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Cutaneous leishmaniasis pattern: A Pakistani perspective

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Abstract

Cutaneous Leishmaniasis is a neglected major disease generally in the world and especially in the Eastern Mediterranean region where 57% of its cases occurs. It is particularly present in rural areas of Pakistan. It is known by different local names such as Delhi boil in India, Saldana in Afghanistan and kaal daana in Pakistan. It is caused by single-celled protozoan known as Leishmania. In Pakistan, it is caused either by *Leishmania tropica* or *Leishmania major*. It is called Anthroponotic and zoonotic in former and later cases respectively. It is transmitted from one vertebrate host to another vertebrate host by a female sandfly of genera *Phlebotomus* and *Lutzomyia* in Pakistan. It has diverse clinical manifestation, however, the skin lesion which appears due to the infection of this diseases have some common clinical features. Size, location, number and type of lesion in cutaneous Leishmaniasis varies. Different factors like migration, socioeconomic factors, climate change contribute to the developing of this disease.

Keywords: Cutaneous leishmaniasis pattern, a Pakistani perspective

Introduction

Leishmaniasis is a primary social problem and public health in Mediterranean tropical and sub-tropical region of the world. In developing countries like Pakistan, it is poverty related disease and affects poor people's [1-12]. Leishmaniasis is stimulated by intracellular parasite of the genus *Leishmania* which have 30 contrasting species (20 in New World and 10 in Old World), of which 21 have been identified to be pathogenic to human [19]. Among them 21 are well known *Leishmania* species infect human beings, while 18 have zoonotic nature, which include agents of cutaneous, mucocutaneous and visceral form of the infection in both the New Worlds and the Old. These species are wide range in all continents exclude Antarctica [8]. The parasite of *Leishmania* was first explained in Calcutta by British Major David Cunningham of the Indian Medical service in 1885 from a tissue taken from an ulcer. In 1898, it was reported from the Tashkent military hospital by a Russian Army physician Peter Fokitsh Borovsky. Many well know physician, Ronald Ross consider malaria is a virulent form of kala-azar. It was not until 1903, when British army doctor William Leishman and Captain Charles Donovan independently described the parasite, while examining the spleen during autopsy of a soldier with visceral leishmaniasis (VL) acquired at Dum-Dum, India (hence the name "Dum-dum fever"). The link between these organisms and kala-azar was further explored by Major Ross, who named them *Leishmania donovani* or Leishman- Donovan bodies. In 1904, Leishman and Royers demonstrated that amastigotes turn into promastigotes in cultures and are related to trypanosomes [4].

Epidemiology

Leishmaniasis is one of the most abandoned disease in the world. It commonly disturbs humble people in emergent countries. World Health Organization (WHO) well-thought-out 350 million people at risk of diminishing Leishmaniasis. Cutaneous Leishmaniasis (CL) is one of the forms of Leishmaniasis. It is a skin infection which is caused by a protozoan. It has diverse clinical features, depending upon the causative species and immune response of the host. It is the most common type of Leishmaniasis in Human beside mucocutaneous Leishmaniasis (ML) and Visceral Leishmaniasis (VL). Cutaneous Leishmaniasis is also known by different names such as Jericho boil, Aeppo button, Bouton de biskra, oriental sore, kaal

daana, Ulcer de los chicleore [13, 27]. There are 1 million new cases each year, however, only a small fraction is reported [31]. According to WHO [1] Pakistan is included in the Eastern Mediterranean region. Most of the cases are reported from Afghanistan, Iraq, Iran, Peru, Saudi Arabia, Algeria and Pakistan [4]. This disease is present in all four provinces of Pakistan along with Azad Kashmir [3-33]. Beside this, it is endemic in Multan, Interior Sind and a large part of Balochistan [2-33]. In Pakistan, it is especially endemic in regions adjacent to war thorn neighbouring Afghanistan and with large numbers of refugees [14]. The geographical distribution of Cutaneous Leishmaniasis foci in Pakistan depends on the presence of Sandfly niches and activities that affects these niches [6, 14] animal breeding [1] and Afghan refugees influx [14, 25].

