Necrobiosis lipoidica and inflammatory eye disease

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DECLARATIONS

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Skin and ocular inflammation can co-exist. We report a case of non-diabetic necrobiosis lipoidica with uveitis and retinal vasculitis.

Case report

Skin and ocular inflammation can co-exist in several inflammatory conditions such as rheumatoid arthritis, sarcoidosis, Wegener's granulomatosis and polyarteritis nodosa.[1] We report a case of non-diabetic necrobiosis lipoidica in whom periods of skin inflammation were associated with exacerbations of ocular inflammation in the form of intermediate uveitis and retinal vasculitis over 20 years.

In July 1988, a 43-year-old Caucasian woman presented with blurred vision and floaters with a three-year history of recurrent iritis in both eyes. Visual acuities were 6/5 in the right eye and 6/6 in the left eye. As she had bilateral inflammatory cells in the anterior chamber and a vitreitis with inferior vitreous aggregates ('snowballs') in both eyes, she was diagnosed with bilateral intermediate uveitis, which over a 9-month period led to cytoid macular oedema in the right eye (visual acuity 6/6). Over the next 24 moths bilateral obliterative peripheral retinal vasculitis occurred, though visual acuity remained 6/9 and 6/6 in right and left eye. Inflammatory markers, infective screen, serum ACE and chest X-ray were all within normal limits. Concurrently she had developed atrophic plaques on the skin of both shins associated with impaired light-touch sensation on the right leg. Her past medical history was significant for granuloma annulare on her hands at age 24 years. Fasting blood glucose and HbA1C were normal and Doppler ultrasound studies of the lower limbs excluded arteriovenous pathology. A skin biopsy confirmed the diagnosis of necrobiosis lipoidica.

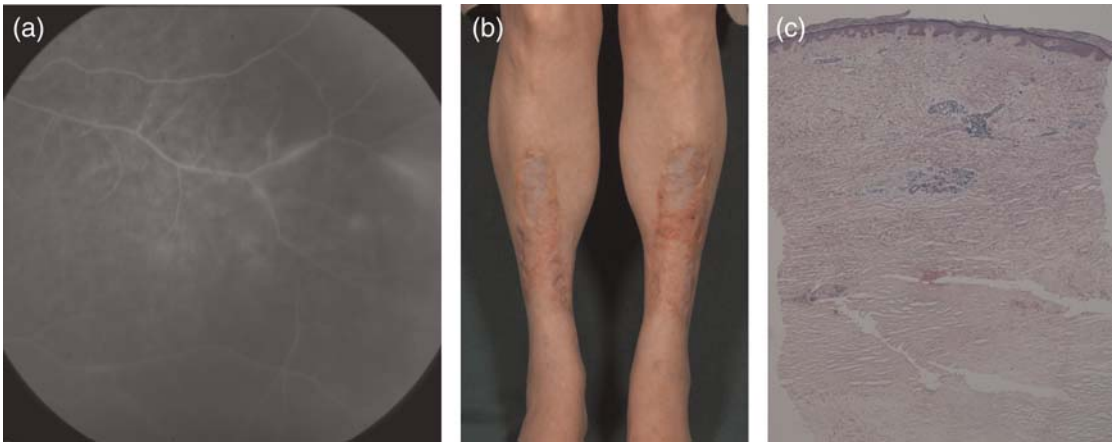
The skin plaques intermittently ulcerated in the years following diagnosis, coinciding with exacerbations of her ocular signs on each occasion. Cutaneous treatments over a 20-year period ranged from intralesional triamcinolone (10 mg/mL) to oral nicotinamide 500 mg tds, clofazime 200 mg od, cyclophosphamide 100 mg bd (3 $mgkg^{-1}$) and topical GM-CSF, each variably effective.

Her ocular inflammation required only topical corticosteroids, until 10 years after first presentation when the retinal vasculitis in the left eye (Figure 1a) led to peripheral retinal neovascularisation, treated successfully with laser panretinal photocoagulation. Visual acuities were 6/9 in the right eye and 6/6 in the left eye. Both ocular and cutaneous inflammation remained controlled for another 9 years, when she had another concurrent recurrence of both bilateral intermediate uveitis and necrobiosis lipoidica (Figure 1b).

