Case Report

Disseminated cutaneous leishmaniasis

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ABSTRACT

Disseminated cutaneous leishmaniasis (DCL) is a condition rarely seen in the Middle East. We report a case of disseminated cutaneous leishmaniasis in a 60-years-old lady. The patient first presented 1996 with an initial lesion, which started on the butterfly area of the face and spread, probably due to immunosuppression, to involve the whole face. The lesions consisted of nodules, which did not ulcerate. The histology showed abundance of macrophages filled with amastigotes (L-D bodies). The patient was started on oral zinc sulphate 10 mg/kg in 3 divided doses daily. The condition showed gradual improvement. Repeated biopsies showed upgrading of the histopathological picture. After 6-months of treatment there was complete clearance of the condition. The patient was followed up for 6-years with no recurrence. However, she presented with a new lesion on the butterfly area again in February 2003. The biopsy again showed abundance of macrophages filled with amastigotes (L-D bodies). A 4-months course of zinc sulphate 10 mg/kg in 3 divided doses daily resulted in complete clearance of the lesions. Zinc sulphate might represent a new treatment for this condition that has no adequate treatment until now.

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Disseminated cutaneous leishmaniasis (DCL) has certain characteristic features. There is an initial lesion that spreads locally from which the disease disseminates to other parts of the skin. Histologically, there is superabundance of parasites in the lesion with a predominance of macrophages full of amastigotes (L-D bodies). Internal organs are not involved, and there is no history of kala-azar. The disease progresses slowly and becomes chronic. Treatment produces only gradual improvement and relapse is the rule. In the Old World this form is due to L.ethiopica.[1] This condition is rarely seen in our part of the world. Reports on the leishmania species in Iraq have indicted that both L.tropica and L.major are responsible for the cutaneous form of the disease.[2] There were no reports of L.ethiopica. Treatment involves the use of pentamidine for many months.[1] Pentamidine is associated with many side effects. Hypotension may develop even after a single injection. Other side effects include pancreatic damage resulting in hypoglycemia or hyperglycemia, hyponatremia and delayed nephrotoxicity.[3] In this communication, we report a classical case of DCL in a patient in an area where L.ethiopica has not been reported. We also report a novel treatment for this disease.

Case Report. A 60-years-old lady presented at the Department of Dermatology in Baghdad Teaching Hospital, Medical City on April 1996 with a history of 6-months of progressive lesions on the face. The condition began 6-months ago where the patient noticed papules on the butterfly area of the face. The papules enlarged to nodules, which spread to involve most of the face with no ulceration. The patient consulted several dermatologists at private clinics and received a myriad of treatments including several local treatments (possibly corticosteroids) and even a course of cytotoxic drugs (possibly due to a diagnosis of discoid lupus erythematosis). The patient had scar of a previous infection with cutaneous leishmaniasis when she was 6-years-old. She was diabetic on oral

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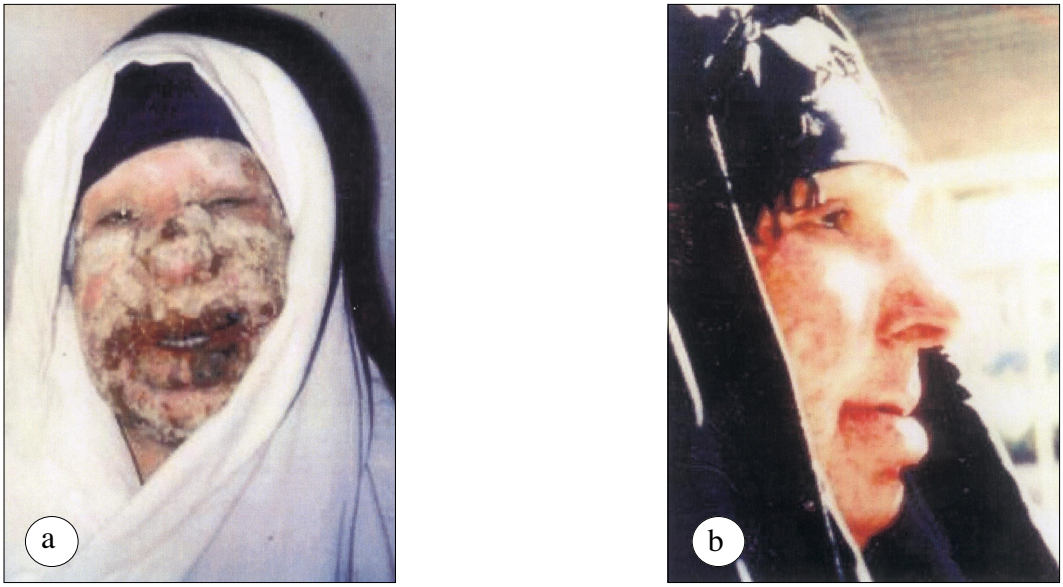

Figure 1 - A photograph of the patient **(a)** Before and **(b)** After 24 weeks of treatment with oral zinc sulphate.

