Treatment of Lupoid Leishmaniasis

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Abstract :

Lupoid Leishmaniasis or Leishmaniasis Recidivans (LR) is seen in about 5-7% of cases of Cutaneous Leishmaniasis[1,2,3,4]. Lupoid Leishmaniasis was diagnosed histopathologically in skin lesion of 5 years duration affecting the cheek of a lady from Ethiopia and was provisionally diagnosed as discoid lupus erythematosus or sarcoidosis. She responded clinically to repeated treatments with Rifampicin and liquid nitrogen spray.

Case Report :

ZOA a 43 years old from Ethiopia-Africa. She reported to the clinic on 3.5.1999. She presented on her left cheek paranasally with a discoid infiltrated reddish brown plaque (Fig. 1 and 2) and was provisionally diagnosed as discoid lupus erythematosus or Sarcoidosis. She gave a history of an ulcer of her left cheek which began early in 1994. There was no scar seen on her left cheek. A punch biopsy was taken from the lesion on 5.5.1999 and was reported to be Luloid leishmaniasis (Fig. 3 and 4). She was treated with liquid nitrogen spray once every 2 weeks from 22.5.1999 till 1.9.1999 when Rifampicin was added in the dose of 1200 mg daily for ten weeks and the plaque showed clinical clearing (Fig. 5 and 6). On 9.4.2000 after nearly 6 months from her clinical cure she reported back with the same infiltrated plaque at the same site of her left cheek and the lesion was re-biopsied and the report showed lupoid leishmaniasis (Fig.7 & 8). She was again treated with liquid nitrogen spray once every 2 weeks and after 6 cryotreatments the lesion had no infiltration and showed post inflammatory hypopigmentation (Fig. 9 and 10) and was considered clinically cured and patient was followed for ten months without recurrence.

Discussion :

Cutaneous Leishmaniasis (CL) is seen in many parts of the world. It is estimated that 3% of travellers to tropical countries develop CL[5]. CL in The Middle East, North Africa and Mediterranian Basin is caused either by L. Major transmitted by Phlebotomus (P) papatasii or L. tropica transmitted by P. Sergenti or L. infantum transmitted by P. Perniciosus. CL in Ethiopia (Africa) is caused by L-aethiopica transmitted by P. longipes or P. pedifer[6]. CL due to L.aethiopica usually affect the central face and rarely look inflamed. The site and clinical character of the present reported case fits with L-aethiopica. L. aethiopica usually heals in 2-5 years[7]. Our patient got recurrence despite treatments and the histopathology showed characteristics of lupoid leishmaniasis.

The different leishmania species are morphologically similar and are distinguished by isoenzyme pattern, DNA analysis and monoclonal antibodies[8,9]. The clinical patterns of CL are not diagnostic of species but certain disease pattern of CL may be commonly associated with a particular species for example L. aethiopica, early ulcerative CL (rural type) which is caused by

L. Major with an incubation period usually less than two months and the late ulcerative clinical form known also as (Urban) type and is caused by L. Tropica and is characterized by an incubation period of more than two months[6].

L-Infantum causes visceral leishmaniasis in children while adults either show self healing CL or chronic non healing ulcers or occasional solitary mucosal lesion may occur [10,11]. Mucosal lesions have been reported in patients with CL in Mediterranian Basin and the Middle East [12]. Severe mucosal involvement in CL was reported from Nepal [13]. Mucosal lesions in leishmaniasis are classically described in American mucosal leishmaniasis and affect between 2 and 40% of patients [12]).

Diffuse CL is a rare variant of acute leishmaniasis where lesions are widespread all over the body surface and the lesions are teaming with leishmania and Montenegro test is negative [2]. It is estimated that 5-7% of CL infections become chronic and

