Disseminated perforating necrobiosis lipoidica: a case report and literature review

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Summary

Perforating necrobiosis lipoidica is an unusual variant of necrobiosis lipoidica, a rare, chronic granulomatous dermatitis. Histopathologically, it is characterized by widespread degeneration of collagen, palisading histiocytes, presence of plasma cells, absence of mucin, and transfollicular or transepidermal perforation. We describe a case of disseminated perforating necrobiosis lipoidica in a 69-year-old insulin-dependent diabetic man. This is the fourth disseminated case to be reported. It can be challenging to make the diagnosis due to the overlap with perforating granuloma annulare, therefore the significant distinguishing clinical and histopathological features are discussed.

KEY WORDS: perforating necrobiosis lipoidica; perforating granuloma annulare; necrobiosis lipoidica; granuloma annulare; disseminated perforating necrobiosis lipoidica.

Introduction

Necrobiosis lipoidica (NL) is an idiopathic, chronic granulomatous dermatitis, first described in 1929 (1). It was originally termed ‘dermatitis atrophicans lipoidica’ by Oppenheim (2), and historically also known as necrobiosis lipoidica diabetorum. It occurs in 0.3% of diabetic adults and 0.06% of diabetic children (3), but also in patients without diabetes mellitus (4). It is three times more common in women than men, and classically presents in early to middle adulthood (1, 3-5). Approximately 85% of cases affect the lower leg only (4), although it has been reported to affect the scalp, face, trunk, upper extremities and genitals (5-7). Mul-

Case report

A 69-year-old retired farmer was admitted with poorly controlled insulin-dependent diabetes and an atypical leg lesion. His past history consisted of ischaemic heart disease, metabolic syndrome, peripheral neuropathy, chronic renal impairment and gout. The patient also had chronic multi-resistant staphylococcus aureus (MRSA) osteomyelitis complicating internal fixation of a left foot fracture. The patient reported his leg lesion had become more inflamed, tender and violaceous over the week prior to admission. On examination, he had a warm, tender, oedematous plaque with secondary violaceous change and several small punctate sinuses draining clear fluid. In addition, the patient was found to have multiple erythematous, annular plaques with a raised, rolled edge, up to ten centimetres in diameter on the extensor surfaces of all four limbs (Figure 1). Many demonstrated central atrophy, hair loss and yellow pustule-like and hyperkeratotic papules studded throughout. The patient also had several late-stage lesions; atrophic plaques with central yellow hypopigmentation and telangiectases. These plaques had developed over many years and were asymptomatic, but the patient was distressed by their cosmetic appearance. He also described occasional spontaneous clear-white ‘cheesy’ discharge from the papules.

The clinical differential diagnosis for our case included infective causes, including botryomycosis, atypical mycobacterial or deep fungal infection, or atypical granuloma annulare (GA). A swab and skin biopsy were taken from the right leg lesion for culture; both yielded growth of MRSA. The deep fungal tissue culture was negative. Punch biopsy of a plaque on the right forearm showed multiple, well defined zones of collagen degeneration, throughout the depth of the dermis, bordered by a palisade of histiocytes. There was epidermal and follicular hyperplasia associated with hyperkeratosis and elimination of necrotic collagen into a dilated hair follicle infundibulum (Figure 2).
A superficial and deep perivascular lymphocytic infiltrate was present accompanied by moderate numbers of plasma cells. No mucin deposition was identified in the zones of necrobiosis. The biopsy of the infected lesion showed more prominent acute inflammatory changes with spongiosis, papillary dermal oedema and neutrophilic infiltrate. The deep dermis and septa of the subcutaneous fat showed sclerosis and a perivascular lymphocytic infiltrate with plasma cells and occasional multinucleate giant cell (Figures 3, 4). NL was favoured over GA due to the clinical feature of residual atrophic scarring, and the histological features of diffuse dermal involvement, a heavy plasma cell infiltrate and absence of mucin. The presence of transfollicular perforation distinguished our case as the rare perforating variant. Botryomycosis was excluded due to the absence of suppurative inflammation and the Splendore-Hoeppli phenomenon on histology. A diagnosis of disseminated perforating necrobiosis lipoidica was made, with secondary MRSA infection of the right leg lesion. Due to our patient's extensive comorbidities, systemic treatments were reserved for use in the event of clinical deterioration. He received antibiotics for the secondarily infected leg lesion and potent topical steroid ointment under occlusion to his lesions with some improvement in cosmetic outcome.