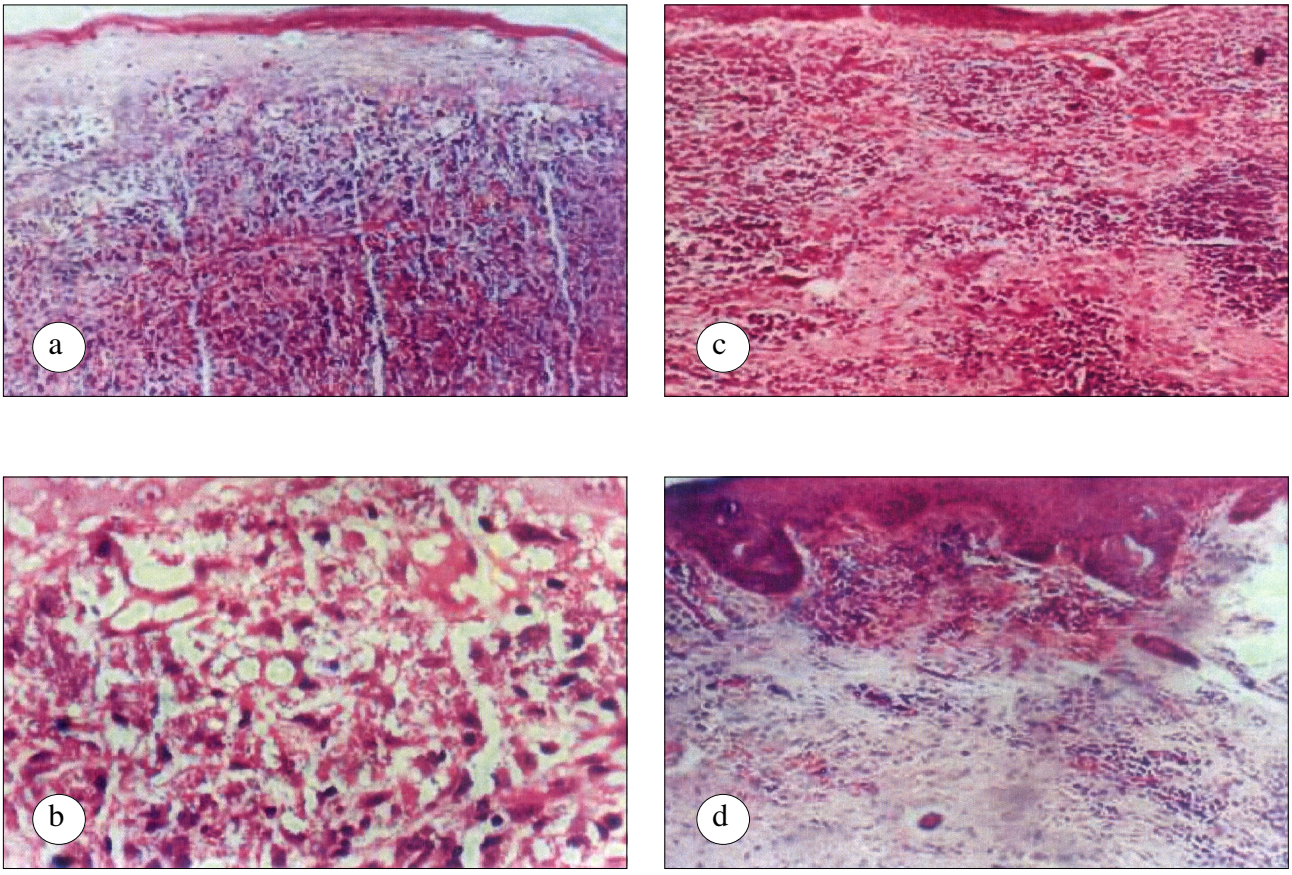

Figure 2 - Photomicrographs of the skin biopsies **(a, b)** Before treatment **(c)** After 12 weeks of treatment **(d)** At the end of 24 weeks of treatment. (32 x A,C,D, 100x B, hematoxyllin and eosin stained)

