

A Case of Pemphigus Foliaceus Co-existing with Psoriasis

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CASE SUMMARY

History

A 37-year-old man first presented in September, 1997 with scaly plaques on the lower limbs, clinically consistent with plaque psoriasis. He was known to be hepatitis B surface antigen positive and hepatitis B e antigen negative. The psoriasis was subsequently treated with topical steroid and acitretin for ten weeks with a good response. He then defaulted follow-up, but re-attended in April, 1998 with widespread erosions and blisters associated with a burning sensation on the body and limbs.

Physical examination

On examination, there were widespread erosions affecting the face, body and limbs with no mucosal involvement. The lesions consisted of annular, polycyclic plaques with overlying scale. Desquamation of these scales resulted in widespread erosions (Figures 1 & 2). In addition, psoriatic plaques were present over both lower limbs (Figure 3).

Investigations

Two skin biopsies were taken. Biopsy from a plaque showed elongation of the rete ridges, spongiosis, hyperkeratosis and parakeratosis in the epidermis. Neutrophilic infiltrates were present in the cornified layer and a perivascular lymphocytic infiltrate was seen in the dermis. The appearance was consistent with **eruptive psoriasis**.

Biopsy from an erosion showed acantholysis in the upper and mid portion of the epidermis including the granular layer. Sparse eosinophils were present

among the acantholytic cells. There were occasional necrotic keratinocytes and exocytosis of lymphocytes in the epidermis. Direct immunofluorescence staining was positive for IgG and C₃ in an intra-epidermal pattern. The histological picture was consistent with **pemphigus foliaceus**.

Anti-skin antibody was positive at a titre of 1:160 and the anti-nuclear factor titre was 1:40. Complete blood picture, chest radiograph, renal and liver function tests were normal.

Progress

The patient was treated with topical steroid and emollient with good effect. The erosions resolved leaving plaque psoriasis on the lower limbs. Systemic



Figure 1: Annular, polycyclic plaques and erosions over the trunk



Figure 2: Close up view of similar plaques and erosions over the back



Figure 3: Psoriatic plaques over the lower limb

steroid was not started as he was HBsAg positive. However, he relapsed six months later in October, 1998 with widespread crusting and erosions affecting the face, body and limbs. He was also febrile and movements were limited by painful erosions. There was no mucosal lesion and anti-skin antibody level was 1:160. He was admitted and dapsone 100mg/day was started. He responded well and was able to tolerate this treatment. Haemoglobin level, reticulocyte count and liver function remained normal. He was discharged two months later with complete resolution of the lesions.

Dapsone was gradually reduced to 50mg/day over the next four months. He remained well-controlled with isolated erosions on the ankles and crusting on the scalp. Psoriasis remained controlled with thin plaques on the lower limbs.

He relapsed with pemphigus foliaceus again in February, 1999 with extensive polycyclic erosions on the chest, back, abdomen, jawline, upper and lower limbs. There was no mucosal lesion. Anti-skin antibody level was 1:40. This time he had no response to dapsone

100mg/day, therefore he was started on prednisolone 40mg/day, while dapsone was continued. The erosions subsided after one month and prednisolone was reduced to 20mg/day with no rebound of psoriasis or pemphigus foliaceus. There was increased scaling of psoriatic plaques on the lower limbs when the dose of prednisolone was reduced to 10mg/day, but apart from isolated erosions he remained under good control. Anti-skin antibody level decreased to 1:20 one month after discharge. Dapsone was stopped as the reticulocyte count increased to 3% and haemoglobin level decreased to 13.9 g/dl (from 14.5 g/dl) one month after discharge.

REVIEW ON PEMPHIGUS FOLIACEUS ASSOCIATED WITH PSORIASIS

Epidemiology

Idiopathic pemphigus foliaceus is an autoimmune blistering disease in which the blisters are located in the granular layers of the epidermis. There is an equal male:female ratio and a mean age of onset of 50-60 years. An endemic form of pemphigus foliaceus known as **fogo selvagem** is found in Brazil. Clinically and histologically it is identical to idiopathic pemphigus foliaceus. Affected patients tend to be young adults and children living in rural areas especially along river beds. The black fly, *Simulium pruinatum*, is found in these areas and is postulated to be a vector of this disease.

Clinical features

In pemphigus foliaceus, there are scaly, crusted erosions on an erythematous base affecting the face, upper trunk and scalp. Early lesions consist of small flaccid blisters which subsequently form erosions. The erosions are accompanied by a burning sensation and are exacerbated by sunlight. However, mucosal surfaces are rarely affected. The disease may remain localized for several years or may rapidly progress to a generalized form.

Histology

Histologically, there is acantholysis just below the stratum corneum and in the granular layer. Direct immunofluorescence is positive for IgG and C₃. Anti-skin antibody is found in pemphigus foliaceus which targets the 160 kd glycoprotein (desmoglein 1) within

the epidermis. The serum level of this anti-skin antibody correlates with the disease activity.

