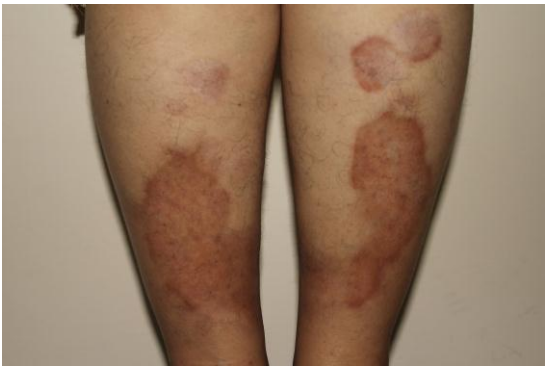
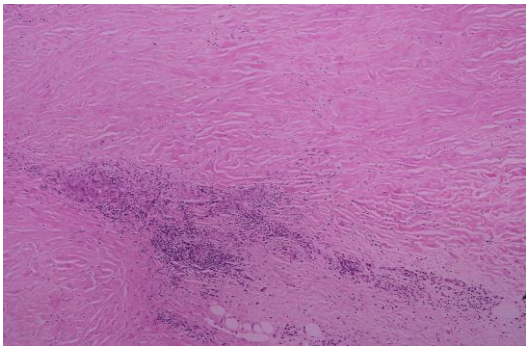
Case 26
A 48-year-old Thai woman from Suradthanee.
Chief complaint: Rashes on both shins for 15 years.



Present illness:
The patient noticed asymptomatic rashes on both shins 15 years ago. The rashes got very slowly enlarging.
Past history: no underlying disease

Skin examination
- 2 large, well-defined, yellow-brown, atrophic plaques with telangiectasias and a slightly elevated hyperpigmented rim, located on both pretibial areas
- 2 smaller plaques in the same features located above

Histopathology: (S13-12291, left shin)
- Nodular and palisading inflammatory-cell infiltrate of histiocytes, multinucleated giant cells admixed with some lymphocytes and plasma cell, in association with homogenized bundles collagen bundles in the dermis and subcutaneous tissue
- Epidermal atrophy with abundant epidermal melanin



Diagnosis: Necrobiosis lipodica

Investigation: Normal fasting blood glucose

Treatment
- Advice about the natural history and prognosis of disease
- Oral pentoxifylline 800 mg/day

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Discussion

Necrobiosis lipoidica (NL) is an uncommon granulomatous skin disorder of unknown origin. It was firstly described in diabetic patients, so it was previously named as necrobiosis lipoidica diabeticorum(NLD). Later, this condition was also reported in non-diabetic individuals, making the term 'necrobiosis lipodica' generally preferred. However, the abbreviation NLD is still widely used.

NL is more common in women rather than men with a ratio of 3:1, and its average age of onset is 30-40 years. Although it has been considered to be strongly associated with diabetes mellitus, particularly type 1, the proportion of NL patients with underlying diabetes mellitus varies from 16% to 65%.[1-3] Furthermore, NL is

present only in a small percentage of the diabetic population, 0.3% to 3%. Interestingly, when compared with diabetic patients who have no NL, diabetic patients with NL have a higher risk of retinopathy and proteinuria[4], so NL patients should be monitored for abnormality in glucose metabolism and possible end-organ damage. Apart from DM, many diseases have been reported to be associated with NL, such as sarcoidosis, rheumatoid arthritis, autoimmune thyroiditis and inflammatory bowel disease.[5]

Clinically, the typical NL is characterized by violaceous to red-brown plaques with elevated peripheral rims, and yellow-brown, atrophic, telangiectatic centers, located on the pretibial region. The lesions are usually multiple and bilateral. NL starts as small red-brown papules that slowly expand and change in the center. Besides anterior shins, NL appears to occur in upper extremities, face, scalp, trunk and penis in the minority of cases.[5] In the less typical locations, lesions tend to be more annular or serpiginous in shape and less atrophic. Even though NL lesions are generally asymptomatic, some patients complain pruritus, decreased sensation or pain. Partial alopecia and hypohidrosis can also be found within the NL plaques.[1]

Ulceration is the most common and hard-to-treat complication of NL, occurring up to 35% of cases.[6] It is usually following a minor trauma. Rarely, squamous cell carcinoma developing within the NL lesions has been reported.[7]

Although the cause of NL remains unclear, two main mechanisms have been postulated in the pathogenesis of NL, vascular abnormality resulting in collagen degeneration and primary collagen disease. In the pole of vascular pathology, several hypotheses have been suggested including immune-complex vasculitis, diabetic microangiopathy, elevated platelet adhesion, increased thromboxane A_2 production and increased blood viscosity.[8]

Histopathological features include multiple areas of degenerated collagen called 'necrobiosis', in association with palisaded and interstitial granulomas within the entire dermis extending into subcutaneous fat. The granulomatous inflammation, comprised of epitheloid histiocytes, multinucleated histiocytes, and inflammatory cells (which are predominantly lymphocytes, admixed with some plasma cells and eosinophils), is aligned parallel to the skin surface showing "layered" appearance.[8]

Although there are plenty of therapeutic options for NL, overall treatment has not proven to be effective in large, double-blind, placebo-controlled studies.[9] Spontaneous remission does occur after many years of disease in less than one-fifth of cases.[2] In case of DM, blood-sugar controlling seems to have no effects on the course of NL. Smoke cessation is recommended to all NL patients.

The important roles of immune cells and inflammatory cytokines in NL pathogenesis make the rationale for immunosuppressive and immunomodulatory agents in NL treatment. The first-line therapy is potent topical corticosteroids and intralesional corticosteroids injected into the active borders, particularly for the early lesions.[8] Other immune-mediated therapies reported to be effective are topical tacrolimus, systemic corticosteroids, cyclosporine, mycophenolate mofetil and phototherapy (topical PUVA and UVA1 phototherapy).[5, 8, 10] As vascular pathology is suspected, the benefits of antiplatelet agents, ticlopidine hydrochloride, and pentoxifylline have been demonstrated.[5, 10] It has been known that TNF-α, a proinflammatory cytokine, has a major role in the formation of granulomas, and treatment with anti-TNF-α agents is effective in many cutaneous granulomatous diseases, including NL.[10, 11] Furthermore, a number of therapies have been anecdotally reported to be helpful in this condition, such as fumaric acid esters, antimalarial agents, thalidomide, and clofazimine.[5, 10]

In case of refractory to medical treatment, fractional CO2 laser and excision with skin grafting are other options.[8, 12]

Our patient is another classic case of necrobiosis lipoidica. The patient is female presented with typical plaques on the classic location, appearing on her 30s. The plaques are indolent and very slowly growing. She is not a known case of diabetes mellitus, and has no abnormality in glucose testing at the presentation. The clinical and histopathological findings recover the diagnosis of late-stage Necrobiosis lipoidica. She is treated with oral pentoxifylline and waiting to see the outcome.

References

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