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Case Report

Atypical Necrobiosis Lipoidica in a Non-Diabetic Patient: A Case Report

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Abstract: Necrobiosis lipoidica (NL) is a rare granulomatous skin disorder commonly associated with diabetes but may also occur in non-diabetic individuals. We present the case of a 52-year-old non-diabetic woman with NL, highlighting the rarity of its presentation and the importance of considering alternative etiologies such as autoimmune disorders and thyroid abnormalities. Clinically, NL manifests as erythematous papules merging into plaques with central atrophy, predominantly affecting the lower limbs. Diagnosis is confirmed through dermoscopy and histopathology, revealing characteristic features such as granulomatous inflammation and necrobiotic collagen. Therapeutically, there are no standardized guidelines for NL management due to its low prevalence. Topical glucocorticoids are commonly used but carry risks of skin atrophy and other adverse effects. Calcineurin inhibitors, such as tacrolimus, offer a safer alternative, especially in atrophic lesions. Biological therapies, including TNF-α inhibitors and Janus kinase inhibitors, have shown promise in severe cases. Despite various treatment options, strict glycemic control does not appear to prevent NL development or progression, and spontaneous resolution occurs in about 19% of diabetic cases after an average of 12 years. This case emphasizes the importance of a comprehensive evaluation in NL diagnosis and highlights the potential of alternative therapies for refractory cases.

Keywords: Necrobiosis lipoidica, diabetes, cutaneous granulomatous disease.

INTRODUCTION

In recent decades, the prevalence of diabetes has steadily increased, making it one of the leading causes of mortality and disability worldwide. Currently, 10.5% of the global population (536 million people) has diabetes, and this figure is projected to rise to 12.2% (783 million) by 2045. In Mexico, the prevalence of diabetes increased from 14.4% in 2006 to 18.3% in 20221. Between 30% and 70% of diabetic patients will develop some form of cutaneous complication during the course of the disease2. Here, we present the case of a 52-year-old non-diabetic female with necrobiosis lipoidica (NL), a rare dermatological condition typically associated with diabetes but unusual in non-diabetic patients3. The significance of this case lies in the rarity of its presentation and its potential to contribute to knowledge of alternative etiologies, expanding the clinical spectrum of the disease and emphasizing the need to investigate other contributing factors.

CASE REPORT

A 52-year-old woman from Mexico City, employed as a nurse, with a history of occasional smoking and recently diagnosed hypertension under adequate control, presented for dermatological evaluation. Two years earlier, she had developed a lesion on the right tibial region, which progressed to ulceration and expanded to the gastrocnemius area (Figure1).

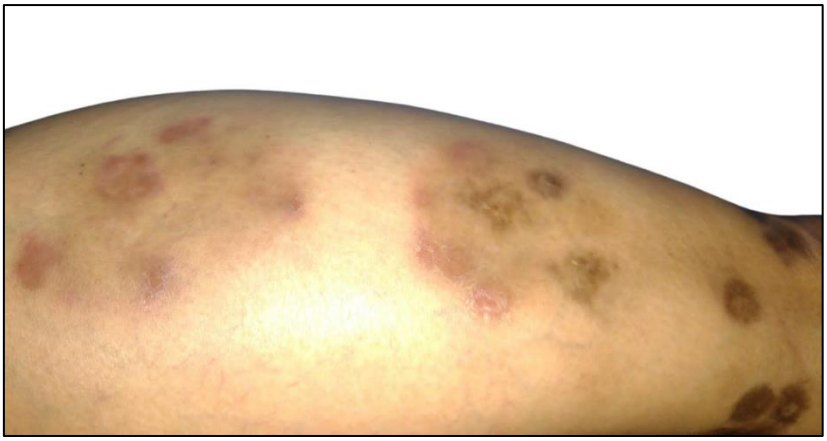

Figure 1: Lesion on the right tibial region

Some lesions had ulcerated centers but were not associated with pruritus or pain. The lesions were in the tibial region of both lower limbs (Figures 2 and 3).

