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Case Report

Diffuse Cutaneous Leishmaniasis Caused by *Leishmania major* as the Initial Presentation of HIV Misdiagnosed as Scabies and Kaposi's Sarcoma: A Case Report

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Abstract

Diffuse cutaneous leishmaniasis (DCL) is a rare and severe form of cutaneous leishmaniasis (CL), particularly uncommon in Uzbekistan. Leishmaniasis remains a major opportunistic infection in immunocompromised individuals, especially in those with HIV, where co-infection with *Leishmania* spp. can result in atypical clinical manifestations, delayed diagnosis, and poor treatment response. This is a retrospective descriptive case report of a single pediatric patient. We report the first known case of DCL in an HIV-infected pediatric patient in Uzbekistan. A 14-year-old boy presented with multiple, non-ulcerative, progressively worsening skin lesions on the face and extremities over six months. Although he had no travel history to known endemic areas, he resided in a region with reported local transmission. Physical examination revealed extensive infiltrative plaques and nodules. Laboratory investigations, including Giemsa staining and PCR, confirmed *Leishmania* infection. Histopathological analysis showed both intravascular and extravascular amastigotes, and species identification revealed *L. major*. Imaging ruled out visceral involvement. Given the patient's immunosuppressed status and the disseminated skin involvement, a diagnosis of DCL was established. Liposomal amphotericin B was initiated as first-line therapy. This case illustrates the diagnostic complexities of leishmaniasis in HIV-positive patients, where initial misdiagnoses (e.g., scabies or Kaposi's sarcoma) may delay appropriate treatment. It highlights the critical need for heightened clinical suspicion, better diagnostic tools, and improved physician awareness in endemic and emerging transmission areas. In the context of rising HIV rates and growing domestic tourism to endemic zones, early screening and structured public health interventions are essential to reduce disease burden and improve patient outcomes in Uzbekistan.

Introduction

Leishmaniasis is a vector-borne disease caused by obligate intracellular protozoan parasites from more than 20 species of *Leishmania*. It is classified into cutaneous leishmaniasis, diffuse cutaneous leishmaniasis, mucocutaneous leishmaniasis, and visceral leishmaniasis (kala-azar) (1). The disease is transmitted through the bites of infected female sandflies of the genus *Phlebotomus* in the Old World and *Lutzomyia* in the New World (2).

Leishmaniasis is endemic in more than 90 countries worldwide. Approximately 1 million new cases are reported annually, primarily in Brazil, Ethiopia, India, Kenya, Somalia, South Sudan, and Sudan (3). The disease causes 20,000 to 40,000 deaths per year (4). Uzbekistan is an endemic country for leishmaniasis, with the Fergana Valley in the east and central and southern regions being the most affected areas of the country (5-7).

According to statistics from the official WHO website, 6,781 cases of cutaneous leishmaniasis (CL) and only 464 cases of visceral leishmaniasis (VL) were reported between 2011 and 2020 (8, 9). However, the incidence and prevalence of the disease are likely higher than reported due to low levels of awareness among healthcare providers, a lack of diagnostic tools, misdiagnosing, and the underreporting or nondisclosure of diagnosed cases to healthcare agencies.

Cutaneous leishmaniasis is caused by over 20 *Leishmania* species with distinct geographic distributions. In the Old World regions (Mediterranean, Asia, Middle East, and Africa), the predominant species include *L. major* (zoonotic), *L. tropica* (anthroponotic), *L. aethiopica*, and *L. infantum*. In the New World (Central and South America), *L. mexicana*, *L. braziliensis*, and *L. guyanensis* are most common (10). DCL is a rare disease, typically caused by *L. aethiopica* and *L. major* in the Old World (11) and *L. amazonensis* and *L. mexicana* in the New World (12). Comparable atypical cases of disseminated cutaneous leishmaniasis in HIV-infected patients have been documented in neighboring Iran, where Hajjaran et al. described four patients whose nodulo-infiltrative lesions closely resembled those in our report (13).

The only case of DCL in Uzbekistan was diagnosed in 2021 at the State Scientific Center of Dermatology and Cosmetology (SSC DC) under the Ministry of Health of Russia (14).

Skin lesions in DCL are characterized by widespread, non-ulcerative nodules that progressively spread across the body. In immunocompromised patients, such as those with HIV, the disease resembles the lepromatous form of leprosy, is often more extensive, resistant to treatment, and prone to chronic persistence**,** making management particularly challenging (15).

