Concomitant Necrobiosis Lipoidica and Morphea: A Case Report and Literature Review

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INTRODUCTION:

Necrobiosis lipoidica (NL) is a relatively rare granulomatous skin disorder, associated with dermal collagen degeneration. When develops in the context of diabetes, it is specifically referred to as necrobiosis lipoidica diabeticorum (NLD).

Skin involvement is commonly characterized by well-defined brownish-yellow indurated plaques with overlying telangiectasias, violaceous borders and atrophic center. It mainly affects the pretibial area but can also present in the upper extremities, trunk, genitalia, face and scalp (1, 2).

Moreover, morphea (also known as localized scleroderma), is a rare and self-limited autoimmune skin disorder of excess collagen production and deposition, causing inflammation and fibrosis of dermis and subcutaneous tissues. Plaque type morphea as the most common form of localized scleroderma, initially presents as slightly elevated, reddish or purplish plaques that gradually expand outward in a centrifugal pattern. In the later stages of the disease, skin lesions develop into dyspigmented, atrophic and sclerotic plaques. Commonly involved areas include the trunk, as well as the inframammary and inguinal regions.

Both necrobiosis lipoidica and morphea are non-infectious inflammatory dermatoses of unclear pathogenesis and etiology(1, 3). As of now, only four cases of concurrent necrobiosis lipoidica (NL) and morphea have been documented in the literature. One case was detailed in a case report, while the other three were included in a retrospective study (4, 5). Herein, we document a case of concomitant NL and morphea in a 43-year-old non-diabetic woman with a history of NL on her elbow, recently developed a plaque-type morphea on her trunk. We also review the literature on other dermatoses that have been reported to coexist with NL.

CASE PRESENTATION:

A 43-year-old woman with unremarkable medical history presented to a university-affiliated dermatology clinic with an 8-year history of an asymptomatic plaque on her left elbow. upon physical examination the plaque was found to be round-shaped, well-demarcated, waxy, yellow-brown with atrophic center and indurated, raised border (FIGURE 1).

Dermoscopically, the elbow lesion was characterized by a diffuse structureless yellowish-pink background and well-defined linear vessels. structureless areas and follicular plugging (FIGURE 3A).

Histopathological examination of the elbow plaque revealed near normal epidermis. The mid to deep dermis featured foci of layered degenerated collagen alternating with palisaded granulomatous inflammation mainly composed of histiocytes, lymphocytes, plasma cells and multinucleated giant cells. Marked lymphocytic and eosinophilic perivascular infiltrate was noted as well (FIGURE 4). Iron colloidal staining revealed no

evidence of mucin deposition in the affected dermis. These clinical, dermoscopic and dermatopathological features confirmed the diagnosis of NL.

In the last 4 months, she noticed the onset of a new hyperpigmented plaque with well-defined borders and noticeable firmness upon palpation on the right upper abdomen (FIGURE 2).

On dermoscopy, the truncal lesion showed ill-defined white clouds (also known as fibrotic beams), scattered pinkish areas, and pigmentary structures, including structureless brownish and reticular brownish areas (FIGURE 3B).

Punch biopsy from her truncal plaque was performed and revealed hyperkeratosis. the dermis featured marked dermal fibrosis with thickened collagen bundles and perivascular lymphoplasma cell infiltrate consistent with morphea (FIGURE 5).

During her initial visit, laboratory tests revealed a fasting blood glucose level of 89 mg/dL (normal range of 70-100 mg/dL), a hemoglobin level of 10.8 g/dL (normal range of 12.3-15.3 g/dL), and an erythrocyte sedimentation rate of 38 mm/h (up to 20 mm/h). Other biochemical tests were normal.

The patient began treatment with topical mometasone furoate 0.1% and tacrolimus 0.01% along with monthly intralesional injections of triamcinolone acetonide. However, after 3 months of follow-up no significant improvement was noted, and she subsequently missed her follow-up appointments.

DISCUSSON:

NL is an inflammatory dermatosis with degenerative connective tissue changes very often linked to diabetes. According to previous reports, diabetes mellitus is a common comorbidity, occurring in greater than 50% of NL patients(5, 6). In 14% of cases, NL emerges before diabetes mellitus is diagnosed. In 24% of cases, NL appears concurrently with the onset of diabetes. In the remaining 62% of cases, NL emerges after diabetes has already been diagnosed. However, our patient did not mention any history of diabetes and her blood glucose levels were within normal range during the visit to dermatology clinic. Additionally, her NL lesion was located on her elbow rather than the more common pretibial area. This represents a deviation from the typical NL lesions being localized to the lower extremities in approximately 85% of NL cases (1).

While the clinical presentation of morphea can vary significantly between patients, there is currently no universally accepted classification system. Kreuter et al.(7) have suggested a five-part categorization of morphea: limited, generalized, linear, deep, and mixed (a combination of at least two prior types). Each of these primary types can be further subdivided into various clinical subtypes. In the case presented, the patient demonstrated plaque type morphea over her trunk. plaque type morphea is classified under limited morphea and is recognized as the most common manifestation of localized scleroderma in adults.

