Correspondence

PUVA therapy of granuloma annulare

Sir, We read with interest the report by J. Setterfield *et al.* concerning granuloma annulare (GA), successfully treated with PUVA.[1] We have also successfully treated three similar cases using PUVA, two with generalized GA and one with localized GA.

Case 1 is a 53-year-old woman who had generalized GA of 4 years duration which had not responded to topical steroids and dapsone. PUVA therapy was administered with a final UVA dose of 3 J/cm^2. Continued treatment was required for 3 months (once per week for 1 month then once every 2 weeks). The dose was 144 J/cm^2. The patient has no history of diabetes mellitus.

Case 2 is a 52-year-old woman who presented with a 4-month history of disseminated GA and no history of diabetes mellitus. The patient had not responded to topical corticosteroid, dapsone or niacinamide therapy. PUVA treatment was started three times weekly with a final UVA dose of 4.5 J/cm^2. Complete clearance was obtained after 48 treatments. A continued treatment was required (twice per week for 1 month). The total dose was 129 J/cm^2. The patient had no reoccurrence during an 8-month post-treatment observation period.

Case 3 was a 51-year-old woman who was treated for primitive biliaris cirrhosis and also had localized GA affecting her legs of 18 months duration. PUVA therapy was administered four times a week with a final UVA dose of 12 J/cm^2. Complete clearance was obtained after 5 months. Continued treatment was required for 2 months (once every 2 weeks). The total dose was 665 J/cm^2. Some scarring remains at the sites of lesions.

In contrast with the case reported by Setterfield, long-term continuous therapy was necessary in order to maintain remission. We conclude, as did Setterfield, that a formal study must be undertaken in order to determine the role of PUVA in the successful treatment of GA. The potential risks for long-term PUVA therapy should be considered. Similar risks are faced with bath PUVA therapy or phototherapy with UVA1, the two methods used successfully to combat this disorder.[2–3]

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Are patients with localized nodular granuloma annulare more likely to have diabetes mellitus?

Sir, Granuloma annulare (GA) can present in a variety of forms, the most common being the localized annular type. Other presentations include generalized, perforating, linear and subcutaneous nodular GA. The relationship with diabetes has been studied extensively and it is generally agreed that in localized annular GA an association with diabetes is unusual. However, there may be subtypes of GA such as the generalized form in which an association with diabetes is more common.[1,2]

We describe four cases of nodular GA in adults, each associated with diabetes mellitus; we question whether this type of GA in adults may be more frequently related to diabetes.

Case 1 is a 41-year-old male with an 8-year history of insulin-dependent (type I) diabetes. He presented with lesions on both hands. He had undergone excision of a number of these lesions 4 years earlier to relieve associated discomfort.

On examination there were nodular plaques on the dorsum

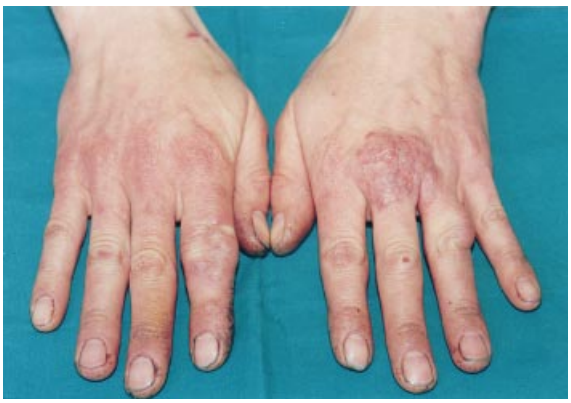

Figure 1 Plaques of nodular GA on the hands (Case 1).

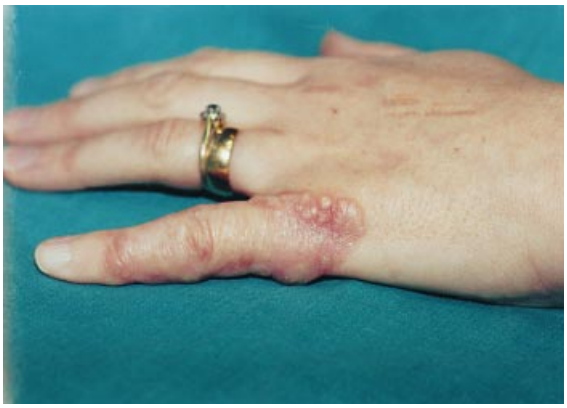

Figure 2 Nodular GA at the base of the fifth digit on the left hand (Case 2).

of the left hand, the left ring finger and also similar lesions on the dorsum of the right index finger (Fig. 1).

Histology showed areas of necrotic collagen surrounded by a pallisaded lymphohistiocytic infiltrate compatible with GA.

