Leishmaniasis: A forgotten disease among neglected people

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Abstract

Although leishmaniasis is almost unknown in North America, it is an endemic disease to more than 80 countries with a global incidence of 1.5 – 2 million cases each year. In the last decade there has been a significant increase in the number of cases of leishmaniasis in the few countries with previously high rates of infection. There were also hundreds of confirmed cases in the United States, most in military personnel whom had returned from Iraq. With more soldiers travelling to Afghanistan, increased cases will likely return to the United States bringing a need for domestic public health to better understand this disease. In this article we review the epidemiology, risk factors, clinical presentations, pschycosocial impact, and methods of treatment and prevention of the disease.

INTRODUCTION

Leishmaniasis is one of the most neglected tropical diseases with current high worldwide incidence. Caused by a group of protozoan parasites belonging to the genus Leishmania, an infection of the disease usually results with a variety of clinical syndromes, and can lead to death.

In this review we discuss the pathophysiology, epidemiology, risk factors, clinical manifestation, diagnosis, treatment, and psychosocial impact of the disease, along with the existing prevention measures.

PATHOPHYSIOLOGY

Humans become infected by the bite of the female sand fly (the vector). Humans may play a part in maintaining the transmission cycle. Sand flies do not live on or near the sand, as their name would imply. Their primary habitat is in forests, the cracks of stone or mud walls, or animal burrows. The sand fly usually bites at night, and typically flies close to the ground. When sandflies take blood meals from an infected host, they take up macrophages infected with Amastigotes. The Amastigotes transforms into Promastigotes in the midgut of the vector fly. They multiply and finally migrate to the fly's pharynx. The feeding sandfly then clears out its pharynx by expelling Promastigotes into the skin of the host, from where they pass into the blood and tissues of the human host (1).

Rodents and/or canines (wild or domestic) serve as the reservoir for most Leishmania species. Infection due to leishmaniasis occurs as a consequence of the interaction between the mammalian reservoirs, the sandfly vectors and humans.

Promastigotes are phagocytosed into macrophages of the human's reticuloendothelial system, where they shed their flagella and become amastigotes again. Amastigtes multiply by binary fission. The infected cells then rupture, causing the infection to spread to other macrophages, and are then carried throughout the body (2).

Leishmaniasis can cause a wide spectrum of diseases ranging from mild skin involvement to severe systematic disease. This probably relates to differing virulence in the various parasite species, and differing immune responses of the host. Temperature plays a role in determining the localization of leishmanial lesions. Species causing visceral leishmaniasis usually grow at core temperatures, while those causing cutaneous leishmaniasis grow best at lower temperatures (See table 1).

Figure 1

Table 1

Subgenus	Complex	Species	Clinical Manifestation
Old World	L. donovani	L. donovani	Visceral leishmaniasis
		L. infantum	Visceral leishmaniasis
	L. major	L. major	Cutaneous leishmaniasis
	L. tropica	L. tropica	Cutaneous leishmaniasis
	L. aethiopica	L. aethiopica	Cutaneous leishmaniasis
New World	L. donovani	L. chagasi	Visceral leishmaniasis
	L. mexicana	L. venezuelensis	Cutaneous leishmaniasis
		L. amazonensis	Cutaneous leishmaniasis
	L. braziliensis	L. braziliensis	Cutaneous and mucocutaneous leishmaniasis
		L. peruviana	Cutaneous leishmaniasis
	L. guyanensis	L. panamensis	Cutaneous leishmaniasis
		L. guyanensis	Cutaneous leishmaniasis

EPIDEMIOLOGY

Leishmaniasis is endemic to more than 80 countries. Incidence is highest in tropical and subtropical regions where conditions are favorable for sandflies. The overall prevalence of the disease is estimated to be about of 12 million cases worldwide (3). The recent estimates from the Center for Disease Control suggests that approximately 1.5 million new cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis occur worldwide each year (4, 5).

Leishmaniasis in the United States is rare. However, it has been reported in areas near the border with Mexico, such as rural southern Texas. Most of the cases found in the United States are acquired by travelers to Latin America. Most recently, Cutaneous leishmaniasis (CL) has been reported in United States military personnel. More than 500 cases of leishmaniasis were diagnosed over an 18-month period in soldiers returning to the United States from the Middle East, especially from Iraq. Most infections were acquired near the borders of Iraq with Syria and Iran (6, 7, 8).

RISK FACTORS

Leishmaniasis infection is strongly linked with poverty. Risk for infection is mediated through poor housing conditions and environmental sanitation, and lack of personal protective measures. And since poverty is associated with poor nutrition and other infectious diseases, the risk that a person will progress to the more serious stage of infection is very high. Lack of access to healthcare causes delays in appropriate diagnosis and treatment and increases leishmaniasis morbidity and mortality (9).

Sandflies have a short flying range and thus must live close to animal reservoirs for perpetuation of the transmission. An important factor in the increase in disease transmission was population migration from rural areas to cities. In Manaus, Brazil, urbanization has resulted in suburbs being built on the edge of the rainforest, placing human populations in close proximity to animal reservoirs of leishmaniasis (10).