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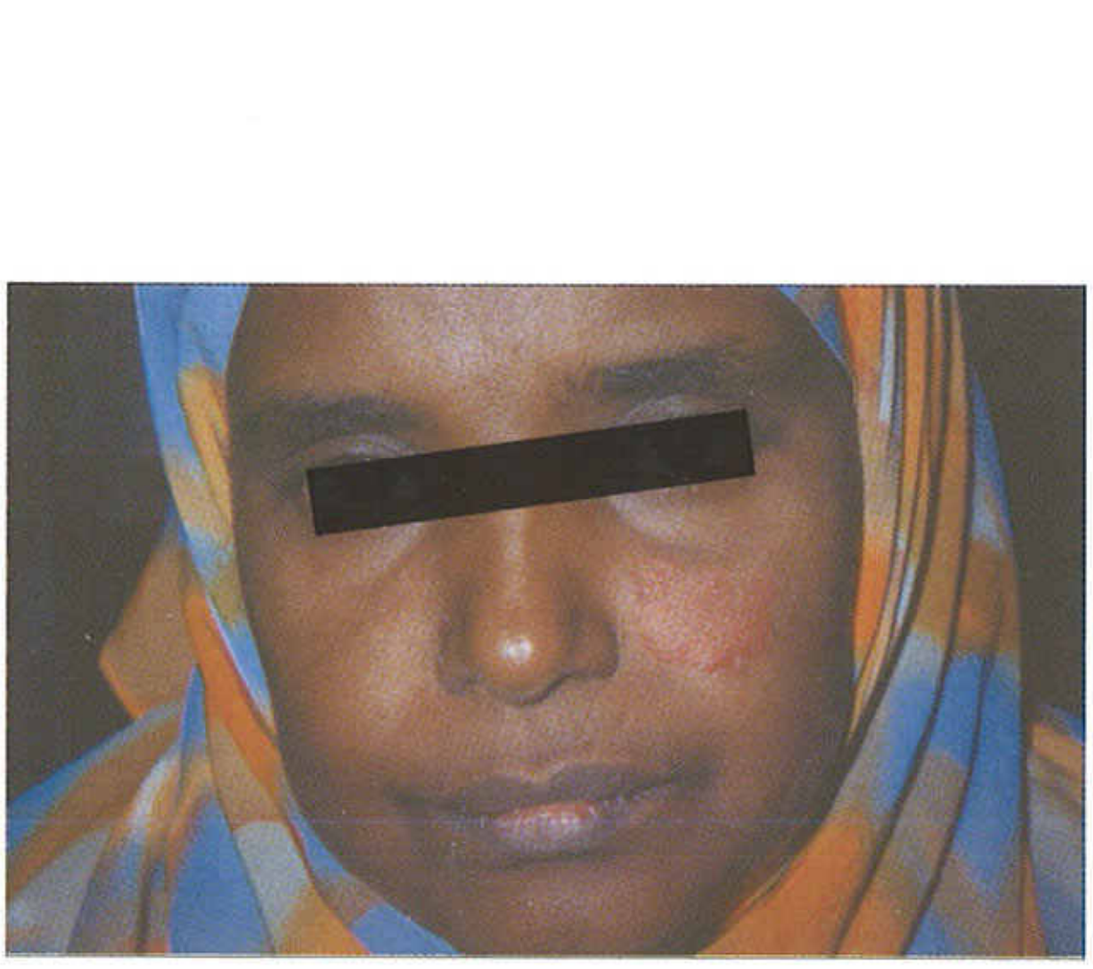