Cutaneous Leishmaniasis is caused by a single cell protozoan parasite called *Leishmania*. Depending upon its presence in the host it exists in two forms known as amastigotes and promastigotes. Amastigotes is a small, rounded and still form which is present in vertebrate host cells while Promastigotes is an elongated motile form that is present in the insect host. Based on its mode of transmission Cutaneous Leishmaniasis is divided into two types anthroponotic and zoonotic. Anthroponotic (also known as urban or dry types) Cutaneous Leishmaniasis is transmitted from human to human while zoonotic (also known as rural or wet types) Cutaneous Leishmaniasis comes from human and animal interaction. In Pakistan both anthroponotic, as well as zoonotic Cutaneous Leishmaniasis is present however later is more prevalent [16, 23]. In Pakistan anthroponotic Cutaneous Leishmaniasis is caused by *Leishmania tropica* (*L. tropica*) while zoonotic by *Leishmania major* (*L. major*) (Bhutto *et al.* 2003). Where *L. tropica* is more prevalent in the urban area, *L. major* is mostly found in rural areas [17].

Classification of leishmaniasis

Leishmaniasis has habitually been divided in triplets, the various scientific forms are; cutaneous leishmaniasis (CL), visceral leishmaniasis (VL) and mucocutaneous leishmaniasis (MCL).

Visceral leishmaniasis

Visceral leishmaniasis, generally known as Sand fly plague, Black fever, Dum-Dum fever, Kala-azar etc., would be the so much far-reaching and tough kind of leishmaniasis really and can be a major reason behind despair and transience, wherein the freeloader invades liver, dislike, and cartilage essentiality [30]. Visceral leishmaniasis, is often because of *Leishmania donovani* convoluted *Leishmania donovani archibaldi*, *Leishmania donovani* (Asia, Africa and Indian sub-continent), *Leishmania donovani infantum* (Latin America, Europe North Africa) and *L.d. chagasi* (America). Occasional cases of VL allow been described to be as a result of *L. tropica* inside the Middle East and *L. amazonensis* in South America. Among many other mammals who can be infected near *Leishmania* species, dogs develop canine visceral leishmaniasis (CaVL) in France and certain other parts of one's world [7, 10, 18]. After infection, promastigotes are internalized by stationery macrophages in spleen, liver and bone marrow. The epidemic is impersonally obvious back of an arrangement cycle of in

general 2-8 months, but flu plus plan cycle as abbreviated as under 2 weeks has been disclosed. A single innovation checked in cases of VL patients within the Indian Subcontinent is hyperpigmentation that may be resulted within the list "Kala-azar" (black fever in Hindi). If not treated VL can be also much at all times incurable and can bring about destruction in 20 months. Death is brought on by severe anemia, hemorrhage, or secondary infection [7, 20, 30]. VL is definitely one of the urbane pollutions a well-known blast HIV-infected individuals. It has a high mortality rate as sharp as 100% if leftist untreated, and is growing in different areas of world owing to intensifying variety of AIDS victims. Approximately 30% of VL patients are guessed at to experience HIV [9].

Cutaneous leishmaniasis

Cutaneous leishmaniasis, generally known as Oriental sore (poach) Aleppo flare, Delhi burn, Chiclero's lesion, Kaldana, Leishmanosa, Saldana, Jericho poach and Mughlai phora. It may be the commonest sort of leishmaniasis attributable to *Leishmania tropica* convoluted (*L. tropica*, *L. aethiopica*, and *L. major*) and *Leishmania infantum* inside the Old World and by *Leishmania braziliensis* complex (*L. guyanensis*, *L. peruviana*, *L. panamensis*, *L. colombiensis* and *L. lainsoni*) and *Leishmania Americana* complex (*L. pifanoi*, *L. Mexicana*, *L. amazonensis*, *L. venezuelensis* and *L. garnhami*) inside the New World [20]. CL is actually an arrange of diseases having a diverse spectrum of objective manifestations, and that cover coming out of limited cutaneous blisters to rough mucosal balance elimination, on a regular basis self-curing inside of 3-18 months, leaving disfiguring scars. *Leishmania* sores tend to be effortless and grow slowly using a granulomatous or smear corrupt and educated margins. Painful sores may hit attributable to bacterial infection. New World CL whichever lines originating skin lesion abrasions mucosal irritation, much accompanied upon resident lymphadenopathy, although Old World CL may today amidst a couple of lesions [30]. Most of one's sores hit on uncovered parts upper limbs, lower limbs, neck, face, forearms, and hands making 89.3% of body parts afflicted. The organisation termination takes coming out of 2-8 weeks as much as a stature of 3 years [10]. The variety of cases has elevated in the course of the past decade because of opportunistic infections with HIV/AIDS and inadequate vector as reservoir control [18]. The extensive of objective manifestations of CL follows

Localized Cutaneous leishmaniasis (LCL): It is in reference to crusted papules or sores whatever crop up a variety of weeks or months the prevention of inoculation of parasite by the bite of sandfly lesions or heal or formed

Diffused Cutaneous leishmaniasis (DCL): It is going from a couple of widespread papules and that start up as a single skin scar. The lacerations don't have ulcerate but having aggregate of spumy macrophages with *Leishmania* parasite.