Children are at greater risk than adults in endemic areas (11). AIDS patients have a greater risk of developing visceral leishmaniasis in certain areas (12).

Although leishmanisis is almost unknown in North America, there is a risk for travelers to infected countries. With more soldiers travelling to Afghanistan, increased cases will likely return to the United States, bringing a need for domestic public health to better understand this disease (13).

CLINICAL MANIFESTATION

CUTANEOUS LEISHMANIASIS (CL)

Cutaneous lesions tend to occur on exposed areas of skin. The lesions are painless, centrally ulcerated, and peripherally indurated and erythematous. They usually heal leaving a scar tissue. Lesion size may vary from 1 to 4 cm. The disease could be localized [Localized Cutaneous Leishmaniasis (LCL)] or could be diffuse [Diffuse Cutaneous Leishmaniasis (DCL)].

MUCOSAL LEISHMANIASIS (ML)

Mucocutaneous leishmaniasis (ML) only occurs in Latin America and is mainly associated with L. braziliensis infection. ML is associated with erosive and scarring disease of mucosal surfaces, most commonly affecting upper airways: nose, nasal septum, or mouth (14).

VISCERAL LEISHMANIASIS (VL)

Also known as Kala-Azar, Visceral Leishmaniasis comes about when the disease involves the human's reticuloendothelial system, causing bouts of fever, hepatosplenomegaly, lymphadenopathy, wasting and weakness, and darkening of the skin (thus, the name Kala-Azar or 'black fever'). VL is caused by parasites of the Leishmania donovani complex. Without treatment, the case fatality rate is >90 percent. Mortality is often due to hemorrhagic or infectious complications. The hemorrhage is secondary to infiltration of the hematopoietic system. The infection is a secondary bacterial infection of mucous membranes, bacterial pneumonia, septicemia, tuberculosis, dysentery, or measles (15).

DIAGNOSIS

In CL cases the diagnosis is made by doing a skin aspirate or biopsy of the lesion. The biopsy will show well-formed granulomas containing numerous lymphocytes and few identified amastigotes in Giemsa stains.

In ML or VL, culture is the best way to obtain an accurate diagnosis. Tissue samples can be taken from the lesions themselves, the lymph nodes, or from a bone marrow biopsy (16, 17, 18, 19).

TREATMENT

Depending upon the form of the disease, there are several drug treatments available. These are usually chosen based on the form of leishmaniasis and the infecting species.

Cutaneous leishmaniasis from Old World parasites does not usually need therapy because of their spontaneous resolution. Treatment is indicated for lesions that are large, multiple, progressing, or in cosmetically important areas. Treatment is also indicated for New World disease, especially in countries where L. braziliensis is found (20).

The pentavalent antimony derivatives are the standard recommended therapy for cutaneous and mucocutaneous leishmaniasis (21). Two agents are available: sodium antimonylgluconate (or stibogluconate, also known as Pentostam) and N-methylglucamine antimoniate (or meglumine antimoniate, also known as Glucantime) (22).

Patients with VL should be evaluated for HIV coinfection. In case HIV is diagnosed as a coinfection, VL should be treated aggressively. Agents with efficacy against VL include amphotericin B, Pentavalent antimonial drugs, and paromomycin. Supportive therapy is necessary to address nutritional status, concomitant anemia, hemorrhagic complications, and secondary infections.

PSYCHOSOCIAL IMPACT

CL and ML can leave scars and cause deformities in the infected area. This may cause severe stigma and trauma, especially for children and women. When women have lesions on their faces, they are often put on the edges of society, not eligible for marriage or work. While this is well-documented in Afghanistan, it is likely true in other countries with conservative societies (23).

In certain societies it may also impact educational promotions, and employment. Testimony from infected women also shows that ‘internalized stigma’, displaying shame, embarrassment, and low self-esteem among infected individuals beyond the views of society. Scars are also considered a widespread mark of low social status, reflecting the underlying poor living conditions and uneducated background of individuals likely to become infected, and carry with them a social stigma.

In some traditional societies there is also a common belief that leishmania is contagious. This may have an extreme negative impacts especially on children, as they are prevented from attending school and stigmatized in their communities. In addition, families have been documented to isolate their children from siblings to stop further spread of the infection.

PREVENTION

The most important action individuals can do is to try to minimize the amount of exposed skin by wearing long-sleeved shirts, long pants, and socks, and/or to use insecticide every night.

Sand flies are very small and they can pass through a standard mosquito net; however, if the net is impregnated with permethrin it will usually be effective in preventing the flies from going through it.

Ideally, an improvement of urban living conditions and environmental hygiene, especially for the urban poor, could do much to decrease the transmission of disease. Awareness campaigns to combat the strong perceptions and associations linking the disease to poverty and low social status would be an important first step in decreasing the current rates of stigmatization and marginalization of infected groups.

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