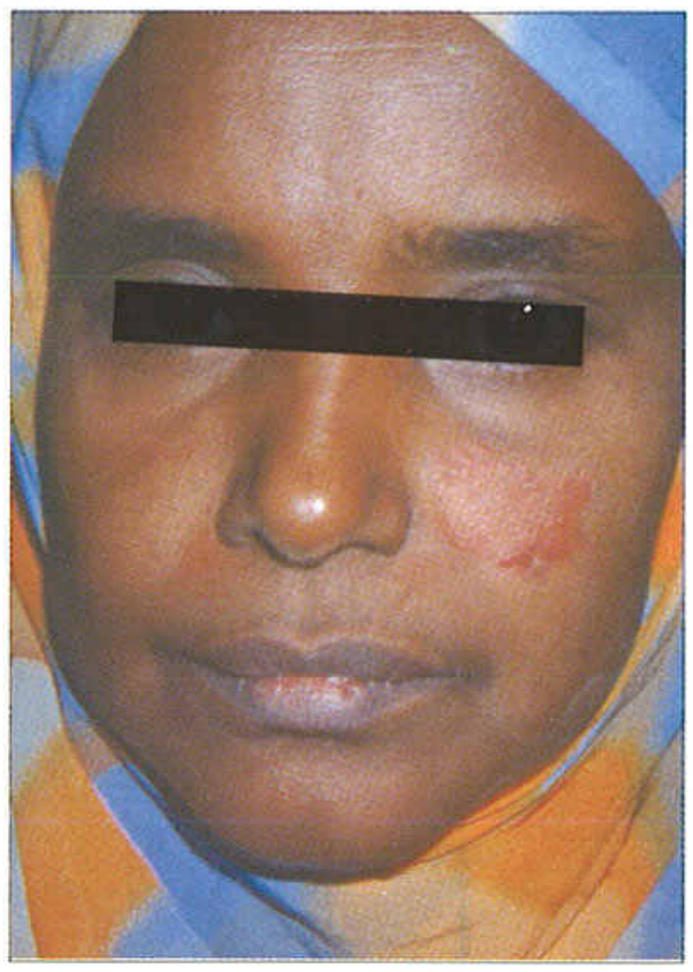
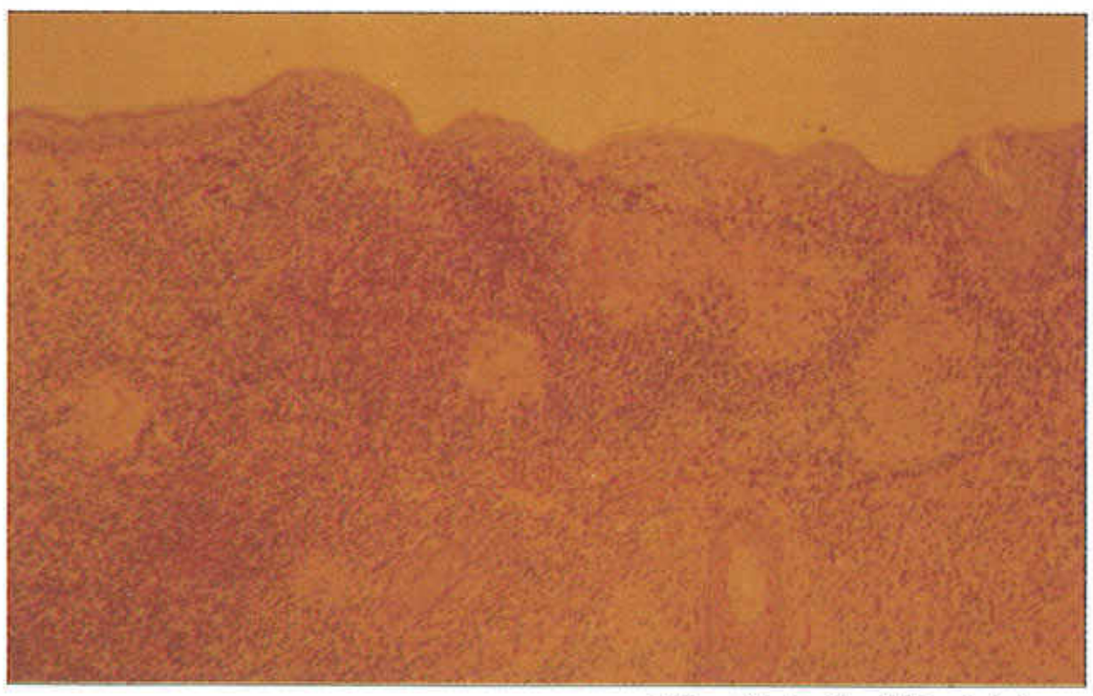


Fig. 1 & 2 : Lupoid Leishmaniasis having a discoid appearance.