Recidivans cutaneous leishmaniasis (RCL): It is containing waxing blisters, badge or sequence of bumps which repair amidst paramount scaring [5].



Cutaneous leishmaniasis lesions on hands, leg and face region of patients attending Mohtarma Shaheed Benazir Bhutto hospital Quetta.

Mucocutaneous leishmaniasis

Mucocutaneous leishmaniasis, often known as mucosal leishmaniasis, espundia, or uta, is most ordinarily linked to *L. braziliensis*, but is usually caused by *L. guyanensis*, *L. panamensis*, *L. amazonensis*, *L. major*, *L. infantum* and *L. tropica*. In litigation of MCL parasite expand to skin and result partial or all loss of mucous membranes of nose (most typical station), mouth, thorax cavities and enclosing tissues. The construction stage is often from 1-3 months, however it may strike a few years afterwards the introductory cutaneous ulcer has healed [18]. MCL strike in 1-10% of localized cutaneous leishmaniasis instances, afterwards 1-5 years of

employment. Risk factors for breakthrough to MCL encompass father sex, massive or a couple of lesions, and lesions exceeding the waistline. Clinical manifestations encompass incurable nasal crowding and bleeding, lesionation and septal granulomas. MCL isn't self-cured and might mature and result in durable or severe complications comparable to soreative extinction of nose, tongue, mouth, gums, lips, gullet, oesophagus, larynx, soft and hard palate, nasal septum rupture and frontal malformation, leading to common imputation. It might be accompanied by respiratory disturbances [20, 26].



Patients of Mucocutaneous leishmaniasis

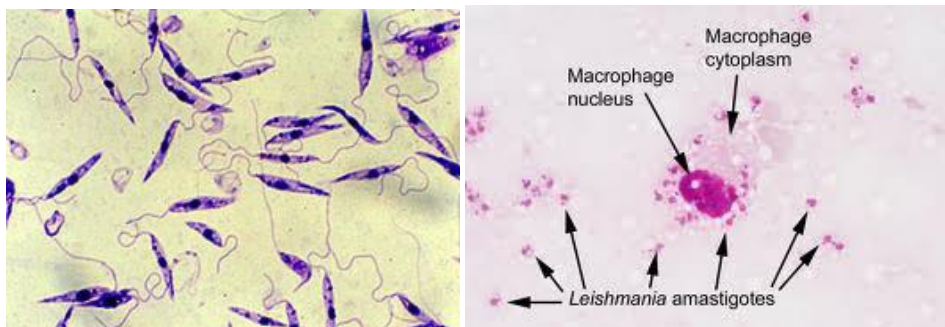
Morphological Forms of Leishmania

Leishmania parasites endure in two the various linguistic forms; the Promastigotes and Amastigotes.

Promastigotes: The promastigotes are motile, extracellular, increased, and flagellated forms; ranging from 10-15 µm in length and located in the gut of sand fly. They possess a paramount nucleus along with a kinetoplast located close to the anterior end [9, 28].

Amastigotes: The amastigotes (Leishman-Donovan bodies) are minor, tour to oblong, obligate intracellular, non-flagellated and non-motile forms; measuring roughly 3-5 µm in diameter and located best within the macrophages of infected vertebrate hosts.

They have a huge nucleus, a popular kinetoplast, as well as a thick axoneme [9, 28].



Amastigote and promastigotes of *Leishmania*

Diagnosis

There are a number of stable characteristic modes for leishmaniasis that are addicted below;

Culture

In this method the *Leishmania promastigotes*, the raised edges of cutaneous lesions are wiped clean, uncontaminated amidst 70% ethanol, along with allowed to dry. A narrow incision is constructed on the cleaned active edge of the lesion, plus a limited amount of one's percolate/scraped stationery is inoculated at the swill step of Novy- McNeal-Nicolle (NNN) art (10% of hare kinship). The society which incubated at 26°C and investigated for parasite production with the help of inverted microscope each and every 4 days in expectation promastigotes are seen, or as much as 7 weeks before throw away as negative [21].