Discussion

Of the 16 cases of PNL described in the literature (2-4, 11-15), only 3 have presented with multiple lesions and can be classified as disseminated (2, 12, 14). Our patient is the fourth such case to be reported. The plaques of PNL retain many of the clinical features of the common variety, as slowly enlarging yellow-red atrophic plaques with purple, serpiginous borders and telangiectases (3). PNL however does have several distinguishing features; it is more frequently described as a red plaque, with a sclerotic, indurated texture (3, 4, 9) and the presence of multiple hyperkeratotic papules or comedo-like plugs dotted throughout (2-4, 9, 13, 14). Earlier lesions tend to show pustule-like foci, which spontaneously drain white or clear material (14), as in our case, and evolve into crusted papules. The end-stage lesions are atrophic, scarred annular areas with hypopigmentation and an absence of hyperkeratotic plugs or papules. Our patient demonstrated lesions at all of the above described stages of evolution. They are typically asymptomatic (2), but can be cosmetically unacceptable (4). The distribution of our patients' plaques may be due to the Koebner phenomenon, which has been reported in PNL (8), as they occurred on the anterolateral legs and dorsolateral forearms, which are common sites for minor trauma.

The pathogenesis of necrobiosis lipoidica remains unclear. A proposed role for autoimmunity exists based on demonstration of IgM and immune complexes within NL lesions and dermal microvessels (5, 7, 9). It may be due to diabetic microangiopathy (1, 6, 7) or a hypoxia-induced vasculopathy (5). Multiple collagen abnormalities have been noted in NL plaques, including abnormal collagen production (1), the accelerated glycation and oxidation of collagen seen in diabetic skin and subsequent increased collagen cross-linking following oxidation (7). Whether it is a primary collagen disorder, or secondary to diabetic changes, NL may be due to collagen degeneration with secondary inflammation and granulomatous change (5, 7).

Transepidermal elimination is the mechanism by which material is actively eliminated through the epidermis, without significant effect on the epithelium (3, 12). It occurs via a dermal-epidermal interaction, with...
the dermis above hair papillae identified as a more sensitive zone of activation for transepidermal elimination (12). Transepidermal elimination may be due to altered dermal connective tissue or abnormal basal layer focal keratinization stimulating a host inflammatory response (2). Fujimoto et al. hypothesized that it may occur due to expression of keratinocyte receptors for minor types of collagen or elastin (e.g. collagen IV, V and VI and the 67-kDa elastin receptor respectively) (16). The material being extruded must be sufficiently foreign to provoke a reaction, yet not so reactive that it stimulates marked inflammation and necrosis (12). In PNL, there have been reports of transepidermal and transfollicular perforation of collagen, elastin, necrotic connective tissue and calcium (3, 11, 15). These foci of perforation correlate clinically to the hyperkeratotic, plugged papules, and transfollicular elimination may account for the absence of hair within plaques (3, 14).

The histopathological differential diagnosis for our case consisted of other dermal granulomatous diseases that may display perforation, such as GA, sarcoidosis and necrobiotic xanthogranuloma. Our patient lacked the other features required to support these diagnoses clinically and histopathologically. Clinicopathologic correlation was also required to distinguish between the two favored diagnoses of PNL and perforating granuloma annulare (PGA). These conditions can be challenging to differentiate, as both are more common in women, have been associated with diabetes and rarely involve the face. It is not possible to distinguish between them on clinical examination alone, as both have been described as red-yellow annular plaques with perforation (1, 6), and tend to have a long clinical course (17). PNL always presents as a plaque, typically on the lower legs and always results in atrophic, hypopigmented

Figure 2 - (A) Low power view of follicular hyperplasia (upper arrow), large zones of eosinophilic staining degenerate collagen (mid arrow) throughout the dermis, and superficial and deep perivascular inflammatory cell infiltrate (lowest arrow), (B) Follicular elimination of necrotic collagen (arrow) and (C) Palisading of histiocytes around zones of dermal collagen degeneration.