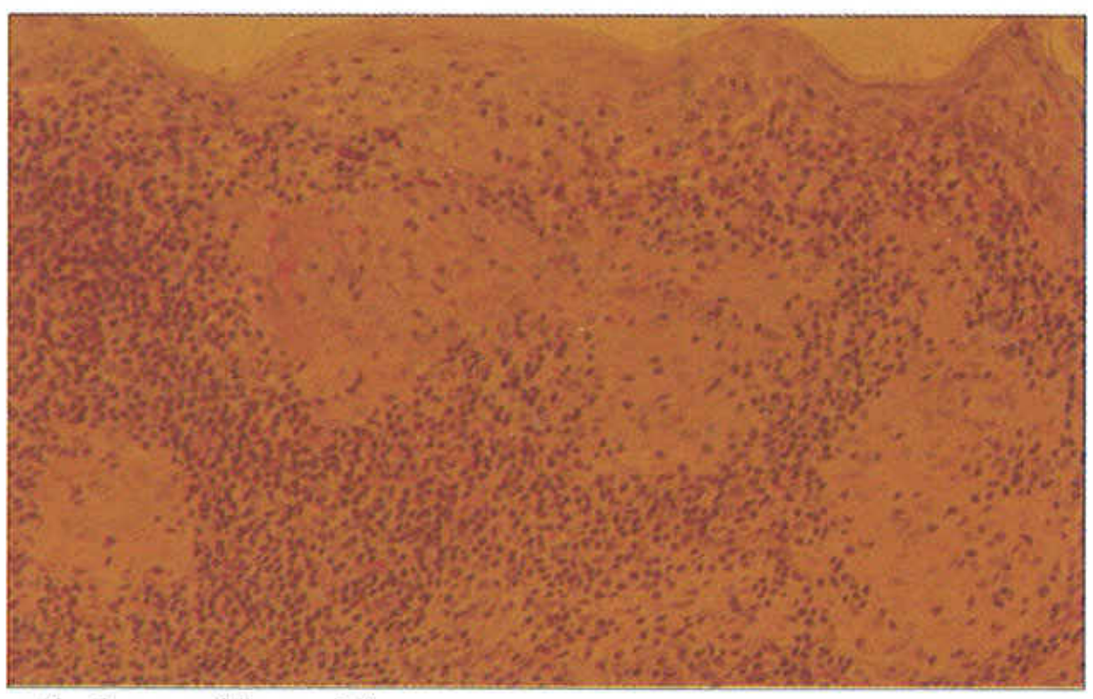
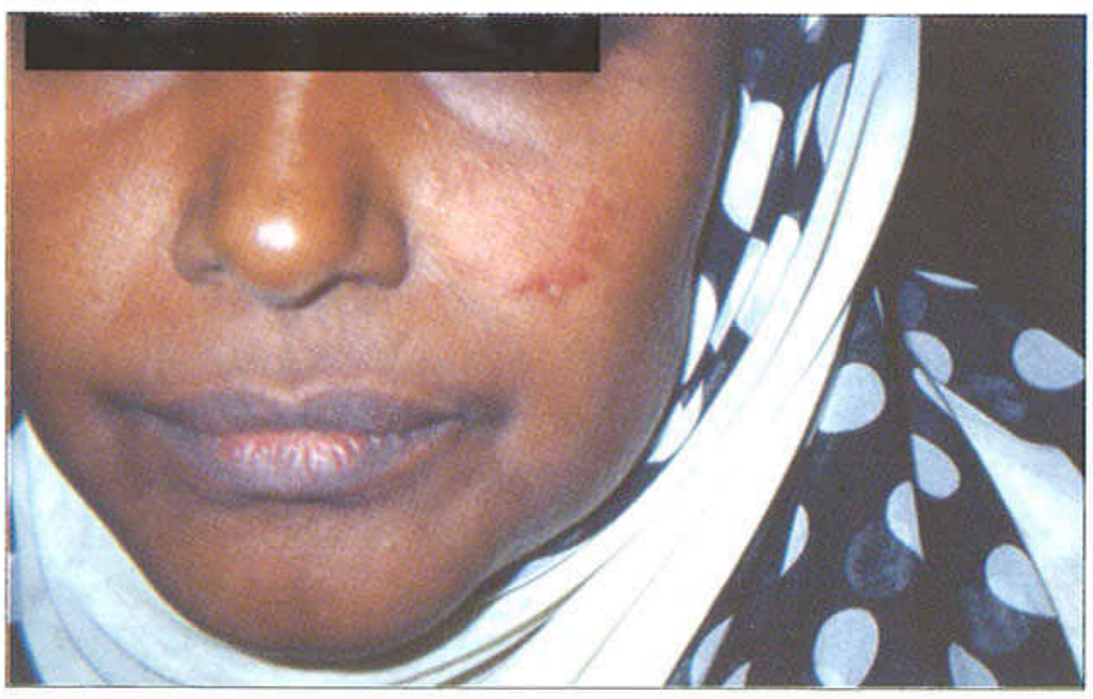