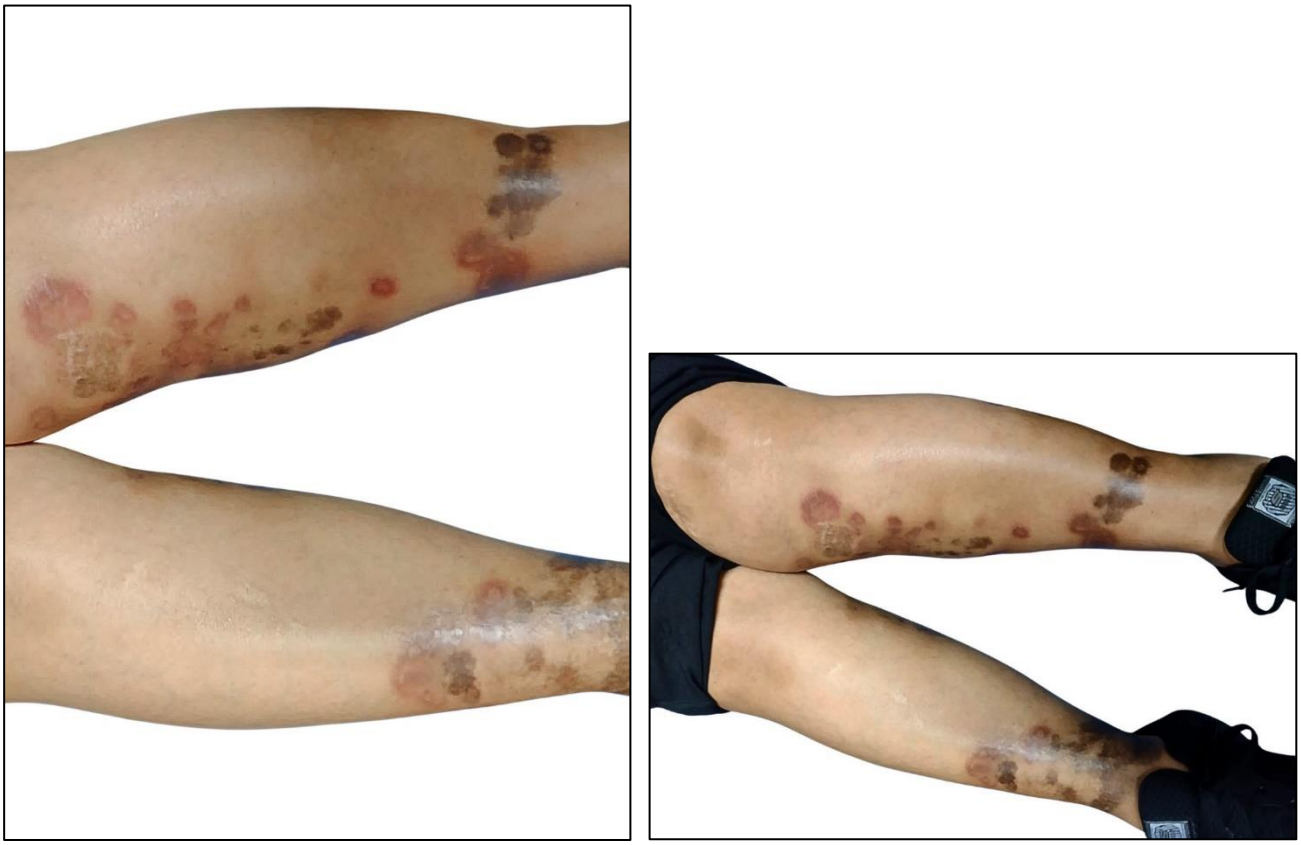

Figure 2 & 3: Erythematous, rounded lesion with an ulcerated center and raised borders, with bilateral progression of the lesions extending to the gastrocnemius muscles

Differential diagnoses included erythema nodosum and necrobiosis lipoidica. Paraclinical tests revealed no leukocytosis, dyslipidemia, or insulin resistance (metabolic syndrome), and a PCR test for tuberculosis was negative. A skin biopsy revealed granulomatous, collagenolytic, and fibrosing dermatitis with diffuse dermal sclerosis, forming a pseudogranuloma. Fitte Faracco staining was negative, consisting with necrobiosis lipoidica (Figures 4, 5, and 6). Treatment was initiated with pentoxifylline 400 mg every 24 hours, hydroxychloroquine 200 mg every 24 hours, and topical calcipotriol/betamethasone every 12 hours, resulting in clinical improvement and complete resolution of the lesions, leaving post-inflammatory hyperpigmentation. To date, the patient remains under follow-up without recurrence of the dermatosis.

