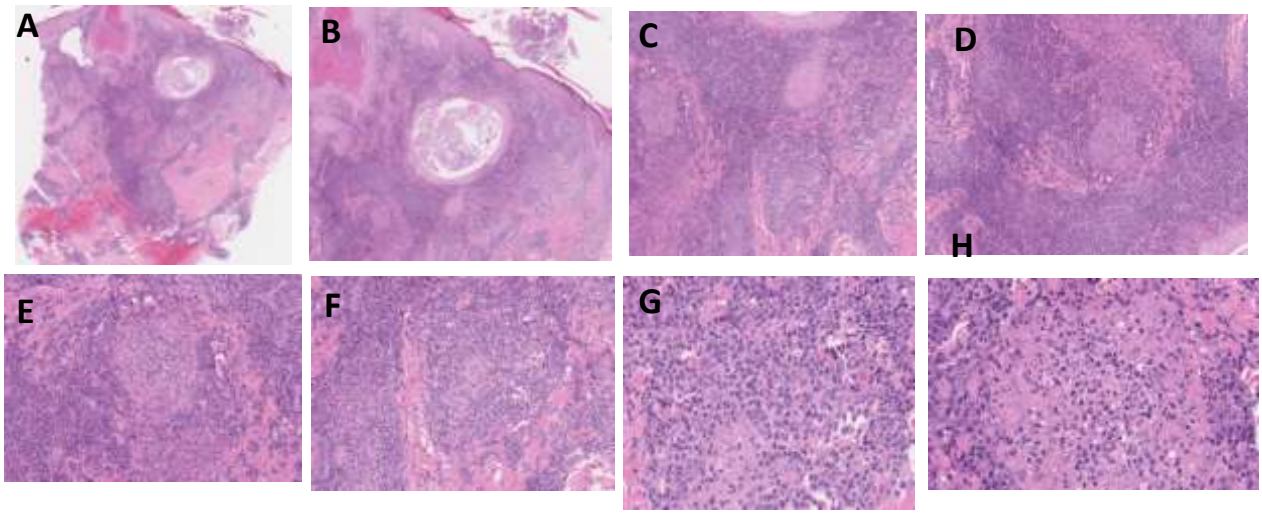

Figure 3: - Microscopic descriptions of skin sections stains by hematoxylin and eosin.
(A- B) low power examination (X40) showed dermal granulomatous inflammation.
(C- D - E) Medium power examination (X 100) showed prominent lymphocytes and histiocyte.
(G -H) High power examination (X 200) showed histiocyte containing oval-shaped, small organisms with bar-shaped paranuclear kinetoplast.

The patient started on weekly cryotherapy that continued for 4 sessions (once a week). The first session was on the 1st of May 2018 (Figure 4; A). She also started on orally Sporanox (itraconazole), 2 capsules twice a day for one week monthly for 3 months.The plan was to start on intralesional pentostam (sodium stibogluconate), but it was not available. (Figure 4; A-D).

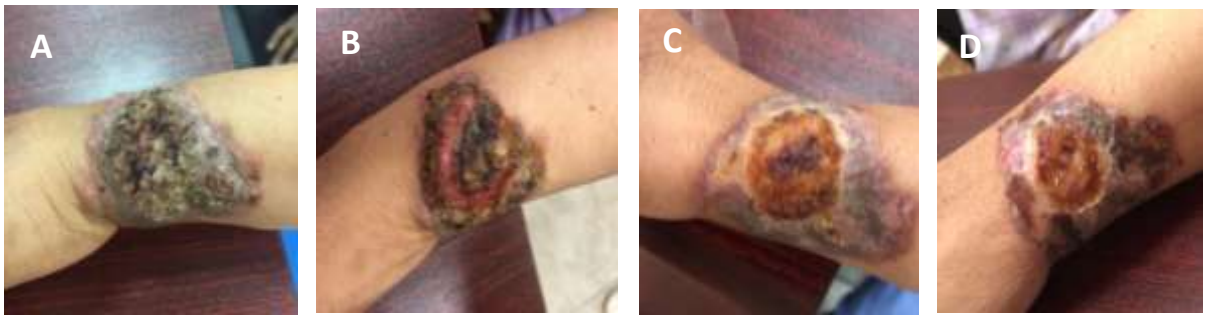

Figure 4:- Cryotherapy sessions.
(A)After the first session on the 9th of May 2018. (B)After the second session on the 16th of May 2018.
(C)After the third session on the 24th of May 2018. (D)After the fourth session on the 29th of May 2018.