Fig. 3 & 4 : First biopsy histopathology of Lupoid Leishmaniosis



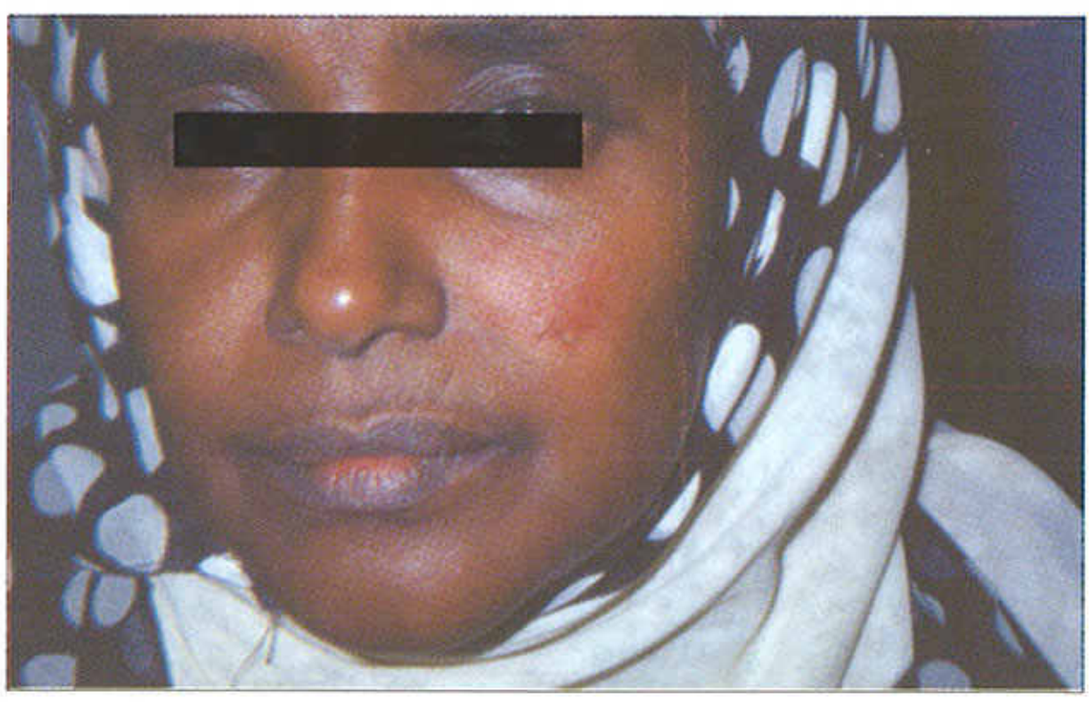


Fig. 5 & 6 : Clearance of the lesion after treatment.