Repeat skin biopsy (Figure 1c) revealed normal epidermis but the dermis showed a moderate, sharply demarcated predominantly plasmacytic perivascular infiltrate with foci of multinucleated giant cells in the deep dermis. The deeper part of the sample showed necrobiotic collagen. There was a small focus of fat necrosis within the collagen and the medium-size deep dermal artery showed moderately thickened media. Mild positive staining for complement C3 was seen in the endothelium of the small dermal vessels on immunohistochemical staining but no obvious

Figure 1

a. Fluorescein angiogram of the periphery of the left eye shows leakage of dye from inflamed retinal veins and peripheral shutdown of the retinal vasculature; b. Necrobiosis plaques on both shins; c. Histology from bunch biopsy of necrobiotic skin. Note plasmacytic perivascular infiltrate with multinucleated giant cells in the deep dermis (haematoxylin & eosin, x20)



IgM deposits were present. There were no features of active vasculitis (i.e. intramural neutrophils, fibrin cuffing, red cell leakage or leucocytoclasis). The overall histological appearances were in keeping with the clinical diagnosis of necrobiosis lipoidica.

Discussion

Several skin disorders can be associated with ocular inflammation, involving the sclera or producing intraocular inflammation.[1] Rheumatoid arthritis is a common systemic autoimmune disease that presents with inflammatory signs in the joints, and can also manifest skin abnormalities in the form of rheumatoid nodules, small painless vasculitic infarcts around the nails and pulp of the fingers and pyoderma gangrenosum, with ulcerative lesions developing especially in traumatised areas. The ocular manifestations of this condition include scleritis, keratitis and dry eyes. Sarcoidosis is a granulomatous disease of unknown aetiology, which affects the skin in up to 35% of patients with manifestations such as erythema nodosum and lupus pernio. In terms of ocular involvement sarcoid can be associated with uveitis, both anterior and posterior, which typically manifests itself as retinal vasculitis. Wegener's granulomatosis is an uncommon multisystem disease characterized by vasculitis and necrotizing, granulomatous inflammation. Up to 50% of the patients will show skin lesions, with palpable purpura or petechial lesions that can progress with ulcerations being the most common. Other forms of skin involvement involve vesicles, pustules, ecchymoses, splinter haemorrhages of fingernails and even gangrene of digits. Ocular manifestations include orbital inflammation, and scleritis as the most common, and also peripheral ulcerative keratitis, uveitis and papillitis. Necrotizing scleritis is a common and destructive form of ocular inflammation. In polyarteritis nodosa, a systemic vasculitis involving small and medium-sized blood vessels, the classic skin finding is that of nodules tracing the course of superficial arteries. The most common lesions are non-specific macules, papules and urticaria. The ocular manifestations, depending upon the site of vascular involvement include retinal vasculitis, papillitis and involvement of orbital vessels.

The pathogenesis of necrobiosis lipoidica remains uncertain although theories include an immune complex vasculitis, a collagen production disorder and a manifestation of diabetic microangiopathy.[2] The association of necrobiosis lipoidica with diabetes mellitus is controversial however. In one large series, two-thirds of patients with necrobiosis

lipoidica had diabetes.[3] In another smaller retrospective study, a much lower incidence of diabetes (11%) was found in patients with necrobiosis lipoidica at the time of presentation.[4]

Clinically, well-demarcated atrophic yellowish plaques are characteristic, typically on the pre-tibial skin. The plaques often have a shiny surface and telangiectasia. Although the condition is usually asymptomatic, hypoaesthesia and hypohidrosis may be found within plaques. Lesions are commonly bilateral, tend to persist and may ulcerate. Squamous cell carcinoma developing in long-standing lesions has been reported.[5]

The co-existence of ocular inflammation and necrobiosis lipoidica has received sparse attention in the literature. To our knowledge this possible association has been reported only in the context of a diabetic patient with sarcoidosis, who developed chronic unilateral iridocyclitis and necrobiosis.[6] Our patient differs from that report in the fact that she developed both skin and ocular inflammation without diabetes.

We would therefore recommend that patients presenting to general physicians and dermatologists with necrobiosis lipoidica should be asked about ocular symptoms and referred to an ophthalmologist for evaluation as appropriate.

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