hypoglycemic treatment (Glibinclamide 5 mg /day) and asthmatic but on no regular treatment. She had no history of travel outside the country for a very long time. She had no history of acquired immuno-deficiency syndrome. Examination revealed a middle-aged lady with endurated nodules involving the whole face. The lesions did not ulcerate. There was a scar of a previous infection of cutaneous leishmaniasis, which was not effected. **(Figure 1a)** The regional lymph nodes were involved. Physical examination was not remarkable. Using a dental broach a smear was taken and stained with Gimsa stain.[4] It revealed macrophages loaded with L-D bodies. A biopsy was taken from one of the nodules. Histopathology revealed that the epidermis showed hypoplasia in some areas with atrophy in other areas. The whole dermis was diffusely infiltrated by macrophages heavily loaded with L-D bodies. There were few scattered lymphoid cell. **(Figure 2a & b)**. No facilities for culture were available at the time. The patient was admitted for further investigation and for follow up to the hospital. Investigations included a complete blood picture and blood biochemistry, which were all within normal except for elevated blood glucose. Screening for human immuno-deficiency virus infection was negative. An ultrasound examination of the abdomen was performed and did not reveal any abnormality. A bone marrow aspiration from the iliac crest was carried out and revealed a normal bone marrow. No L-D bodies were identified. Due to the unavailability of either sodium stibogluconate or pentamidine at that time, a decision was made to use oral zinc sulphate to treat the patient. Zinc sulphate was found to be effective in the treatment of cutaneous leishmaniasis in an open trial performed between 1994-1996.[5] The consent of the ethical committee in the hospital as well as the patient's consent was obtained before beginning of the treatment. The patient was started on oral zinc sulphate 10 mg/kg in 3 divided doses. After the first week of starting treatment all the lesions showed swelling. The swelling subsided in 3 weeks. The patient was discharged and followed up weekly in the outpatient clinic. She showed gradual improvement on follow up. After 12 weeks from starting of treatment, a smear was repeated and was negative for L-D bodies. A biopsy was also taken and revealed that the epidermis was atrophic in most areas. The dermis showed patchy infiltration, diffuse in some areas with a tendency for granuloma formation. The infiltrate consisted mainly of lymphocytes mixed with plasma cells. No macrophages with L-D bodies or Langerham's cell were seen. Capillaries were dilated with a patchy infiltrate around blood vessels **Figure 2c**. Treatment was continued for a period of 24 weeks. At the end of the treatment period, all lesions were cleared leaving a hypopigmented area **Figure 1b**. A biopsy taken at the end of treatment revealed a normal epidermis while the dermis showed a patchy infiltrate both in the superficial and deep dermis of lymphoid cells with no plasma cells. No macrophages or LD bodies were seen **Figure 2d**. A smear showed no LD bodies. At this point treatment was stopped. During the treatment period, the patient did not show any side effect. The patient was followed up every 3-months for one year and then every 6-months. During this period, there was no re-occurrence of the lesions. In February 2003, the patient presented with a symmetrical rash on the butterfly area of the face consisting of hard indurate nodules. Re-occurrence was suspected. A biopsy was taken from one of the nodules and revealed massive infiltration of the dermis with macrophages filled with LD bodies. She was restarted on oral zinc sulphate 10 mg/kg in 3 divided doses for a 4-month period. At the end of the treatment all lesions were cleared.

Discussion. The case reported represents a classical case of DCL in all respects except that it was probably caused by a species other than L ethiopica. The possibility that this case was caused by L.ethiopica is far fetched since L.ethiopica has never been reported in Iraq.[2] Iraq is geographically far from areas where L.ethiopica is endemic. In addition, the patient has not left the country. The most probable factor, which leads to the development of this condition, was the immunological state of the patient. The patient had a previous scar of CL, but it is known that re-infection can occur after the passage of several decades.[6] On the other hand, the patient was diabetic. It has been reported that both the cellular and humoral immunity is depressed in diabetic patients.[7] Another factor, which might have contributed to immune suppression, was the fact that the patient was asthmatic. A common practice among practitioners in our country is to treat asthmatic attacks with corticosteroids. This might have added to the immune suppression in the patient. Added to all the above, the patient received many local treatments in the form of steroids as well as a course of cytotoxic therapy. Treatment added to the immunosuppression already present.

In the case reported one notices several gaps in the history of the patient before consulting our department. In Iraq, as well as several other developing countries, there is no organized health service. Patients can consult any private clinic or hospital at their own discretion. There are no records of any diagnosis or treatment given except what the patient recalls. Zinc sulphate was reported

to be effective in the treatment of acute CL.[5] This therapeutic effect of zinc is due to a combination of a direct antileishmanial effect,[8] as well as an immunomodulatory effect of zinc.[5] Ongoing research in our institution has indicated that zinc in vitro increased the phagocytosis of L-D bodies by macrophages. These observations explain both the swelling observed at the beginning of treatment as well as the upgrading in the histopathological picture observed. Thus, histopathologicaly the picture moved from one end of the spectrum; such as the anergic type with macrophages filled with L-D bodies to the other end such as, the granuloma with no L-D bodies.[9] This has been described in the classical DCL.[1]

Although this is a report of a single case but it might encourage a pilot study of zinc sulphate in the treatment of DCL due to L.ethiopica. Compared to pentamidine, zinc has 2 advantages. It can be given orally and has no major side effect similar to pentamidine. With increasing age of the population together with increasing health problems, an important lesson from this case report is to keep CL always in the differential diagnosis of skin conditions in endemic areas.

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