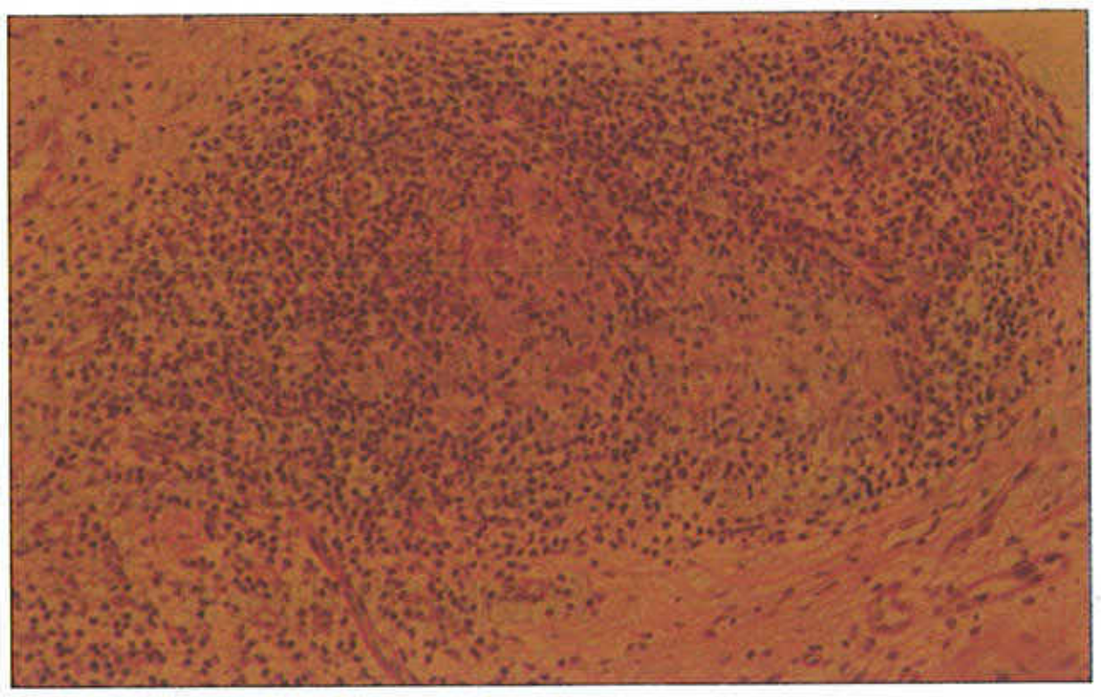
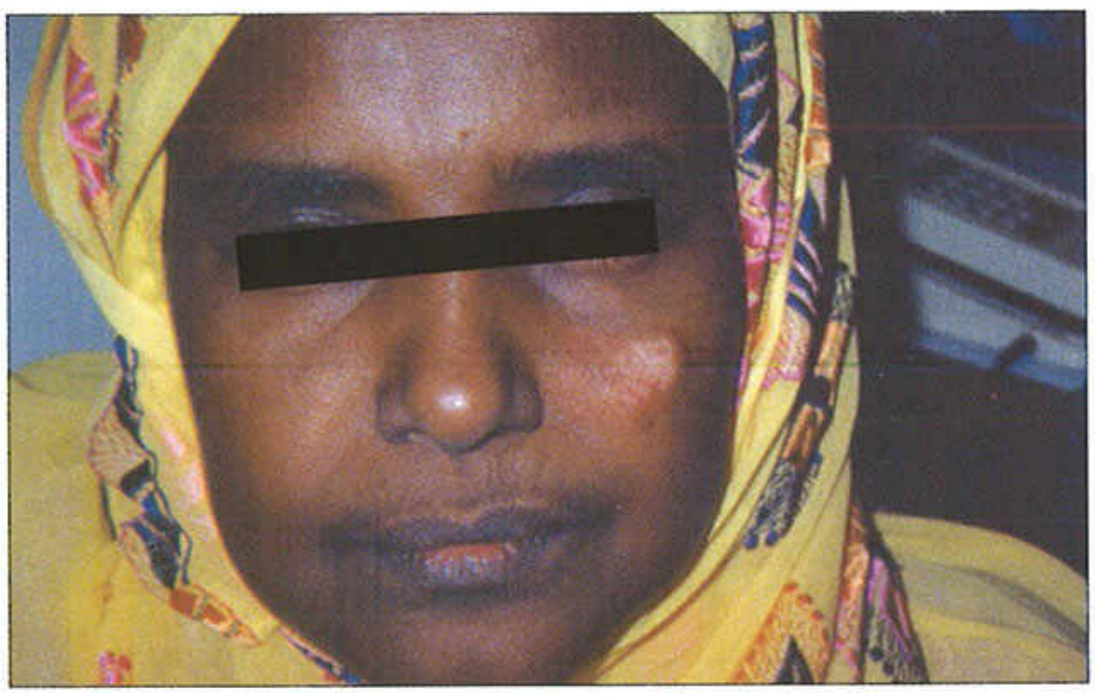


Fig. 7 & 8 : Histopathology of second biopsy taken 6 months after clinical clearance ñ showing Lupoid Leishmaniosis.