Although the plan was to continue the cryotherapy for a few more sessions to get a better result, the patient decided that she was satisfied with the result (Figure 5) and decided to stop the treatment.

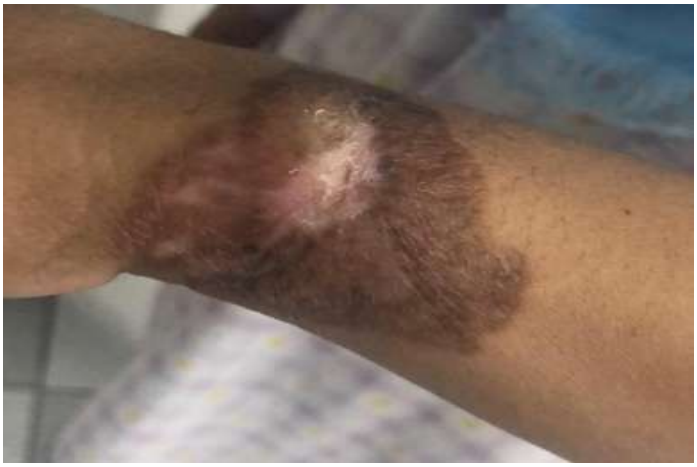

Figure 5:- On 16th of July 2018.
Resolution of the original plaques leaving scar and hyperpigmentation.

Discussion and Review Of Literature:-

Our case is a case of cutaneous leishmaniasis.We chose this case since it was our first interaction with the disease. Our patient was a female, which is unusual in our region as according to a health report published in 1991 in Saudi Arabia, approximately 25% of the reported cases were females [5].

A study published in 1980 in Kuwait stated that cutaneous leishmaniasis is endemic in Kuwait and that attributed to several factors at that time. First, the location of Kuwait in the middle east surrounded by endemic areas of CL, including Iraq, Iran, and Saudi Arabia. Second, the rapid increase in economic activities. Third, the number of travelers and immigrants. Finally, the rapid urbanization and change of ecological conditions and nature of habitat for the sandfly vectors [4].

Nowadays such cases are not commonly seen in dermatology clinics in Kuwait as we mentioned earlier. However, there is no available record. There were no available recent studies generally about Leishmaniasis in Kuwait. But, a recent study in Saudi Arabia, which is considers a similar lesion, showed that the average number of cases between 2006 and 2015, was ~2500/year and ranging between 1464 and 4131 cases. In general, the incidence of leishmaniasis worldwide is 1.5 to 2 million new cases occur every year [1].
Leishmaniasis has three forms: visceral, muco-cutaneous and cutaneous [2,3]. Each one has a different incubation period and clinical features. Visceral leishmaniasis (VL) usually has an incubation period of 3 to 8 months (it can range from 10 days to 34 months). It manifests as fever, weight loss, hepatosplenomegaly, lymphadenopathy,

pancytopenia, hypergammaglobulinemia and sometimes, skin pigmentation.Muco-cutaneous Leishmaniasis (ML) has an incubation period of 1 to 3 months but it may occur many years after the initial cutaneous ulcer has healed and it usually involves the nose, oral cavity, and pharynx which can result in difficulty in swallowing. Cutaneous Leishmaniasis (CL) has incubation period ranges from several months up to 3 years.[2]

In cutaneous leishmaniasis, the lesion starts as erythematous papule at the site of sandfly bite that associated with swelling, a local increase in temperature and sometimes there is pruritus but painless [3].

It usually ranges from 1 to 10 mm in diameter at the beginning then, within a few days, it changes into a vesicle and later into a pustule.

At a pustule stage, it either ruptures spontaneously or by trauma (e.g. scratching), resulting in rounded ulcer with nodular and raised borders.

The base of ulcer shows granulation tissue covered by whitish pseudo-membrane. Sometimes the lesion becomes painful when there is a secondary bacterial infection [3].

The management approach of CL according to recent guidelines begins with establishing the clinical severity of infection either complicated or uncomplicated infection [6,7]. Multiple factors affect the response to the treatment; type of species, host immune response and pharmacological factors [8].

There are two treatment options for CL local therapy and systemic therapy.

