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A Case of Unhealing Skin Ulcer with Iatrogenic Cushing's Syndrome

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Abstract:

Cutaneous Leishmaniasis is a rare disease in South-East Asian countries like Bangladesh, often presenting as skin lesions, ulcers or granulomatous plaques on the arm or back. As the disease is uncommon, high index of suspicion is required for the diagnosis. We are presenting a case of cutaneous Leishmaniasis in a migrant Bangladeshi worker in the Kingdom of Saudi Arabia (KSA). The case was initially treated with antibiotics, emollients and systemic steroid for a long time. However, the disease progressed, and the patient developed features of iatrogenic Cushing syndrome. The diagnosis was confirmed with a skin biopsy, which revealed Leishmania parasite. He received treatment with Injectable liposomal Amphotericin B (LAmB) and oral Miltefosine with promising clinical response. Clinicians should be vigilant while treating non-healing ulcers, and consider CL when there is history of travelling to CL endemic areas.

Keywords: Cutaneous Leishmaniasis, Cushing syndrome, LD body, Bangladesh

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Introduction:

Bangladesh is considered an endemic country for visceral leishmaniasis, which Leishmania DonovaniLeishmania Donovani causes causes. Cutaneous leishmaniasis (CL) caused by *Leishmania major/ Leishmania tropica* is rare in south Asian countries like Bangladesh because of the absence of its vector. CL cases are imported into our country from different endemic countries. Therefore, diagnosis of CL is difficult in non-endemic countries like Bangladesh[2]. However, in endemic countries, clinical diagnosis is straightforward. Possible differential diagnosis of cutaneous leishmaniasis could be mycobacterial infection, deep fungal infection, malignancy or autoimmune skin diseases[3]. In Bangladesh, where tuberculosis is more prevalent, cutaneous leishmaniasis is very likely to be mistreated as cutaneous tuberculosis, especially lupus vulgaris[4]. Another problem of this rare case might often lead to different diagnoses like autoimmune disease and result in long-term prescription of steroids, causing harmful side effects like iatrogenic Cushing's syndrome. Here we present a case of cutaneous Leishmaniasis in a migrant worker who returned from the KSA and developed iatrogenic Cushing syndrome due to long term steroid therapy.

Case Report:

A 36-year-old man, a migrant worker in the Kingdom of Saudi Arabia (KSA) for five years, was admitted to our hospital with a history of two non-healing ulcers on his left arm and around his left elbow for 22 months accompanied by features of Cushing syndrome. The patient stated that he was working in a garden of date palm in KSA, where flies bit him in several times. He noticed that, following the fly bite, there was the an itchy skin lesion over his left elbow and another lesion developed over the left arm. Both the lesions gradually became reddish and papular, which ultimately converted into ulcer. He consulted a dermatologist in KSA and took several oral and topical medicines without any improvement. When his disease aggravated, he was sent back to Bangladesh. In Bangladesh,, he initially saw several physicians. He took other oral and topical antibiotics, anti-fungal drugs, and a 3-month course of oral prednisolone in a dose of 20 mg/kg. There was no

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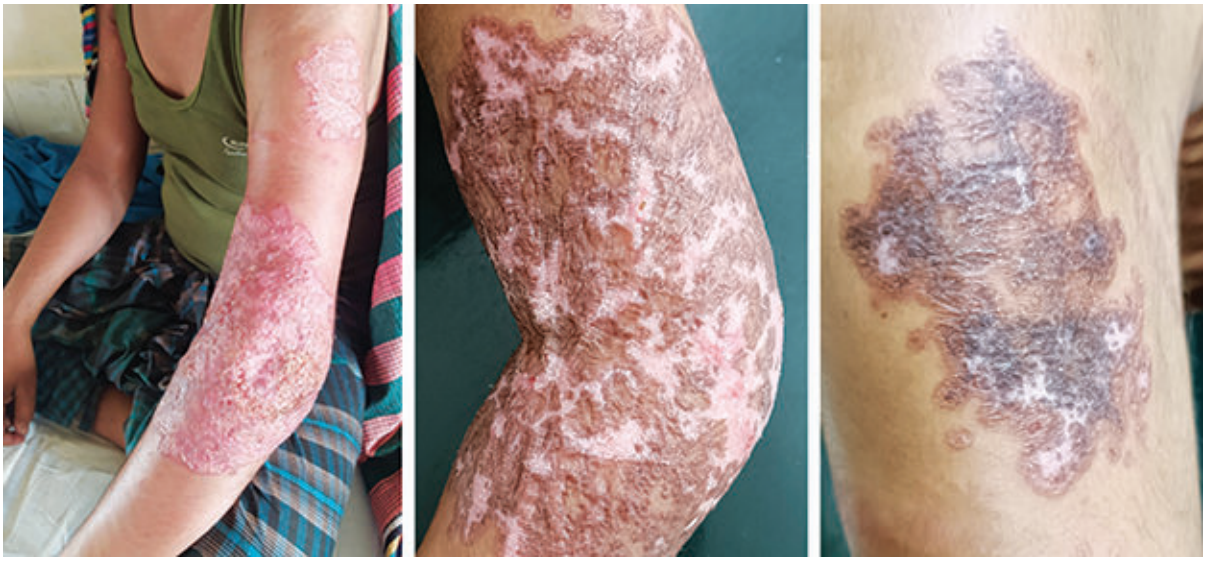

