

QUIZ

Recurrent asymptomatic nodules and plaques

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Report of a case

A 42 year old Bahraini woman presented with history of recurrent skin lesions over legs, forearms, arms and upper back of seventeen years duration. The lesions were asymptomatic and healed with depressed scar. Several previous attempts at treatment had been unsuccessful. She had suffered from insulin dependent diabetes mellitus since the age of 25 years.

Cutaneous examination revealed multiple erythematous nodules and plaques distributed over forearms, dorsa of hands, arms, upper back and left thigh (Fig. 1). Lesion over left wrist was annular, with central clearance (fig-2). There was a hypopigmented, depressed scar over left forearm (fig-1). General examination was

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1. Clinical photograph showing multiple erythematous nodules and plaques over upper limbs

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within normal limits. Fasting blood sugar was 7.4 mmol/L (normal 3.6-5.8 mmol/L). HbA1c level was 8% (normal 4.3-5.8%) Other routine investigations were within normal limits.

Biopsy was performed from the lesion on the right hand. (Fig-3, 4).

What is your diagnosis?

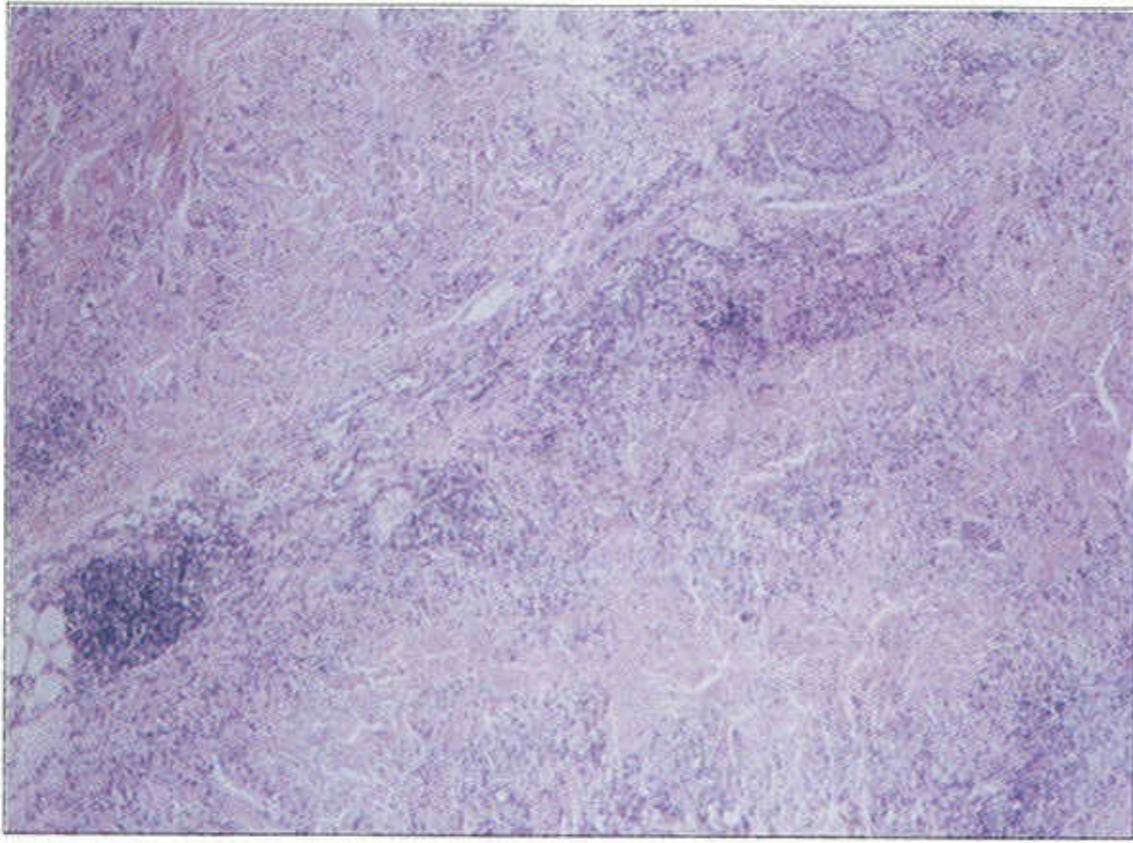
Answer; Necrobiosis lipoidica diabetorum (NLD)

Microscopic findings; Epidermis was atrophic. Dermis showed areas of necrobiosis, characterized by altered collagen, which appeared homogenous, splintered, and with loss of nuclei (fig-3). Alternating with these areas of necrobiosis, there were areas of cellular infiltration around blood vessels, composed of lymphocytes, histiocytes and foreign body giant cells (fig-4). Some giant cells contained refractile bodies. Few foam cells were also seen. Verhoeff stain for elastic tissue showed fragmentation of elastic fibres. Blood vessels showed prominent endothelial cells. These changes were present throughout dermis.