Case 2 is a 39-year-old female with a 15-year history of insulin-dependent (type I) diabetes. She presented with lesions on the left thigh, heel and hand and right calf, that had been present for approximately 5 years. On examination she had nodular GA on the left hand (Fig. 2). There were also annular GA lesions on the left heel and necrobiosis lipoidica on the left thigh and right calf.

Case 3 is a 69-year-old male with a 7-year history of type II diabetes that is controlled with gliclazide and metformin. He presented with a pruritic lesion on the right arm which had developed over the past year. Examination revealed a pigmented nodule with a slighty warty surface of 11 mm diameter on the right forearm. The clinical appearance was suggestive of a dermatofibroma; however, histology from an excision biopsy showed characteristic histology of GA.

Case 4 is a 41-year-old male with a 5-year history of insulin-dependent (type I) diabetes. He presented with lesions on both hands which had enlarged slowly over the past 4 years. Examination revealed a nodular lesion overlying the fourth metacarpophalangeal joint of the right hand which measured 3.5 × 2 cm and a similar lesion over the fourth proximal interphalangeal joint of the left hand. An incisional biopsy of the former confirmed the clinical suspicion of GA.

Annular localized GA is only rarely associated with diabetes mellitus and as both are common disorders the association may occur by chance. We report four adult patients with nodular localized GA and diabetes. Three of the cases had type I insulin-dependent diabetes whereas case 3 had type II diabetes controlled by oral medication. Localized nodular GA is an unusual variant of GA and we have been struck by the fact that that all four of our most recent consecutive cases of localized nodular GA in adults have had diabetes. Therefore we suggest that localized nodular GA in adults may have a genuine association with diabetes. One large retrospective study did show an association between localized GA and diabetes but did not specify whether the lesions were of the annular or nodular type.[3] To clarify this point future studies of GA should specify the clinical subtype of GA involved, and also record whether the patients have type I or type II diabetes.

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Pemphigoid gestationis with intra-uterine death associated with foetal cerebral haemorrhage in the mid-trimester

Sir, Pemphigoid gestationis is a rare auto-immune blistering disease of pregnancy. Estimates of incidence vary from 1 in 10 000[1] to 1 in 50 000[2] pregnancies. This rarity has made it difficult to study the potential risks to the foetus. Whereas one early study showed an increased risk of foetal death and premature delivery,[3] others showed no increase in foetal mortality,[4,5] but several reveal an increase in prematurity and small-for-dates infants.[6,7] More recently, a marginal increase in spontaneous abortion (mainly first trimester) and has been reported.[8] There have been no reports of increased risk to the foetus following use of systemic steroids.

We report a patient who has had four pregnancies, all with the same partner. The first was an uncomplicated pregnancy resulting in a normal male infant in 1992. In 1994, she underwent termination of pregnancy at 8 weeks. Two years later, she developed moderately severe pemphigoid gestationis in the 30th gestational week of her third pregnancy. Typical pruritic papulovesicular lesions appeared over her hands, feet and trunk, which resolved 4 weeks postdelivery of another normal male infant delivered prematurely at 34 weeks. Direct immunofluorescence revealed linear C3 and IgM deposited at the basement membrane zone. Indirect immunofluorescence revealed epidermal binding of C3 and IgG on salt-split skin. Other investigations revealed a thyroid microsomal antibody titre of 1 : 6400, with normal thyroid function. (The association of pemphigoid gestationis with other autoimmune diseases is well documented.[8])

In February 1999 she became pregnant with an IUCD *in situ*. The IUCD was removed at 10 weeks gestation, and at 14 weeks gestation she noticed the appearance of intensely pruritic vesicles over her fingers and toes. This rapidly deteriorated into florid pemphigoid gestationis confirmed by

histology and immunofluorescence studies but presenting 16 weeks earlier than in her third pregnancy. Treatment with potent topical steroid ointments helped initially, but within 3 weeks of development of the blisters, she required oral prednisolone (20 mg daily) to control her symptoms and to allow her to continue to work.

At 22 weeks gestation, an ultrasound scan (performed when the midwife failed to pick up a heartbeat) revealed foetal death. Post-mortem examination revealed a normal weight-for-dates female baby with evidence of several day old cerebral haemorrhage. It could not be elucidated whether there was an underlying vascular malformation or whether cerebral ischaemia preceded the event. The placenta showed signs of mild acute chorioamnionitis (nonspecific inflammation found in many 'normal' placentae), but was otherwise normal. The patient's thrombophilia screen including activated protein C resistance, antithrombin 3, lupus anticoagulant, proteins C and S and anticardiolipin antibodies were normal or negative. There were no other risk factors for foetal cerebral haemorrhage.

There is no previous report of foetal cerebral haemorrhage occurring in pemphigoid gestationis. This association may have occurred by chance, but it is unfortunate for two such rare disorders to have occurred together in one patient.

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