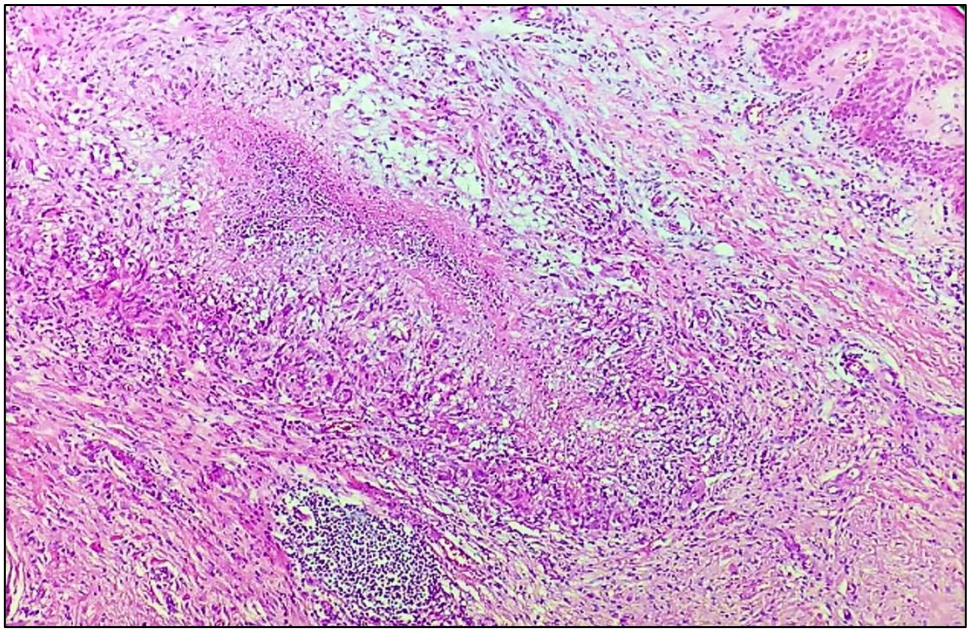

Figure 4: Purple granulomas with inflammatory infiltrate, Perivascular lymphoplasmacytic aggregate adjacent to "palisading" granuloma. H/E 400X

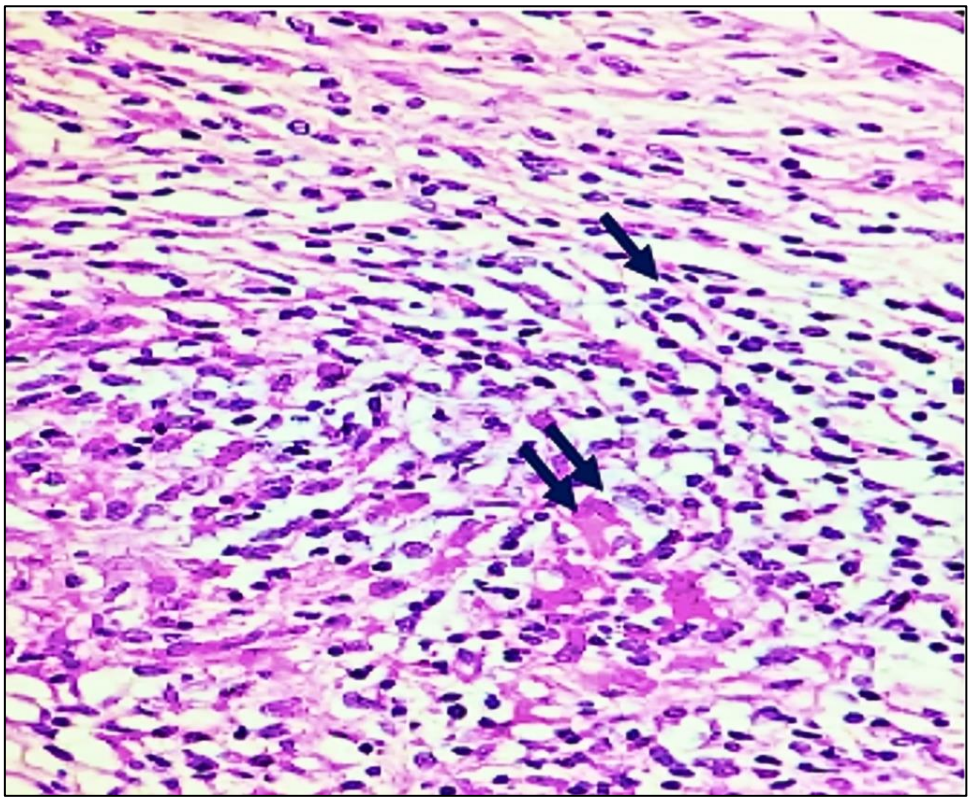

Figure 5: Interstitial lymph histiocytic infiltrate distributed among sclerotic collagen bundles (arrow). Multinucleated giant cells focally aggregated (double arrows)