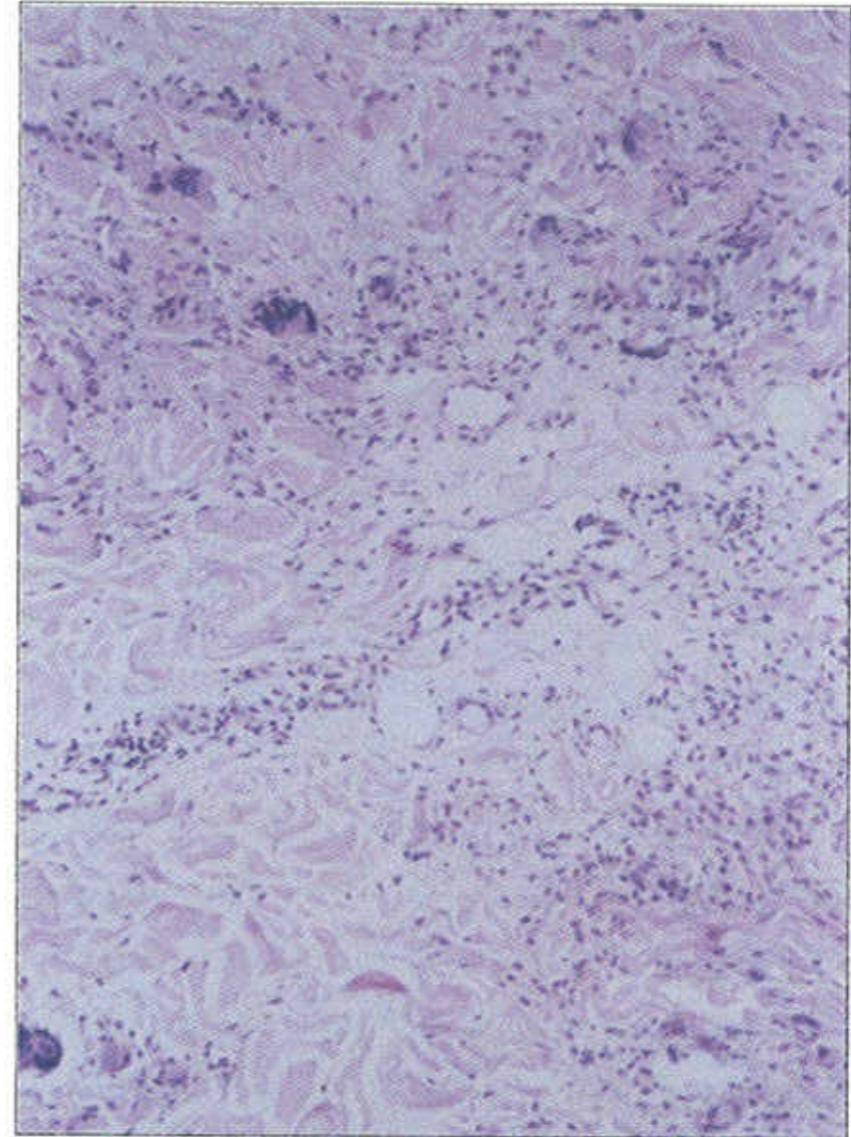
Course; Patient has been treated with several treatments, including local steroids, chloroquine and PUVA therapy, with out significant benefit.



2. Clinical photograph showing erythematous nodule and an annular plaque over left forearm and wrist. There is a depressed scar over upper forearm.



3. Photomicrograph (20X) showing areas of necrobiosis and cellular infiltration



4. Photomicrograph (40X) showing necrobiosis, cellular infiltrate around blood vessels, and multiple giant cells.

Discussion;

Necrobiosis lipoidica is a chronic condition, characterized by yellowish atrophic plaques distributed over shins, common in women and often associated with diabetes mellitus¹. The lesion starts as an erythematous fleshy nodule, which slowly expands to form a yellowish-brown plaque with irregular outline, which may become atrophic. The lesion may ulcerate and healing may occur with the formation of an atrophic scar. Though classically distributed over legs, lesions can occur over other areas, such as forearms, arms, back, chest, and rarely, scalp, nipple and glans penis^{2,3,4}. The lesions in these atypical locations are often annular. It has been reported that such atypical distribution is not associated with diabetes mellitus. Other clinical variants include NLD with comedones, granuloma annulare like and diffuse variant of NLD²⁻⁴. A high degree of awareness is necessary for diagnosis of these atypical lesions.

Histological features^{1,5}; Epidermis is often atrophic. Transepidermal elimination (which appears clinically as comedonal lesions) of elastic fibres⁶ and cholesterol crystals⁷ have been reported. Dermal pattern may be of two types; a necrobiotic type and a granulomatous type. The former shows areas of necrobiosis, seen as splintered, homogenous staining collagen, often without nuclei. Areas of necrobiosis may also contain mucin, which stains with alcian blue. In addition

there is an infiltrate of lymphoid cells, histiocytes, fibroblasts. Elastic fibres may show degeneration. Blood vessels show prominent endothelial cells with mild thickening of vessel walls. PAS positive, diastase resistant material is often seen around blood vessels, suggesting the deposition of fibrin. Granulomatous pattern, reported more often in lesions over atypical sites, shows focal collection of mononuclear cells, foreign body giant cells, and often foam cells. Giant cells may contain refractile material. Lesions with prominent granulomatous reaction are thought to be less often associated with diabetes mellitus and have been referred to as Granuloma disciformis of Meischner⁸.

The pathogenesis of the condition is poorly understood. Several studies have demonstrated the association of this condition with diabetes mellitus (both insulin dependent and noninsulin-dependent types) and with impaired glucose tolerance^{1,4,9}. However, the association is highly variable and a significant percentage of patients do not have diabetes mellitus^{10,11}. It has been reported that presence of necrobiosis lipoidica in patients with type 1 diabetes mellitus may signify risk for retinopathy and nephropathy⁹. It has also been suggested that the collagen changes are secondary to vascular changes found in diabetes. Abnormal glycation and glycoxidation of collagen may also contribute to the pathogenesis¹⁰. Demonstration of immunoglobulins,

complement, and fibrin by direct immunofluorescence in the vessel walls suggests an underlying immunological mechanism^{1,5}.

Treatment of the condition is unsatisfactory. Several treatments, such as local and intra lesional steroids,

hyperbaric oxygen¹², local tretinoin¹³ have been tried. Systemic drugs reported to be of benefit include steroids¹⁴, pentoxifylline¹⁵, and cyclosporin¹⁶. There is no correlation of disease activity with control of hypoglycemia in cases associated with diabetes.

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