This report describes a 14-year-old patient with HIV who initially presented with symptoms resembling scabies but was later diagnosed with DCL.

Case Presentation

A 14-year-old boy was brought to the clinic by his parents with complaints of widespread nodular rashes. The rashes were distributed across the forehead, cheeks, perioral and perinasal regions, elbows, dorsal aspects of the hands, palms, fingers, gluteal region, knees, dorsal surfaces of the feet, and toes. Mild pain was reported in the affected areas (Fig. 1).

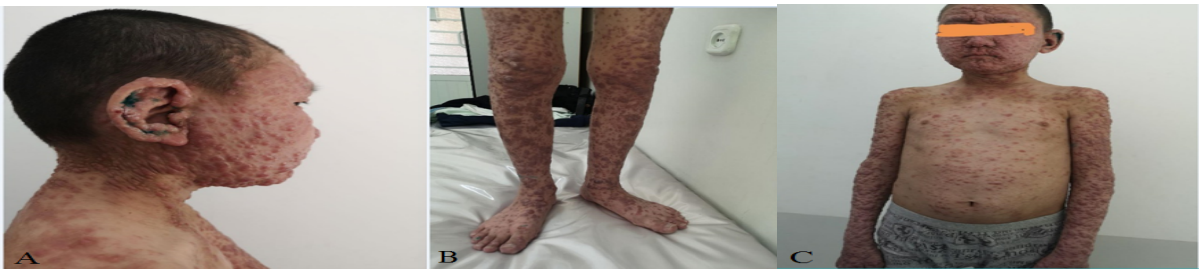

Fig. 1: Diffuse Cutaneous Leishmaniasis lesions in an HIV Patient: (A) Facial Lesions, (B) Lesions on Lower Limbs, (C) Lesions on Abdomen and Chest

The patient was born in the Jizzakh region, an endemic area for cutaneous leishmaniasis in Uzbekistan. He has never moved or traveled to other countries, including neighboring Asian nations. He received all recommended vaccinations, including essential, age-appropriate, and routinely administered immunizations, ensuring broad protection against preventable diseases. There is no history of blood transfusions or invasive procedures.

The patient's condition began in June 2021, initially appearing on both palms without any specific cause identified. After a while, symmetric rashes appeared on the elbow areas, accompanied by intense itching. The mother contacted the local clinic, and the patient was diagnosed clinically with "Scabies" and prescribed sulfur ointment and Permethrin cream (5%), but no injections were administered. The rashes on the palms, fingers, and elbows wholly healed, leaving behind hyperpigmented spots.

In November 2021, nodular rashes reappeared on the face, palms, elbows, buttocks, knees, and dorsal surfaces of the feet. Initially, the lesions presented as smooth, raised, flesh-colored papules and nodules, symmetrically distributed on both upper and lower extremities. Over time, the lesions progressively increased in number. The patient sought medical attention at the local clinic and was subsequently referred to the AIDS center for further evaluation. HIV testing, including antibodies to HIV-1/HIV-2 (Tridot; J.Mitra & Co., New Delhi, India) and p24 antigen detection by ELISA returned a positive result, and antiretroviral therapies (dolutegravir, Tenofovir alafenamide, and Lamivudine) were prescribed. After being diagnosed with HIV, the patient was referred to the Republican Specialized Scientific and Practical Medical Center of Dermatology, Venereology, and Cosmetology, and a skin biopsy was obtained in the clinic to identify the underlying cause. The patient was initially misdiagnosed with Kaposi's sarcoma**,** a common neoplasm in HIV-positive individuals. The presence of multiple infiltrative skin nodules and vascular proliferation on histology likely contributed to this diagnostic confusion. The patient was advised to undergo chemotherapy; however, the recommended treatment was delayed due to the COVID-19 pandemic.