Microscopy

For construction smear, a minor cleft is made within the clean lifted boundary of lesion with all the points of the uncontaminated lancets. The cutter (lancets) is bend 45 degrees and scraped forward the cut margin of the incision to take away and obtain the exudates, that exudates are coat on a glass slide. After drying they're fixed using absolute methanol, allowed to dry then, and stained by Giemsa's stain for microscopic diagnosis [21].

Polymerase Chain Reaction (PCR)

Polymerase chain reaction (PCR) will be the most typical structure for nature special recognition of leishmaniasis usually and will be the so much delicate approach than microscopy and culture. DNA is extracted this one originating at the Giemsa's imprints or from promastigotes on glass slides, isolated amidst check motivation and live agarose gel. It is and then blend upon radio enthusiastic labeled basal specialized for *Leishmania* type [29].

Leishmanin skin test (LST)

Leishmanin verifying test was introduced in 1926 by

Montenegro. It include intradermal management of *Leishmania* antigen followed respectively dimension of indurations. *In vivo*, it is used as an indicator of cell-mediated immunity against *Leishmania* parasites. Leishmanin inoculation within the skin of any person in whom unfounded infection has brought about a expound of cell-mediated indemnity character bring about a delayed-type allergy feeling going from erythematic and indurations at the site of antigen injection after a few hours [21].

Clinical features

The clinical features of CL are very varied it includes atypical morphologies and unusual sites. However, lesions in cutaneous Leishmaniasis showed the following features:

- There is infiltration of the skin to some extent i.e. the skin of lesion or around appears thicker as compared to normal
- They evolve slowly and takes more than 1 week to reach the final size
- Its shape is more or less of a disk or an oval shape
- Their colour appeared abnormal and is mostly dark or red
- Their borders are mostly well demarcated

Beside these common features, different aspects of the lesion in Cutaneous Leishmaniasis is an outcome of an infecting parasite species. Lesion in cutaneous Leishmaniasis caused by *L. tropica* is mostly dry and takes 1 year or longer to heal. It often leaves disfiguring scars. On another hand, lesion in cutaneous Leishmaniasis caused by *L. major* appears as extremely inflamed and ulcerated and takes 2-8 months to heal.

Lesions in cutaneous Leishmaniasis usually occurs on exposed parts of the body like arm, legs, neck and face although it also appears on body parts that are normally well covered such as the abdomen. Moreover, there appears single or multiple lesions. Like appearance, its size also varies and ranges from 0.5 cm to 3 cm in diameter.





Cutaneous leishmaniasis gallery

Major risk factors

Socioeconomic factors

Poverty may contribute to the development of cutaneous Leishmaniasis in a certain area. Poor housing with unhygienic sanitary conditions may favour the breeding of sandfly. Also, living of large numbers of people in the small area may attract sand flies. While houses with cracks wall those made of grass may provide favourable conditions for the breeding of sand flies. On another hand, socioeconomic factors may force a people to migrate from one place to another place which may contribute to another risk factor for developing of cutaneous Leishmaniasis.

Migration

Over the course of time, people do migrate from one place to another place due to several reasons. Epidemics of cutaneous Leishmaniasis may cause due to the introduction of a person from an endemic area to non-endemic area. These migrations may cause threats or transmission of the disease to the area which is previously known to be non-endemic. Introduction of a large number of Afghan refugees to different parts of Pakistan especially Balochistan and Pakhtunkhwa provinces lead to the developing new foci of cutaneous Leishmaniasis in those areas.

Environmental factors

Cutaneous Leishmaniasis is sensitive to climate and develop in a specific environment. Changes in climate such as rainfall, global warming, humidity, atmospheric temperature etc strongly affect cutaneous Leishmaniasis by effecting vectors, host and caustic parasitic species in different ways.

Prevention

Currently no pharmaceutical opposed to leishmaniasis is

obtainable. The handiest precautions are protection opposed to sand fly bite, its eradication as well as abolition of reservoir hosts. Some of the measures are as follows:

1. Reducing breeding places of sand flies feel like crevices, uneven floors, humid, and thatched roof areas containing humus.
2. Screening of doors and windows and use of good mesh mosquito nets having a pyrethroid-containing insecticide.
3. Use of insect repellent admire DEET (N, N-diethyl-metaltolouamide).
4. Reducing outside activities deriving out of dusk to dawn
5. Eradication of sand flies by the use of insecticides sprays sold in market in brand names prefer Baygon, Aldrin, Bop and Mortin.
6. Destruction of burrows of ants and habitats of other reservoir ^[20-24].

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