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Cutaneous leishmaniasis: Review Article

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ABSTRACT

Leishmaniasis is a protozoal infection caused by a number of different species in the Leishmania genus. Sandflies are the vectors for the transmission of these protozoa to humans. When macrophages are triggered into a leishmanicidal state, a clinical recovery occurs. In particular, the T-helper cell type 1 (Th1) response is responsible for this, and it is also responsible for preventing the recurrence of latent chronic infection. Regardless of the disease's clinical manifestation, antimonial drugs are the treatment of choice. Amphotericin B is the second-best treatment option. This study focuses on the pathology and treatment of cutaneous leishmaniasis.

Keywords- *Cutaneous Leishmaniasis* (CL).

I. INTRODUCTION

1.1. Leishmaniasis:

The intracellular, singlecelled, flagellate protoz oa of the type Leishmania are accountable for the disease known as leishmaniasis (order Kineto-plastidae).

There are 21 different types of leishmania that c ause a wide variety of clinical syndromes. These syndro mes can be categorized into three main categories [1]:

- **Mucocutaneous leishmaniasis** (MCL, espundia)
- **Visceral leishmaniasis** (VL, kala-azar-Hindi for black fever)
- **Cutaneous leishmaniasis** (CL oriental sore, chiclero ulcer, Baghdad boil, wet cutaneous sore, uta and other names)[2].

Different strains can be distinguished from one another based on virulence, biologic, epidemiologic properties, and tissue tropism, as well as serologic, and biochemical criteria, Certain species are known to be capable of inducing many disease syndomes omes (e.g., visceral leishmaniasis from organisms of visceral leishmaniasis). In a similar manner, a single clinical disease can be brought on by a variety of distinct agents [24].

1.2. Cutaneous Leishmaniasis:

Cutaneous leishmaniasis This disease is caused by a protozoan that comes in three different varieties, including Leishmania aethiopica, Leshmania Mexicana, and Leshmania brasiliensis. Leishmania ethiopica. In atheopai, leishmania aethiopica are the pathogens responsible for the disease [3].

1.3. Clinical features:

The typical incubation period is two to three months (range 2 weeks to 5 years). A papule grows at the place of the vector bite in all types of CL [4]**.**

Box 1: **Old World cutaneous leishmaniasis subtypes**

Leishmania spp.	Host	Clinical features
L. tropica	Dogs	Slow evolution, less severe
L. major	Gerbils, desert rodents	Rapid necrosis, wet sores
L. aethiopica	Hyraxes	Solitary facial lesions with satellites

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The tiny, red papules can appear singly or in clusters, and their diameters will grow to be between 2 and 10 centimeters over time. A crust covers a granulated ulcer with raised edges (Fig.2.). Ulcers of this type appear several weeks or months after the bite. Infections with L. major and, less frequently, L. tropica can cause satellite lesions (Fig.1.) [5]. Secondary bacterial infections, pain, pruritus, and regional lymphadenopathy have been reported [3] [1].

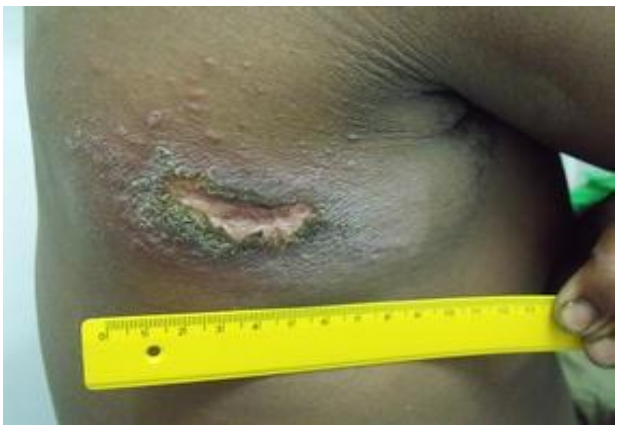

Figure 1: Satellite injuries present in CL. Local dispersion of Leishmania parasites from the chief lesion to the neighboring skin can result in the development of satellite lesions [5].