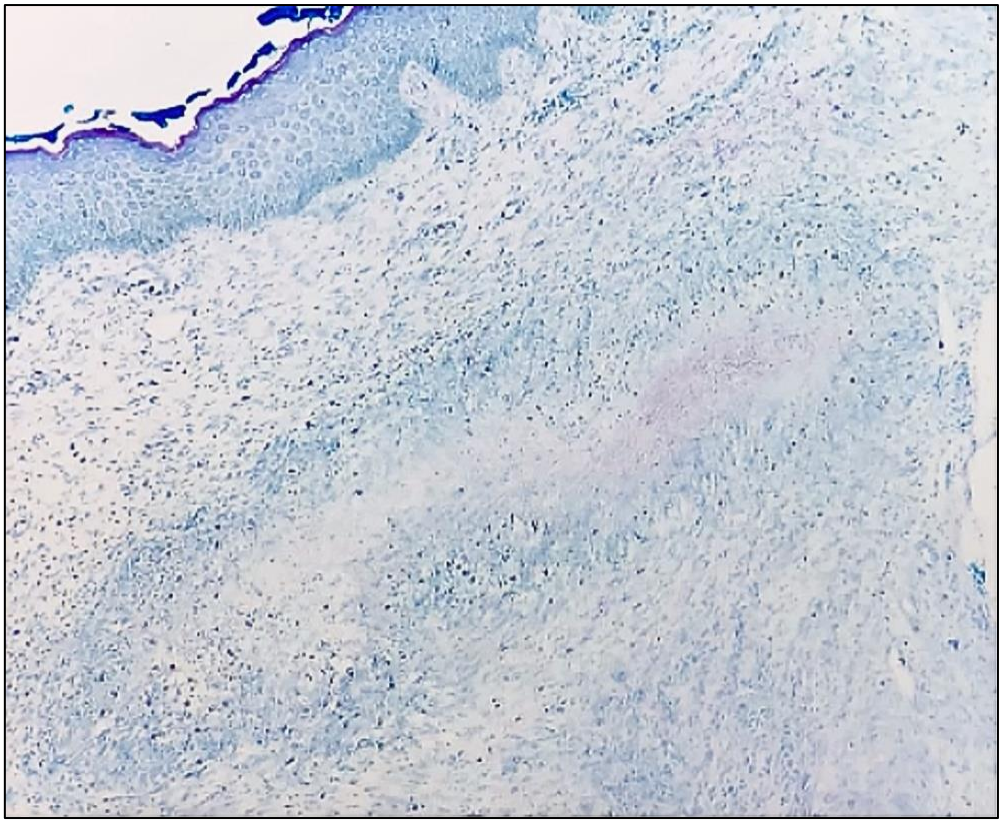

Figure 6: Ziehl-Neelsen stain: negative. Z-N x200

DISCUSSION

Necrobiosis lipoidica (NL) is a rare chronic granulomatous skin disorder characterized by collagen degeneration, granuloma formation, and thickening of vascular walls4–6. It was first described by Oppenheim in 1929 and was initially linked exclusively to diabetes. In 1935, the first case of NL in a non-diabetic patient was documented3. The etiopathogenesis of NL remains uncertain, though proposed mechanisms include microangiopathy, immune complex deposition, collagen production abnormalities, and aberrant neutrophil migration [2, 5–7]. NL may coexist with thyroid disorders, autoimmune diseases such as sarcoidosis and rheumatoid arthritis, and metabolic syndrome. However, its most common association is seen in insulin-dependent diabetic patients [3].

