Leishmaniasis: Its Changing Pattern and Importance as an Imported Disease

During the past few decades, the parasitic diseases such as leishmaniasis, malaria and trypanosomiasis have not been considered priority public health problems or to be of medical importance in Japan and in other developed countries. Therefore, such diseases were sometimes relegated to the status of simply an academic curiosity in these countries, and few physicians or parasitologists felt the need to understand the details of the diagnostic procedures and treatment regimens associated with these parasitic infections. Recently, however, increasing worldwide travel has raised the numbers and a variety of parasitic diseases have been imported into non-endemic areas of the diseases. In such a circumstance, imported cases of a variety of parasitic diseases should be adequately diagnosed and treated by knowledgeable medical personnel. Here, the changing pattern of leishmaniasis and its importance as an imported disease are briefly discussed in order to stimulate the interest of medical personnel in the field of parasitic diseases.

See also p 502.

Leishmaniases are caused by a unicellular organism of the genus *Leishmania*, and transmitted by phlebotomine sandflies, the genus *Phlebotomus* in the Old World and the genus *Lutzomyia* in the New World. There are at least 20 different species of *Leishmania* that cause human infections (1). The protozoan parasites, *Leishmania* spp., produce a wide range of clinical infections in both humans and vertebrate animals as zoonosis. In humans, clinical leishmaniasis ranges from a simple, often self healing cutaneous form to those producing destructive mucocutaneous ulcers of nasopharynges, uncurative diffuse cutaneous lesions, and a visceral form known as kala-azar, the severe chronic infection of the reticuloendothelial system, which is often fatal if left untreated. The disease is endemic in many tropical and subtropical regions, and is classified as one of the six tropical diseases targeted by the World Health Organization (WHO) for study by the Tropical Disease Research Programme (TDR). It is estimated that there could be some 12 million infected people in the world, and 370 million at risk, of whom some 0.4 to 1 million will be infected each year in 67 countries affected (2, 3). Some 90% of the visceral leishmaniasis cases are reported from two regions, a wide zone in northeast India, Bangladesh and southern Nepal, and Sudan; and 90% of the cutaneous cases including mucocutaneous and diffuse ones are found in Afganistan, Iran, Saudi Arabia and Syria in the Old World, and Brazil and Peru in the New World (2, 3).

In non-endemic areas of leishmaniasis such as Japan or U.S.A., most people have never heard of the disease. Moreover, because many physicians in non-endemic areas of the disease are usually unfamiliar with such a parasitic disease, they may not consider leishmaniasis even if their patients have traveled to the endemic areas. In this respect, it is relevant that in the current issue of the Journal, Kawakami et al (4) report a visceral leishmaniasis misdiagnosed in Boston, MA, U.S.A. as malignant lymphoma; this is an important case from India, firstly imported to U.S.A. and then to Japan. According to Kawakami et al, in this case (30-year-old Japanese female), the findings of fever of unknown origin, hepatosplenomegaly, leukopenia, increased serum lactate dehydrogenase and erythrocyte sedimentation rate and the presentations of liver and bone marrow biopsy might have led the U.S. physicians to the misdiagnosis. Furthermore, they commented that administration of prednisone after splenectomy might have concealed the clinical manifestations such as high grade fever, splenomegaly and hypergammaglobulinemia. They also commented that the administration of prednisone have resulted in active proliferation of *Leishmania* parasites accelerated by humoral and cellular immunosuppression. In patients who are immunosuppressed by immunosuppressive agents or who are co-infected with HIV, both the diagnosis and treatment are especially difficult (5). In such an "exotic" disease like leishmaniasis, furthermore, therapy only aimed at symptomatic relief makes it more difficult to make a definitive diagnosis without the knowledge or interest on imported parasitic diseases as pointed out by Kawakami et al (4).

Since the mid-1980s there has been a dramatic increase in the number of leishmanial infections in HIV-positive patients concurrent with the spread of the viral epidemic to areas traditionally endemic for leishmaniasis in the world (6). In Europe, for example, especially in Spain, Italy and France, leishmaniasis is a growing problem with several hundreds of HIV co-infection cases (5). Similar problems are frequently reported from India, Bangladesh and Nepal where the severe visceral leishmaniasis is highly prevalent (3). Thus, visceral leishmaniasis is now established as an HIV-associated infection. Usually, in these patients, clinical manifestations are unusual and diagnosis difficult, showing atypical secondary localizations in the gastric mucosa, rectum or skin, either in lesions or in normal tissue (6); these patients need prolonged treatment and are liable to relapse (7). In Spain where the disease has been a compulsorily notifiable disease since 1982,

almost 80% of the Spanish visceral leishmaniasis cases were immunodepressed patients, 60% of whom were HIV-positives and the rest were basically divided between haematological disorders of the white blood cells, transplants, autoimmune disease and alcoholic hepatopathies (8, 9). In the endemic area of leishmaniasis of southern Europe, intravenous drug abusers, who represent 60% of the HIV-positive cases, operate in periurban areas, where the drug traffic is uncontrolled. Therefore, the opportunity for both diseases, HIV and leishmaniasis, to overlap in these areas is optimized (9).

Recently, a retrospective study was undertaken to characterize the U.S. travelers who acquired cutaneous leishmaniasis in the Americas and to highlight problems they encountered in seeking medical care from U.S. physicians (10). It was reported that patients consulted from one to seven physicians (mean, 2.1 physicians) before leishmaniasis was diagnosed. In the situation of increasing worldwide travel, it was emphasized that travelers to the endemic areas and medical personnel in developed countries need to be aware of the risk of infections, preventive measures and appropriate medical management of leishmaniasis and other parasitic diseases.

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