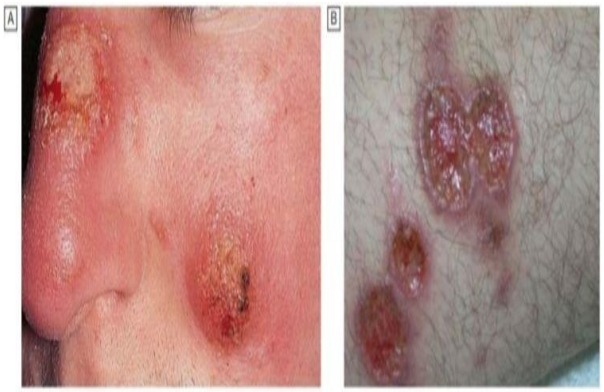

Figure 2: Cutaneous leishmaniasis. A Papule. B Ulcer.

II. LEISHMANIA TRANSMISSION

Most clinical syndromes are brought on by zoonotic parasites that are spread from animals (most often rodent and canine reservoirs) to humans by means of phlebotomine sandfly vectors [6] (Fig.3.A). Major vesicular leishmaniasis hotspots on the indian subcontinent and among injection drug users have a single, consistent reservoir: humans beings (anthroponotic persone- toperson transimmission), [7] (Fig.3.B and C). There are between 0.9-1.3 million new cases of leishmaniasis per year (25% viseral Leishmaniasis), and it is found in about one hundred countries.

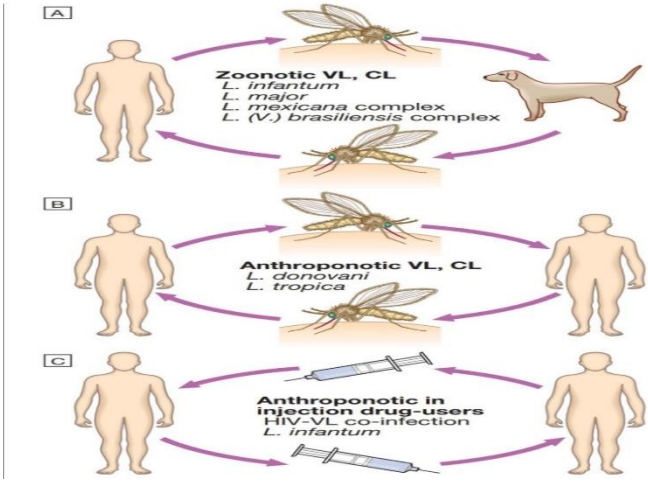

Figure 3: The process by which leishmaniasis is sprea d. A transmission caused by zoonotic agents. B Trans mission through human contact. C Transmission of a nthroponotic pathogens by intravenous drug use. (CL = cutaneous leishmaniasis; VL = visceral leishmaniass) [1].

III. PATHOLOGY

Leishmania's life cycle is depicted in figure5, which can be found here. While feeding, the female sandfly spreads flagellar promastigotes [8], which Rangein size from 10 to 20 micrometers. The promastigotes are ingested byneutrophils, which then undergo apoptosis and are swallowed by macrophages, where they change into amastigotes (2-4 micrometers in length; Leishman_Donovan body) (Fig.4). This multiplies, which leads to the death of macrophages, and cellular infection. Sandflies acquire amastigotes from their hosts once they feed on diseased humans or animal reservoirs [9]. The parasite in the sandfly undergoes a metamorphosis into into flagellated promastigote in the vector's digestive tract, where it multiplies via binary fission, and migrates to the proboscis to infect a new host [4] [1]

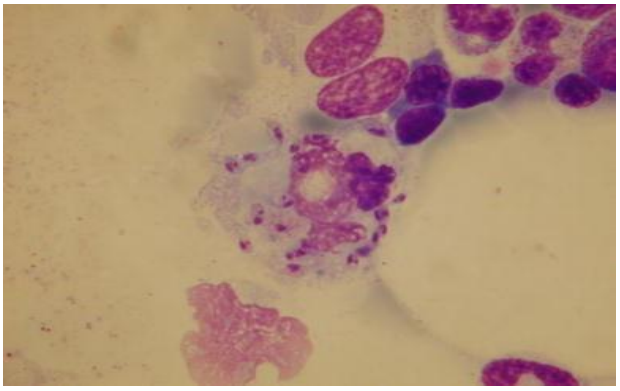

Figure 4: An amastigote form of leishmaniasis. Amastigotes are small, intracellular bodies that can range in size from 2 to 4 m and are easily recognized by their nuclei and kinetoplasts [5].