The available local therapies are cryotherapy, thermotherapy, intralesional injection of sodium stibogluconate, topical paromomycin and photodynamic therapy. Combined topical therapy specially with intra-lesional pentavalent antimony give a better results.Local cryotherapy can be used alone for uncomplicated, not ulcerated lesions. It also can be used for recently developed lesions, less than three months duration, smaller than 3 cm in diameter, nodular lesions, and patients unfit for systemic treatments [9,10].

Thermotherapy - is a good alternative to cryotherapy for uncomplicated lesions smaller than 25 mm in diameter. Both cryotherapy and thermotherapy can help in healing residual lesions treated by systemic therapy [11].

Intralesional injection of sodium stibogluconate or meglumine antimoniate - is most effective for management of lesions (≤1 cm) caused by CL species not associated with mucosal or lymphocutaneous involvement. Guidelines favor an injection of 0.2 to 5 mL per session every three to seven days, in combination with cryotherapy [7]. A total of five to eight treatment sessions is appropriate or until observation of clinical healing [11].

Topical paromomycin (or aminosidine) - is a topical aminoglycoside cream or ointment that is most useful in treating ulcerative infection of lesions ≤ 5 cm [11].

Photodynamic therapy - generates reactive oxygen species, which interfere with normal cell function and destroys tissues. It consists of administrating a photosensitizing compound that accumulates in the target tissue then follow that with irradiation [11].

Systemic therapies include oral options; azoles and miltefosine, and parenteral options; Parenteral pentavalent antimony, Amphotericin B and Pentamidine isethionate.

Azoles drugs - work by modifying the components of the *Leishmania* parasite membrane [13]. Azoles efficacy depends on species of leishmaniasis.

Ketoconazole is effective in treating CL caused by *L.L. mexicana, L.V. panamensis*, and *L.L. major*. It has significant risks of hepatotoxicity or QT prolongation [13-15]. Whereas Fluconazole works effectively against *L.L. major* in Saudi Arabia, and in higher doses may benefit in *L.L. major* in North Africa and Iraq [11].

Miltefosine - an oral anti-leishmaniasis, alkylphosphocholine, drug; that is active against all three types of leishmaniasis [16]. Miltefosine interacts with parasite membrane components and can inhibit protein kinase B [17]. Miltefosine also interferes with glycosylphosphatidylinositol anchors [17].

It got the FDA approval in 2014 for the treatment of ML, VL, which caused by *L.L.donovani*, and CL that caused by *L.V. braziliensis*, *L.V. guyanensis*, and *L.V. panamensis* for individuals >12 years old. The efficacy of miltefosine varies among different species [11].

Parenteral pentavalent antimony - There are two available agents: sodium stibogluconate (sodium antimony gluconate, Pentostam) and meglumine antimoniate (N-methyl glucamine antimoniate, Glucantime) [18,19]. The pentavalent antimonial drugs affect ATP synthesis and may inhibit glycolysis, affecting fatty acid oxidation [20]. Sodium stibogluconate has effects on *Leishmania*-infected macrophages [21].

Amphotericin B - There are two formulations of amphotericin B used in the treatment of CL: amphotericin B deoxycholate and liposomal amphotericin B (Ambisome). Amphotericin B is a polyene antibiotic; works by increasing parasite membrane permeability resulting in cell death [22].

Pentamidine isethionate - is an alternative parenteral therapy. It is an aromatic diamidine compound; works by interfering with DNA synthesis, causing fragmentation of mitochondrial membranes [23].

Healing of CL is slow and rarely complete. It might continue even after the completion of the treatment.Flattening of the skin lesion is the early and first sign of healing. The first two to three weeks of treatment, some patients may express the paradoxical increase in local inflammatory response. That can be difficult to differentiate from the failure of treatment.

The size of the lesion usually decreases by more than 50 percent after four to six weeks of treatment, and ulcers start healing and re-epithelializing. Edema and inflammation subside with no development of new lesions [24].

In our hospital, we followed the guidelines and started the patient onlocal therapy(cryotherapy) in conjunction with oral systemic therapy (Sporanox). We have also planned to start the patient on intralesional sodium stibogluconate (Pentostam)but it was not available.

Conclusion:-

CL is a purely cutaneous disease caused by a sandfly bite. That seen in Kuwait due to several factors such as the location which near endemic areas, travelers and immigrants, and changes in ecological factors.The main issue in CL is the disfiguring lesions. There are several treatment options available, including local, systemic or a combination treatment depending on the severity of lesions, species of leishmaniasis and host immune response. Recently, healing is better with available therapies. However, complete healing is rare.

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