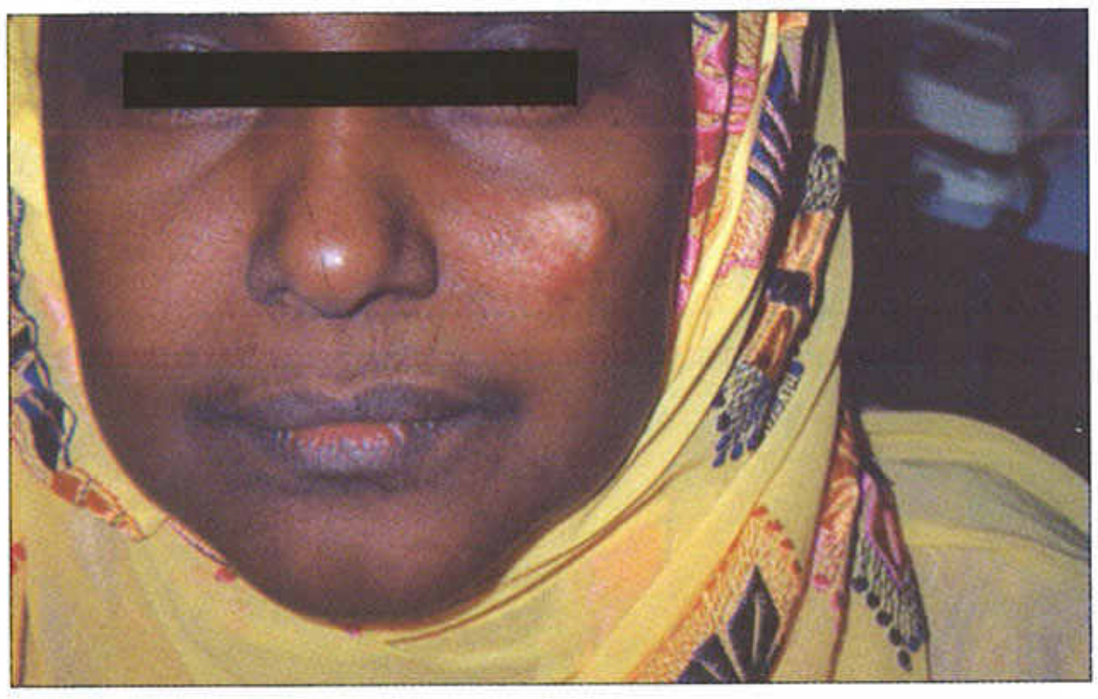


Fig. 9 & 10: Clinical clearance after repeated treatment with post Inflammatory hypopigmentation.

persistant form known as lupoid leishmaniasis or leishmaniasis recidivans (LR). This clinical form of cutaneous leishmaniasis is a problem in diagnosis and management. Lupoid leishmaniasis evolves from acute CL lesions and papulonodular satellites appear in a circinate pattern around or in a preexisting scar of an apparently healed CL and on diascopy the nodules give apple jelly color. Sometimes the initial nodules in LR change to form a plaque that resemble discoid lupus erythematosus [14] with summer exacerbation and winter remission [2]. A verrucous variety of LR is also described. The variations in the clinical appearance could be due to various factors including the immune response of the host, the leishmania species and the size of the inoculum of the organism [16]. In chronic cutaneous leishmaniasis caused by L-tropica the lesions may persist for two years or more before ultimately clearing clinically [17,18]. LR is characterized by recurrent healing and reactivation over prolonged time up to 71 years [2]. This pattern of reaction is related to the immunity of patients whose T-lymphocyte activity is defective and the macrophages cannot completely eliminate the amastigote parasite [2] and it has been suggested that acid phosphatase surface membrane enzymes may sheild the protozoa from normal immune mechanisms. The lesion of LR may be mistaken for lupus vulgaris, discoid lupus erythematosus or plaque sarcoidosis. Direct smears of LR is negative for leishmania and it is difficult to culture the leishmania from LR on Nicolle-Novy-Mc Neal medium (3 N Medium). A tuberculin test if done is invariably positive and Montenegro test is always positive. The histopathologic features of LR is that of a non caseating tuberculoid granuloma which shows infiltration with macrophages,

lymphoid cells and very few or no plasma cells and leishmania organism are not usually seen on routinely stained sections [20].