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However, in cases of diffuse CL, the infection can spread to deeper tissues or reappear in the mucous membranes of nose, the mouth, and pharynx. The sand fly acts as a vector for the sexual reproduction of Leishmania amastigotes, which it picks up when feeding on an infected host and develops into promastigotes. T cells play a crucial role in the immune system's response to CL. In most cases, this causes a varied inflammatory cell penetrate at the place of contamination, with Leishman-Donovan bodies (amastigotes within macrophages) being the greatest prominent. Epithelioid granulomata by little visible parasites characterize more prolonged lesions with an overall immune response [10] . In contrast, a diffuse macrophage infiltrate and many visible parasites characterize more prolonged lesions and a weak immune system. Multiple cytokines have been linked to primary Th1 lymphocyte responses, which are related with superior consequences compared to primary Th2 lymphocyte reactions [5][11]**.** Sandflies lay their eggs in decaying matter, and they prefer warm, humid climates where they can hide in the crevices of mud or straw homes. Those in such settings are at greater risk of developing leishmaniasis. The female sand fly feeds primarily on animals throughout the night, with humans serving as accidental hosts.

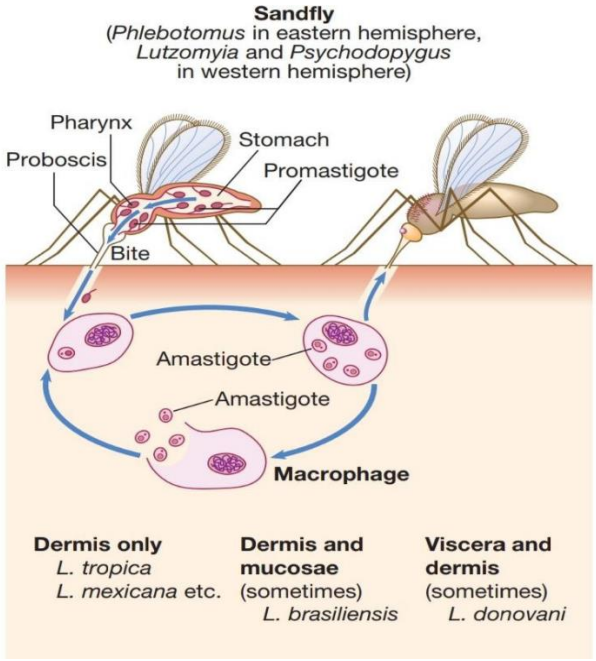

Figure 5. Leishmania's life cycle Parasitic disease in man, according to Knight R. Churchill Livingstone, Elsevier, 1982 [1]