Management

Systemic steroid is the mainstay of treatment for pemphigus foliaceus. Doses used are similar to pemphigus vulgaris (for example, oral prednisolone 60-80mg/day). Other treatments include dapsone, azathioprine and gold. Plasmapheresis has been reported to be effective in isolated cases.

Pemphigus foliaceus co-existing with psoriasis

Psoriasis has been reported to be associated with systemic lupus erythematosus, bullous pemphigoid, myasthenia gravis and ulcerative colitis, suggesting that there is a predisposition to immune disease. Bullous pemphigoid is the most common blistering disorder reported to be associated with psoriasis. Its association was previously attributed to the treatment modalities used, such as ultraviolet B (UVB) phototherapy, psoralen-ultraviolet A (PUVA) photochemotherapy, anthralin or tar. However, there are two points against this hypothesis. Firstly, one would expect immunobullous disease to be associated with psoriasis more often than observed as these are commonly used treatments. Secondly, in a study of nine patients who developed both psoriasis and bullous disease (bullous pemphigoid, pemphigus vulgaris, cicatricial pemphigoid), Grunwald et al found that bullous pemphigoid developed in one patient with psoriatic arthritis who had not received any of these treatments.¹ Furthermore, none of the other patients in his series were treated with phototherapy, anthralin or tar, suggesting that other mechanisms are responsible for the association.

Pemphigus vulgaris is a known immunobullous disease associated with various autoimmune diseases such as myasthenia gravis and pernicious anaemia. However, there have been few case reports of its association with psoriasis, while it is even rarer in pemphigus foliaceus. A summary of reported cases of pemphigus foliaceus associated with psoriasis is given in Table 1.^{2,3,4} In patient 1, lesions of pemphigus foliaceus developed at the sites of previous psoriatic lesions, suggesting an inducing function of the previous psoriatic lesions. In the third case there was relapse of psoriasis when the dose of prednisolone was less than

Table 1. Reported cases of pemphigus foliaceus (PF) and psoriasis vulgaris

Age/sex	Distribution of PF lesions	Interval between psoriasis and PF	Direct IMF	Anti-skin antibody titre	Treatment	Outcome
F/40	erosions on the trunk, extremities, sites of previous psoriasis	10 years	Inter-cellular IgG, C ₃	1:80	topical steroids, methotrexate 25mg/wk	remission of psoriasis and PF
F/34	eczematoid patches on the flank, extremities	2 weeks	Inter-cellular IgG	1:80	prednisone, azathioprine (dosage not mentioned)	remission of PF
M/51	bullae, erosions on the neck, axillae, trunk	1 year	Inter-cellular IgG, C ₃	1:256	prednisolone 60mg/day	relapse of psoriasis with prednisolone < 15mg

15mg/day, highlighting the problem of rebound of psoriasis on steroid withdrawal. Immunosuppressive drugs (prednisolone, methotrexate, or azathioprine) were effective for controlling both pemphigus foliaceus and psoriasis. It could be seen that the cases reported were between 30-50 years of age and the average interval between onset of psoriasis and pemphigus foliaceus was four years (range: 1-10 years). In contrast, Grunwald et al found that psoriasis preceded the appearance of bullous pemphigoid or pemphigus vulgaris by an average of 20 years.¹

There has been increasing evidence that an immune mechanism is responsible for the development of psoriasis. Decreased suppressor T lymphocyte function has been reported in psoriatic patients.⁵ An increased ratio of helper to suppressor T lymphocyte function has also been described.⁶ In addition, psoriatic patients show depressed reactivity to sensitization with contact allergens. This abnormality returns to normal with treatment.⁷ Antibodies to stratum corneum together with rheumatoid factor have been found in psoriatic lesions,⁸ while antibodies against the nuclei of the basal layer in unaffected skin have been reported. In addition, streptococcal infection is known to cause an exacerbation of psoriasis. As streptococcal antigen is known to be a superantigen, it can act as a trigger in some psoriatic patients. Increased levels of γ interferon, interleukin 6, and interleukin 8 have also been reported,^{9,10,11} and drugs which suppress T lymphocyte

function (cyclosporin A, FK 506) are effective for psoriasis. Thus, it has been hypothesized that the immune dysregulation in psoriasis may provide a favourable environment for the expression of pemphigus antigens.² Alternatively, inadequate suppression of the humoral system due to decreased suppressor T lymphocyte function may result in the production of anti-skin antibodies, leading to bullous disease.⁴

Learning points:

Co-existence of pemphigus foliaceus and psoriasis is rare but has been reported. Systemic steroid is often required for control and there is a risk of flare of psoriasis on steroid reduction. Topical steroid may be used to control psoriasis in these cases.

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