Fig.-1: *A. Before treatment, elbow & Arm, B. After treatment, elbow, C. After treatment, arm*

significant improvement of his ulcer instead the patient developed features of iatrogenic Cushing syndrome, including central obesity, abdominal stria, and weight gain. There was no history of fever, joint pain, weight loss, bowel abnormality, contact with smear-positive pulmonary tuberculosis patient or unsafe sexual exposure. At this stage in August 2022, he was admitted in our hospital. We found two large non-healing ulcers over the left elbow and left arm (Fig:1A). Ulcer floors were erythematous, covered with unhealthy granulation tissue, the base was mildly indurated and non-tender. He was hemodynamically stable with features of Cushing syndrome. There was no lymphadenopathy, no organomegaly, and other part of the skin, including genitalia, was normal. His routine haematological and biochemical investigations were regular. Basal cortisol level was 4.4 nmol/L (Normal value: 100-450 nmol/L). A short synaesthete test was compatible with adrenal insufficiency. A total thickness skin biopsy from both the ulcer was taken, and histopathology report revealed features of cutaneous leishmaniasis with the presence of intracellular and extracellular Leishmania parasites (Fig 2). He was put on a physiological dose of prednisolone (7.5 mg/kg body weight daily). Injection LAmB was given in an amount of 21 mg/kg body weight in five divided doses in at interval of 2-3 days, followed by oral Miltefosine 100 mg daily for the next three months. He was followed up monthly,, and the ulcer was significantly improved (Fig 1B & 1C). Features of Cushing syndrome also gradually disappeared.

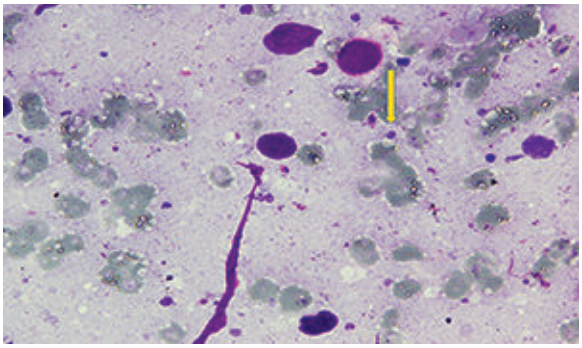

Fig.-2: *Leishmania parasite*

Discussion:

Cutaneous leishmaniasis is a chronic protozoan skin infection caused by more than 20 Leishmania species. It primarily involves the mononuclear phagocytic system but can also affect the skin. Female sand-flies transmit it and it is endemic in the European Mediterranean basin[5]. Diagnosis of CL in immunosuppressed patients can be challenging because of its clinical pleomorphism, which depends mainly on the host immune response rather than the parasite species. That leads to misdiagnosis of CL with inflammatory and malignant conditions. CL diagnosis is also challenging in countries like Bangladesh, where many infections like tuberculosis

and deep fungal infections are endemic, which quickly creates confusions with other infectious diseases[6,7].

Leishmaniasis has an extensive geographical distribution. It is prevalent on all four continents and considered endemic in 67 countries of the Old World and 21 countries of the New World, including Bangladesh, Brazil, Afghanistan, Iran, Saudi Arabia, Peru, Sudan, and India[8,9]. Leishmaniasis in the Old World is endemic in the Mediterranean Sea and the neighbouring countries. The annual incidence worldwide is about 400,000 cases, with a prevalence of approximately 350 million people infected[10]. Tourists and workers from endemic areas have an increased incidence of CL. CL is mainly imported to endemic countries by immigrants and returning travellers. Patients with non-healing skin lesions and a travel history to an endemic region should be considered for CL. Diagnostic confirmation may be made by culture but is principally achieved by direct microscopic detection of Leishmania amastigotes in skin biopsies; serologic testing is unreliable. With high-level specificity for Leishmania DNA, polymerase chain reaction (PCR) testing of lesion specimens is particularly useful when parasite burden is low and is currently the most accurate method of diagnosis in CL[11]. The management of CL has not been standardised, although attempts are now being made by European investigators[12–14].

Our patient suffered from two non-healing ulcers for about two years before its diagnosis. Moreover he developed iatrogenic Cushing syndrome from inappropriate steroid therapy. A high index of suspicion is required for provisional diagnosis[15]. CL should be considered in any case of chronic non-healing ulcers especially if there is a travel history to endemic countries. Delayed diagnosis not only increases the sufferings of the patient but also leads to the development of treatment-related complications and substantial economic burden.

The treatment of CL involves either an intralesional injection of 8.5% meglumine antimonite (Glucantime) or intravenous LAmB[16]. LAmB was approved for the treatment of leishmaniasis in June 2009 in Japan. As our patient had large and chronic skin lesions and was experiencing severe symptoms, we chose to use intravenous LAmB (20 mg/kg, in five divided doses) as recommended by different guideline[17–19]. We also used oral miltefosine for another three months as our experience of treating CL patients with LAmB monotherapy was not satisfactory. The combination treatment in this patient results in excellent recovery of the patient.

Conclusions:

Cutaneous leishmaniasis is a rare disease in Bangladesh. Because of higher rate of travel and work abroad, an increased number of sporadic cases of cutaneous leishmaniasis in non-endemic areas should be taken into account. Clinicians should be vigilant regarding treating such cases, and CL should be charge while treating any cases instancesof skin ulcers in patients who returned from CL endemic countries. We think this case report will give important message to the clinicians and will make awareness of CL.

Ethical consideration

Written informed consent was taken from the patient for publishing the history and pictures. Utmost respect and sympathy were shown to the patients during treatment.

Conflict of interest

There was no conflict of interest.

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