IV. PATHOGENESIS

Pathogenesis is governed by a complicated web of interactions between many components, many of which are set off by the hosts innate, and acquired immunological responses (e.g. neutrophils, macrophages, dendritic cells, natural killer cells)[12]. Dermal lesions are caused by the cutaneous form of leishmania at the point of sandfly inoculation. This includes: Leishmania tropica, leishmania Mexicana, leishmania braziliensis, leishmania major, and others. Before the infection enters the skin, and produces ulceration, the infection affects the dermal layers, causing infiltration of cells, intracellular production of amastigotes, and extracellular spread. Some cases of cutaneous leishmaniasis (the hypersensitivity or recidivans variety) manifest as satellite lesions, which are characterized by the absence of parasites, resistance to treatment, and a severe granulomatous scarring response [24]. Disease manifestation is mediated by inflammatory responses, which can cause asymptomatic or subclinical infection, spontaneously resolving LCL, or chronic leishmaniasis (eg, DCL, leishmaniasis recidivans, and mucosal leishmaniasis). Dermal macrophages consume inoculated parasites [2], where they multiply and serve as a focal point for lymphocytes, epithelioid cells, and plasma cells. Depending on the etiological pathogen, the lesion may heal on its own through macrophage necrosis infection, or chronicity due to ulceration of the skins surface [1]. When macrophages are triggered into a leishmanicidal state, clinical recovery occurs. The T-helper cell type 1 (Th1) reaction is primarily accountable for this effect, and it is also responsible for preventing the recurrence of latent chronic infection. Antigen-presenting CD8+, dendritic cells, and CD4+ T cells that respond, and the production of pro-inflammatory cytokines (such as interleukin-12, interferon-gamma, and tumor necrosis factor-alpha [TNF-alpha]) are the hallmarks of the Th1 response. Th2 reactions are characterized by their ability to downregulate cytokines (e.g. interleukin 4, interleukin 13, interleukin 10, and transforming growth factor [TGF]), thereby deactivating macrophages and preventing the overproduction of protective cytokines [12] [13]. Despite the fact that the Th2 response likely prevents widespread skin damage, it also favors intracellular contamination. The maintenance of a memory cellular response dependent on continuous antigen presentation may be necessary for lifelong protection against reinfection, as evidenced by the identification of live parasites (e.g., Leishmania subgenus Viannia DNA in scars and blood of clinically healed patients) [14][15]and repeated challenges by parasites, most commonly through new bites of infected sand fly vectors. After the primary lesion has healed, recurrence due to repetition of determined infections or trauma is possible [16], and in some cases, additional cutaneous lesions appear in other areas of the body [17]. L. Mexicana pifanoi is responsible for a cutaneous disseminating form in Venezuela. Leishmania aethiopica, endemic to Ethiopia, is responsible for a similarly nonulcerating, blistering, spreading cutaneous leishmaniasis. Large numbers of parasites can be found in dermal blisters in both types, and both are typically anergic and nonreactive to skin test antigen [24].

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V. EPIDEMIOLOGY OF LEISHMANIASIS

Leishmaniasis has a complex epidemiology, that includes not only various parasite species but also parasite strains. The majority of leishmaniasis types are zoonotic. Human involvement varies considerably from region to region [3]. Ninety percent of all cases of cutaneous leishmaniasis (CL) occur in only seven countries: Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia, and Syria [18] [9]. The parasite genus Leishmania is divided into the following categories, according to a European perspective:

- **Old World species:** Three different species of L. from the Old World: L. infantum, L. (L.) major, and L. (L.) tropica (prevalent around the Mediterranean basin, the horn of Africa, the Middle East, and the Indian subcontinent). Most cases of several Old World types result in self-limiting lesions.
- **New World species:** L. (L.) amazonensis, L. (V.) braziliensis, L. (L.) mexicana L, L. (V.) naiffi, L. (L.) chagasi, and L. (V.) guyanensis are all examples of New World species (endemic in Middle and South America). Diseases triggered by New World types are collectively referred to as American tegumentary leishmaniasis. This term encompasses not only CL but also MCL and the extremely uncommon forms of diffuse and disseminated cutaneous leishmaniasis (DCL)[19] [2]**.**

Cutaneous leishmaniasis, also called "oriental sore," is found both in the New World (the Americas), and the Old World (Africa, Asia, and Europe) . The New World form of Cutaneous Leishmaniasis, triggered by the L. mexicana complex, is more severe and can lead to disfiguring scarring of the face, especially around the nose, ears, and mouth (comprising L. mexicana, L. amazonensis and L. venezuelensis). CL is less severe in the Old World. It lives in the Middle East, the Mediterranean basin, and Central Asia up to sub-Saharan Pakistan, Sudan, and West Africa (Fig.6). Travelers from endemic areas of the Old World or Central or South American forests should raise the possibility of cutaneous leishmaniasis in the differential diagnosis of an ulcerating skin lesion.

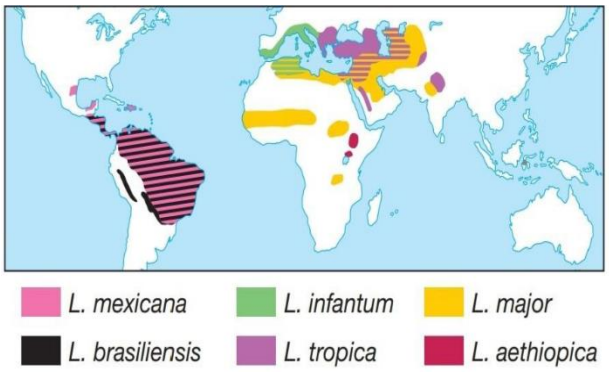

Figure 6: World distribution of cutaneous leishmaniasis [1].