Between 11% and 87% of individuals who develop NL have diabetes, while only 0.3% to 1.2% of diabetics will develop NL [3, 8]. Information regarding the prevalence of NL in non-diabetic patients is limited in the literature8. The condition is more common in women, with a female-to-male ratio of 3:19. In individuals with type 1 diabetes, NL typically appears in the third decade of life, whereas in those with type 2 diabetes and in non-diabetic individuals, it generally presents in the fourth decade [5].

Clinically, NL presents as erythematous papules that merge to form plaques with red-purple borders, central atrophy displaying a yellow-brown hue, and surface telangiectasia. It predominantly affects the lower limbs, particularly the pretibial region, though it can also involve the face, scalp, upper limbs, and trunk. NL is generally asymptomatic but may present with pruritus, hypoesthesia [2], or pain, especially when ulceration occurs, which is seen in about one-third of cases [2, 6]. Ulcers can become secondarily infected or progress to squamous cell carcinoma (SCC)[2]. The Köebner phenomenon may be observed in surgical scars or areas of previous skin trauma. Even rarer clinical variants include perforating NL and periorbital NL [3].

In inconclusive cases, a biopsy can assist in ruling out differential diagnoses such as necrobiotic xanthogranuloma, granuloma annulare, or sarcoidosis [6].

Histologically, in non-diabetic NL, tuberculoid-type lesions are frequently observed3. However, NL coexisting with diabetes is characterized by granulomatous inflammation organized in horizontal palisades[8,10], interspersed with dermal fibrosis and eosinophilic necrobiotic collagen, following a pattern described as "layered like a cake"[10,11]. Lymphoplasmacytic infiltrates are often observed at the junction between the dermis and the panniculus. The epidermis is generally unaffected, although in rare cases, it may appear atrophic or ulcerated [10].

Dermoscopy is a valuable tool in diagnosing NL. In the early stages of the disease, comma-shaped vessels can be observed on a pink background with brown-orange areas and a thin superficial vascular network. As the disease progresses, a network of vessels is identified on a pink background with homogeneous yellow-orange areas. In the final stage, branched linear vessels appear on a light brown background, accompanied by whitish areas and a heterogeneous pigment network[3].

Three key dermoscopic findings that suggest NL include: branched linear vessels associated with epidermal atrophy and dilation of the papillary dermis vessels; a background of structureless yellowish areas corresponding to dermal granulomas; and white linear streaks indicative of fibrosis [12].

Due to the low prevalence of necrobiosis lipoidica (NL), there are no unified therapeutic guidelines for its treatment. Topical glucocorticoids are the most commonly used drugs, although their use is limited by adverse effects such as skin atrophy, which restricts their application to atrophic lesions. Other side effects include striae, rosacea, perioral dermatitis, acne, purpura, hirsutism, pigmentation changes, delayed wound healing, and increased risk of infections. Moreover, prolonged use over large areas can disrupt metabolism, particularly in diabetic patients. In contrast, calcineurin inhibitors, such as tacrolimus, do not cause skin atrophy, enabling their use in atrophic areas and on facial skin. These agents have demonstrated efficacy in treating ulcerated NL, making them a valuable therapeutic option in more severe or refractory cases of the disease [3].

Other therapeutic options include photodynamic therapy [13], fumaric acid esters, dapsone, antimalarials (chloroquine, hydroxychloroquine), cyclosporine, doxycycline, and pentoxifylline. Biological therapy is reserved for cases in which other treatments have proven ineffective or are contraindicated. Most biologic trials have focused on TNF-α inhibitors, such as adalimumab, infliximab, and etanercept. In recent years, successful cases have been reported with biologics targeting other molecular pathways, such as ustekinumab and secukinumab, as well as Janus kinase inhibitors (JAKi) and the aryl hydrocarbon receptor (AhR) agonist, tapinarof [3].

Unfortunately, strict glycemic control does not seem to prevent the development or progression of necrobiosis lipoidica (NL). Approximately 19% of NL cases in adults with diabetes resolve spontaneously after an average duration of 12 years [6].

CONCLUSION

Necrobiosis lipoidica (NL), although classically associated with diabetes, can occur in individuals without this condition, highlighting the need to investigate alternative etiological factors such as autoimmunity, thyroid disorders, or metabolic syndrome. This case expands the clinical spectrum of NL and emphasizes the importance of a comprehensive evaluation for its diagnosis and management. Additionally, the use of alternative therapies, such as calcineurin inhibitors and biological agents, opens new therapeutic options for more severe or refractory cases.

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