At the time of presentation to our clinic, the patient's general condition is moderately severe, with clear consciousness. All vital signs and physical examination were normal. Skin examination showed symmetrical, chronic inflammatory nodular lesions on the face, hands, gluteal region, lower extremities, auricles, neck, torso, genitals, and upper extremities. These nodules ranged in size from 0.3 to 2.0 cm, were round, and varied from pinkish-flesh-colored to brownish. Badirzadeh et al. subsequently reported the first mixed *L. major*/*L. infantum* coinfection in an HIV-AIDS patient, underscoring the possibility of dual-species dissemination and the diagnostic complexity it creates (16). They had smooth, shiny surfaces with well-defined borders and a dense consistency. On the face, numerous eruptions were noted along with diffuse infiltration and pronounced skin folding, forming a "lion face" (facies leonina). Lesions on the gluteal region exhibited scaling and crusting. Palpation revealed no tenderness or discharge from the nodules, and sensory functions over the lesions, including temperature, pain, and tactile sensitivity, were intact.

Early differential diagnoses included sarcoidosis, disseminated cutaneous lesions of secondary syphilis, leprosy, histoplasmosis, and cutaneous tuberculosis.

A laboratory investigation was conducted to detect syphilis, toxoplasmosis, cytomegalovirus, hepatitis B and C. Tests included an anticardiolipin test, detection of antibodies to *Treponema pallidum* using the passive hemagglutination assay (PHA), total antibodies to hepatitis C virus (HCV) by ELISA, HBs-antigen by ELISA. Laboratory investigations revealed anemia (hemoglobin: 8.6 g/dL) and lymphopenia (20% of total white blood cells). Monte-

negro test for leishmaniasis was unavailable, but the Mantoux test for tuberculosis (TB) was negative. All other investigations, including liver and renal function tests, chest X-ray, and ultrasonography (USG) of the abdomen, were found to be normal.

Oral consent was obtained from the patient's parents for the skin biopsy to be performed on the lesions again. Punch biopsies were obtained from multiple body regions, including the upper and lower extremities, trunk, gluteal areas, and face. Microscopic examination hematoxylin and eosin (H&E) revealed numerous *Leishmania* (amastigotes) both intracellularly in macrophages and extracellularly (Fig. 2). Tissue samples were sent to the Research Institute of Microbiology, Virology, Infectious and Parasitic Diseases for Polymerase Chain Reaction (PCR), which released the organisms as Leishmania major.

Molecular species identification**:** DNA was extracted from paraffin-embedded biopsy tissue and the *Leishmania* ITS-1 locus was amplified with primers LITSR / L5.8S using a standard 35-cycle PCR protocol. The resulting ~320 bp product was visualized on 2% agarose, purified, and Sanger-sequenced. BLAST analysis showed 99.8 % identity to *L. major* (GenBank MHOM/IR/2014/LJ2014). A reference *L. major* DNA sample served as the positive control; water blanks were negative in every run, confirming assay specificity. The epidemiological history, clinical presentation, PCR result, and laboratory findings, including microscopic and histological studies, established the diagnosis of DCL.

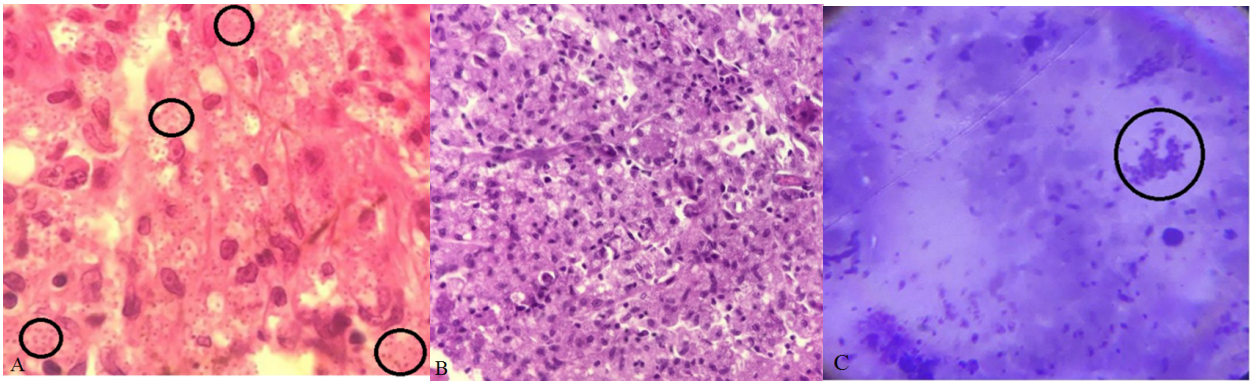

Fig. 2: Histopathological images of leishmaniasis at different magnifications. A. High-power view (×400, H&E): multiple amastigotes visible within macrophages (circled areas). *(Note: taken at ×400; oil-immersion ×1000 not available).* B. Low-power view (×200, H&E) showing numerous intracellular *Leishmania* amastigotes within macrophages. C. Giemsa-stained smear of skin lesion (×400): clusters of Leishmania amastigotes are visible within macrophages, though finer structural details (kinetoplasts) are not well resolved at this magnification