VI. INVESTIGATIONS OF CUTANEOUS LEISHMANIASIS

Clinical features of the lesions are often used to make a diagnosis of cutaneous leishmaniasis. However, because clinical symptoms may resemble those of other infections, parasitological confirmation is crucial. Stained Giemsa smears of slit skin or cultures of early-stage sores reveal amastigotes. L. brasiliensis, the parasite responsible for the vast majority of cases in Brazil, appears to make it particularly challenging to isolate parasites from lesions. In general, touch preparations based on biopsies and histopathology lack sensitivity. Among the many material culture methods, fine needle aspiration has been found to be the most sensitive [1]**.**

VII. TREATMENT OF CUTANEOUS LEISHMANIASIS

In most cases, small lesions will heal by themselves or after being frozen with liquid nitrogen or surgically removed (curettage). An ideal antimicrobial therapy does not exist. treatment of CL depended on the following: Pathogenic organism, Availability of drugs, Intensity of the lesions, Local resistance patterns, and Patient tolerability of toxicity. The available treatments for cutaneous leishmaniasis are as follows:

- Paromomycin 15% and methylbenzethonium chloride 12% applied topically are effective. Patients with cardiac, liver, or renal diseases can safely receive intralesional antimony (Sb 0.2-0.8 mL/lesion up to 2 g), and it appears to be rapidly effective in appropriate cases.
- Multiple or permanently damaging lesions in CL are best treated by parenteral Sb at a dosage of 20 milligram/killogramg/day (normally administered for twenty days for CL), or with conventional or liposomal amphotericin B. Sb is also recommended to prevent the development of mucosal disease if there is any possibility that a lesion acquired in South America was caused by a strain of L. brasiliensis.
- An amphotericin B preparation is recommended for the treatment of refractory CL.
- It's possible that additional treatments will help. To combat Cutaneous Leishmaniasis produced by L. guyanensis in the New World, 2 to 4 doses of pentamidine (2-4 mg/kg) given on alternating days are effective.
- The antifungal drug ketoconazole (600 mg once daily for four weeks) has shown some effectiveness against L. mexicana infections. Fluconazole (200 mg once daily for six weeks) sped up patients' recoveries from CL caused by L. major and cured 79% of them in Saudi Arabia. In India, patients with CL responded well to itraconazole treatment (200 mg once daily for six weeks). [6] [1]**.**

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VIII. DISCUSSION

CL is an inflammatory parasitic disease that causes perivascular infiltration both superficially and deeply, with or without granuloma formation. Seeing Leishmania bodies is a standard clinical diagnosis, this agrees with [20] study. Macrophages show a crucial role in Leishmania infection due to their ability to act as antigen presenting cells, produce molecules that stimulate inflammatory reaction, and potentially kill the parasite, this in agreement with [21] study. Macrophages efficiently eliminate parasites and control parasite growth without tissue damage, whereas macrophages from patients with cutaneous leishmaniasis permit parasite survival and produce inflammatory molecules that stimulate and enlist other cells, resulting in pathology. The mechanisms underlying these findings are not fully understood, but they present a fascinating research topic. The Th1 immune response regulate parasite multiplication and spread in CL, but it does not eliminate the Leishmania infection, this in agreement with [22]. Leishmaniasis treatment should be selected based on several factors, including the presence of a pathogenic organism, the severity of the injuries, the availability of treatments, local resistance patterns the patient's, and acceptance of toxicity. In most cases, simple cutaneous leishmaniasis cures without therapies and confers immunity to subsequent infections caused by a similar parasite species. Antimonial drugs are the therapy of choice. The second-best therapie is amphotericin B, this in agreement with [23] study.

IX. CONCLUSION

Leishmaniasis is produced by a complex interplay between the host, the vector, and the parasite. Cuteneous leishmaniasis patients' macrophages allow parasite survival and produce inflammatory molecules that stimulate and recruit many cells, leading to pathology, whereas healthy macrophages effectively eradicate parasites, and regulate parasite expansion without skin injury. Critical factors in selecting a treatment for leishmaniasis include Patient tolerability of toxicity, the prevalence, and type of local resistance seen in the disease.

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