Several studies have investigated NL comorbidities including cutaneous comorbidities. We conducted a PubMed search for articles containing "necrobiosis lipoidica" in the title or abstract. Additionally, no limitations were placed on language or year of publication for the included articles. We detected 11 retrospective articles focusing on NL comorbidities (table 1). Severson KJ et al.'s (5) research on 328 NL patients revealed that, psoriasis, scleroderma and morphea were reported as coexisting dermatoses. Similarly, a study by Jockenhöfer et al. (8) examined 262 NL patients and found psoriasis, erysipelas and other local infections of skin and subcutaneous tissues as comorbidities. In a smaller study by Erfurt-Berge et al. (9) involving 52 NL patients, cutaneous sarcoidosis was the only reported coexisting dermatosis. Finally, Marcoval, J., et al. (10) conducted a study on 35 NL cases and found granuloma annulare to be the sole cutaneous co-diagnosis. Other studies mainly focused on non-cutaneous comorbidities such as diabetes, hypertension, dyslipidemia and thyroid disease, thereby did not offer any insights into cutaneous comorbidities. These studies collectively imply that the coexistence of inflammatory and autoimmune dermatoses with NL is not uncommon. This association is likely attributable to the underlying dysregulation of the immune system, which may predispose individuals to multiple autoimmune manifestations.

Specifically, Coexistent NL and morphea has been documented only 4 times in the literature. As mentioned

above, the retrospective study conducted by Severson KJ et al.(5) found that among 328 NL patients, only 3 cases were reported to have coexisting morphea. Additionally, Acebo E et al (4) reported a 59-year-old woman with morphea affecting her breast who also developed NL lesion over the scar from an appendectomy she had undergone 38 years earlier. Similar to our case she did not develop any NL lesions on pretibial area.

NL and morphea are 2 separate disease entities with noteworthy similarities and differences. Both diseases are inflammatory dermatoses with different patterns of inflammation and collagen abnormalities. Histopathologically, NL is marked by necrobiotic collagen surrounded by layered granulomatous inflammatory infiltrate. This granulomatous reaction mainly consists of dermal and subcutaneous infiltrate of histiocytes, epithelioid cells, and multinucleated giant cells with epidermis often remaining unaffected (8, 11). In contrast morphea is defined by an autoimmune fibrosing disease characterized by excessive collagen production and the presence of perivascular lymphocytic inflammatory infiltrate, particularly evident in the early stages of the disease.(4, 7). Both conditions also show a female predominance, with morphea having a female-to-male ratio of around 4:1 and NL having a ratio of around 3:1.

Dermoscopically, both NL and morphea exhibit vascular abnormalities albeit with distinct patterns. Morphea features linear branching vessels along with scattered whitish fibrotic beams and brownish reticulated areas. On the other hand, NL lesions are characterized by comma-shaped vessels during the initial phase, transitioning to arborizing vessels in the final phase, all against a yellow-white background (1, 3, 12).

Given the role of immune system dysfunction in the pathogenesis of both NL and morphea, the mainstay of treatment for these conditions is corticosteroids and immunomodulators. Additionally, phototherapy-based therapies were shown to be effective in alleviating both conditions. In fact, ultraviolet light exposure exerts anti-inflammatory effects via modulating inflammatory cytokines and depleting certain inflammatory cells (3, 7, 12).

CONCLUSION:

Necrobiosis lipoidica and morphea are two distinct skin conditions that share some similarities but also have notable differences. In rare cases, patients have been found to have both NL and morphea concurrently, suggesting a potential overlap in their underlying pathophysiological mechanisms. Both diseases are marked by distinct patterns of inflammation and collagen abnormalities, with NL featuring necrobiotic collagen and morphea exhibiting collagen overproduction leading to sclerosis. Additionally, female predominance and similar treatment approaches including immunomodulators and phototherapy, further highlights their shared pathophysiological mechanisms involving immune system dysregulation.

Table 1 : NL & associated cutaneous comorbidities

References	Studied population	No. of NL Patients	Gender (F/M)	Gender (%)	DM status	cutaneous
					DM	No DM
Heite 1959 (13)	NL patients	265	209/56	78.9/21.1	160	105
Muller 1966 (11)	NL patients	171	131/40	77/23	111	60
O'Toole 1999 (14)	NL patients	65	63/2	96.9/3.1	8	57
Erfurt-Berge 2012 (9)	NL patients	52	40/12	79.9/23.1	24	28
Erfurt-Berge 2015 (15)	NL patients	100	77/23	77/23	43	57
Marcoval J. 2015 (10)	NL patients	35	29/6	82.8/17.1	23	12
Hammer 2016 (16)	DM1 patients	161	108/53	67.1/32.9	161	0
Jockenhofer 2016 (8)	NL patients	262	166/96	63.4/36.6	90	172
Hashemi 2019 (6)	NL patients	236	200/36	84.7/15.2	138	96
Erfurt-Berge 2022 (2)	NL patients	98	82/16	83.7/16.3	53	45
Severson 2022 (5)	NL patients	328	282/46	86/14	167	131

DM: Diabetes mellitus DM1: Diabetes mellitus type 1 – F/M: Female/Male – No.: Number – NOP: number

of patients

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