Areas of necrosis are seen or absent and the epidermis is either atrophic or may show pseudo epitheliomatous hyperplasia [21,22]. Polymerase chain reaction studies were useful in identifying amastigote in 47.6% of cases of LR and the presence of DNA molecules of leishmania amastigote in formalin fixed paraffin embeded tissue obtained from patients with LR samples [20].

Regarding treatment of CL the world literature is confusing and contradictory [23] and this may be due to the known fact that isolates from different parts of the world can have different drug susceptibility [24]. Pentavalant antimonials are the drugs of choice in acute forms of CL but are less effective in LR. The mechanism of action of antimonials is not clear and it is suggested that antimonials inhibit an enzyme phosphofructokinase thus blocking the production of adenosine triphosphate in the parasite [25]. Meglumine antimoniate (Glucantim) has been used successfully to treat CL and LR [22,26,27,28]. Intramuscular sodium stibogluconate (Pentostam) combined with intralesional steroid was used successfully in late cutaneous leishmaniasis [29]. There is some variability in response of patients with CL to treatment with sodium stibogluconate (Pentostam) given intramuscular according to the patients rate of excretion of the drug as it was found that the response was less with rapid eliminators and higher with slow eliminators[30]. Rifampicin has been used to treat CL and LR [31,32,33] Rifampicin given at 1200 mg daily dose for one or more 10 days courses has been met with more success in treatment of mild acute disease [2,34]. Other systemic drugs used are Dapsone[35], Itraconzole [36,37], Ketoconazole in the dose of 400 mg daily for 4 to 12 weeks gave response 0% in L.tropica, 70% in L-major and 1-6% in American Leishmaniasis [38,39]. Combination of alupurinol and meglumine antimonate (Glucantim) was reported to be effective in 95% of cases of LR. The doses given were 20mg alupurinol per kg per day for 30 days and meglumine antimoniate in the dose of 70mg/kg/day for 15 days and the lesions were considered cured when they show complete clinical healing, no papules and no relapse after one year [25].

Intralesional treatments were tried using amphotericin B [40]; emetine hydrochloride[41], pentavalant antimony preparations [2,42] and intralesional hypertonic saline given at 7-10 days intervals was very effective in acute CL with 96.05% cure rate and most lesions needed only one injection and intralesional sodium stibogluconate gave 96.42% cure rate [42]. Removal of the lesion was used to treat CL either by electrocautery[43,44,45], Cryotherapy [46,47] and surgical excision and grafting [2].

Levamisole for immune modulation was also tried in CL [49]. Topical aminosedine (Paromomycin) was found to be inadequate to accelerate recovery of CL and the ointment should not be used in the present formation to treat zoonotic CL [50]. Topical clotrimazole 1% was reported to be effective in simple CL lesions and 15.7% of 89 lesions healed fully while 47.2% were reduced in size and 22.5% showed no change and 14.6% got worse [51].

Conclusion

Lupoid leishmaniasis is a chronic form of cutaneous leishmaniasis that occurs mainly in Middle Eastern urban communities especially in Iran and Iraq. It is a troublesome, and chronic lesion that relapses frequently and may persist for many years. It evolves usually from the ìoriental soreî. Clinical and histopathological appearances of the lesion may mimic lupus vulgaris or sarcoidosis[52]. Therefore, clinical history and evolution of the lesion is, extremely important for arriving at a correct diagnosis. Organisms are scanty or absent by routine techniques. Serological tests for leishmania antibodies are either negative or yield only slightly raised titers compared to normal population. However, majority of cases exhibit a strong delayed hypersensitivity response to leishmanin skin testing [16,52,53,54]. Histologically it is characterized by well-organized non-caseating epithelioid granulomata surrounded by lymphocyte with very few or no plasma cells.[16,53]

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