Considering this patient's clinical features, diffuse dissemination of lesions, the presence of HIV infection, and PCR confirmation of Leishmania major, Liposomal Amphotericin B was prescribed at a dose of 4 mg/kg/day IV on days 1–5, 10, 17, 24, 31, and 38 (10 doses over 38 days), for a total dose of 40 mg/kg. Additionally, fluconazole (200 mg daily for 6 weeks) was included as adjunctive therapy due to its potential antifungal and immunomodulatory effects**,** which may help suppress secondary fungal infections in immunocompromised patients (17). Depending on the patient's response to the initial treatment, adding a pentavalent antimony compound (glucantime) was planned as a further treatment option. After five doses of liposomal amphotericin B (total 40 mg/kg) lesions softened, erythema faded, and no new lesions appeared. Renal function stayed stable. One infusion-related

fever (38.2 °C) subsided with paracetamol. Follow-up beyond day 38 was not possible.

Discussion

Cutaneous leishmaniasis is the most common form of leishmaniasis in Uzbekistan. The clinical case of DCL in an HIV-infected patient described in this report is the first of its kind to be diagnosed in the Republic of Uzbekistan.

Several healthcare professionals conducted a retrospective research analysis in 2022 to determine the geographical distribution of the disease (18). An analysis of the disease incidence rates across different regions revealed that most cases were recorded in the central and western areas of the Republic, accounting for 165 (85.9%) and 22 (11.5%) patients, respectively. In contrast, the eastern region reported only sporadic cases, with 5 (2.6%) patients identified. Notably, some individuals in this region had previously visited endemic zones. Most cases were concentrated in the Kashkadaryo, Surkhandaryo, Bukhara, and Jizzakh regions, which are highly endemic areas. The ongoing intensive development of previously uncultivated lands in these regions has led to increased epidemic activity in the natural foci of the disease. A retrospective analysis of medical histories and outpatient charts revealed that the urban type of the disease was documented in 21 patients (10.9%). In comparison, the rural type was observed in 171 patients (89.1%), indicating that the disease vectors are predominantly found in rural areas. Emerging Iranian data also show rising visceral-cutaneous coinfection rates among HIV-positive cohorts (Shafiei et al.), reinforcing the need for regional cross-border surveillance and early screening protocols (19).

Leishmaniasis is the third most common parasitic infection after toxoplasmosis and cryptosporidiosis in HIV-infected patients (20). Consistent with our observations, Jafari et al. documented disseminated lesions due to *L. tropica* in Iranian HIV-positive patients, demonstrating that profound immunosuppression facilitates widespread cutaneous involvement regardless of species (21). It is the primary systemic opportunistic infection along with toxoplasmosis in HIV-infected patients (22). However, due to its prolonged latent period, leishmaniasis is often overlooked in favor of other opportunistic infections associated with immunosuppression (23). Diagnostic steps such as histopathological examination, PCR testing, and serological tests can help differentiate leishmaniasis from these other conditions and improve early diagnosis. Without timely therapy initiation, the prognosis for patients with DCL is unfavorable (11).

To improve patient outcomes and prevent further cases, healthcare providers in Uzbekistan must improve their awareness and recognition of leishmaniasis, particularly in immunocompromised patients. Recommendations for public health authorities include the development of national guidelines for diagnosing and treating leishmaniasis, along with targeted training sessions for healthcare professionals. These initiatives could help ensure that leishmaniasis is recognized and treated early, reducing misdiagnosis and improving prognosis. Public health campaigns aimed at raising awareness in endemic regions and among tourists and pet owners could also play a vital role in controlling the spread of the disease.

Conclusion

Diffuse cutaneous leishmaniasis may be an early manifestation of HIV infection, often mimicking other dermatologic conditions. Enhancing physician awareness and public health initiatives is critical to improving early diagnosis and prevention, particularly in vulnerable populations.

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Conflict of Interest

Non-declared

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