Figure 3 - (A) Epidermal hyperplasia and parakeratosis. Perivascular lymphocytic inflammatory cell infiltrate and focal multinucleate giant cells (arrow), (B) Numerous plasma cells (arrow) associated with the lymphocytic perivascular infiltrate.
scars (17). Traditionally, PGA is usually seen as annular arrangements of comedo-like, plugged papules on the dorsal hands or lower legs (1). However, Penas et al. published a review of 58 cases of PGA in 1997 that proposed several alternative clinical conclusions; namely that the perforating variety is more often disseminated and that approximately one third of PGA lesions will resolve with scarring (17). Since this time, only sparse reports of PGA and PNL have appeared in the literature, particularly cases with a disseminated distribution. The histopathology of NL and GA is a granulomatous dermatitis associated with degeneration of dermal collagen, histiocytes arranged in a palisade around zones of necrobiosis and interstitially between collagen fibres, and a perivascular chronic inflammatory cell infiltrate (6, 17-19). The perforating variants show transepithelial elimination of necrotic material. It may be that some cases included in Penas’ review actually represent misdiagnosed PNL, as in the review the distinguishing histological features for 52 out of the 58 cases were not discussed. Despite the histological similarities, there are many potential distinguishing features between the conditions. NL shows diffuse dermal as opposed to patchy involvement of the dermis seen in GA. There is frequent extension into the superficial subcutis in NL. Plasma cells accompany the lymphocytic perivascular infiltrate in NL and are not a feature of GA. Eosinophils maybe seen in GA. Mucin deposition is absent in the zones of necrobiosis in NL but typically present in GA (2, 3, 5, 6, 11, 14). There is discordance between Authors whether to accept transfollicular perforation within the spectrum of PGA (3, 18, 19), however it is widely accepted in PNL. In late lesions of PGA, resolution may occur with restoration of normal cutaneous structures, contrasting with the dermal and subcutaneous sclerosis seen clinically as atrophic scarring in PNL. The potential complications of PNL include ulceration (1, 6), often secondary to trauma (8) and scarring leading to joint contractures or alopecia (9). There are rare case reports of malignant transformation, to squamous cell carcinoma or epidermoid carcinoma occurring within ulcerated or perforating NL, with an associated poor prognosis (4, 15). Although the role of glycaemic control in PNL remains unclear, diabetic patients with the condition do have higher frequencies of nephropathy and retinopathy (3, 4), consistent with our case. Ulcerated NL lesions can become infected, similar to other chronic wounds on the lower leg (1). Secondary bacterial infection of the perforating variant has not previously been reported, yet the foci of transepithelial perforation represent a vulnerability in the skin barrier. Our patient was predisposed to infection as he was colonised with MRSA, may have unwittingly traumatised the lesion due to his peripheral neuropathy and had consistently poor glycaemic control. Treatment of both NL and PNL is often unrewarding. Anecdotally, many treatments have been used with lit-
tle success, from conservative measures such as optimising glycaemic control, to topical therapies such as retinoids or oral immunomodulators and antiplatelet agents (1-4, 7, 12). Some improvement with intralesional corticosteroid or potent topical corticosteroids under occlusion has been reported (3, 13). This is an illustrative case of a very rare presentation of necrobiosis lipoidica, with features of dissemination, perforation and secondary bacterial infection. In variants of NL characterized by a scarring process such as ulceration or perforation, early biopsy of any concerning areas is mandated to detect malignancy (15). Given that the vast majority of PNL reported so far have occurred in diabetic patients, we would recommend screening all patients newly diagnosed with PNL for diabetes. PNL can be a challenging diagnosis to make with significant histological overlap with PGA. It is possible that it has previously been under-recognised and misdiagnosed as PGA in the literature. We have sought to highlight the distinguishing features between the two conditions to aid dermatologists and pathologists with future diagnoses. While it would not significantly influence clinical management, the development of standardised diagnostic criteria for these perforating, palisading granulomatous dermatoses would provide diagnostic clarity and reveal their true prevalence.

References