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Pemphigus Foliaceous Successfully Controlled with Plasma Exchange During 10 Years

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A case of pemphigus foliaceous is presented, where the disease has been successfully controlled with plasma exchange therapy alone for 10 years. ***Key words: apheresis; autoantibodies; immunobullous diseases.***

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Plasma exchange as a treatment for pemphigus has been described for many years past. It has been suggested as an adjuvant therapy secondary to other alternatives (1–3). In the following, we describe a case where plasma exchange alone has been a successful treatment for over a decennium.

CASE REPORT

A 47-year-old man who, in 1981 at the age of 31, consulted the family physician for scaling and redness of the scalp. Seborrhoeic dermatitis was the preliminary diagnosis. Topical treatment with 0.05% betamethasone dipropionate solution was unsuccessful. Initially, only the scalp was involved, but during the following years new itchy lesions appeared on the back, chest, abdomen, axilla and groins. The face became intensely red. The lesions were macromorphologically described as round erosions, 0.5–2 cm in diameter, with vesicules. Scales and crusts were present at the borders. Nicolsky's sign was positive. Symptoms were provoked by exposure to sunshine. After intensive topical therapy (0.05% betamethasone dipropionate ointment) for 1 month on a dermatology ward, the patient improved, but relapsed 1 month later. The distribution of the lesions was as before, but more severe (Fig. 1). No mucosal lesions were found. Laboratory data, including antinuclear antibodies, were normal. Microscopically, skin biopsy showed subcorneal acantholytic bullous disease. Intercellular keratinocyte deposits of IgG antibodies and C3 were detected with immunofluorescence in both healthy and lesional skin. During the initial investigation, no circulating antibodies to intercellular substance or basal membrane were present but, in 1992, antibodies to intercellular substance were demonstrated for the first time (titre 1/100). A diagnosis of pemphigus foliaceous was established and therapy was instituted with 30 mg prednisolone daily. Recurrence and high doses of prednisolone encouraged us to combine the steroid medication with azathioprine. Doses as high as 150 mg daily of each drug were required for control of the disease. In 1982–1987, the disease was controlled by adjusting the dose of these two drugs. During that period, the patient had relapsing folliculitis and developed pneumonia on one occasion. Concomitantly with systemic treatment, topical steroid ointments were used.

In January 1987, plasma exchange therapy was started (see below). In the beginning it was given every third week and later on at longer intervals. His skin condition immediately improved and it became possible to reduce both the dose of prednisolone and the azathioprine. Six months later, systemic treatment was discontinued. After 18 months, the interval between plasma exchange sessions was increased to 5 weeks. After a relapse, treatment was given at 4-week intervals. Since then, he also improved after exposure to sun. Two years later the disease could be controlled by plasma exchange alone every 6th week. After 5 years, the treatment was given every 8th week and, after 10 years, the treatment interval was 10 weeks during the summer and 8 weeks in winter. Since 1987, he has worked full-time. He has been nearly free from lesions, except at times some days before treatment and when the interval has been too long. No therapy other than mild topical steroid ointments has been used in combination with the plasma exchange.

Apheresis

Plasma exchange was performed with a discontinuous cell separator, Haemonetics V50 Pheresis System (Haemonetics Corporation, 400 Wood Road, Braintree, MA, USA). From January 1987 to June 1997, a total of 96 treatments were given. During each session, only about 2 l (mean $\pm$ SD; 2008 $\pm$ 86 ml) patient plasma was removed. Usually, one plasma volume (or more) is exchanged at each therapeutic plasmapheresis, which is considerably more than the 2 l exchanged in our patient. The patient's plasma volume can be estimated by the following calculations based only on weight and haematocrit: *Patient's weight in kg* $\times$ *70 ml* $\times$ *(1.0-haematocrit, as a decimal)*. The weight of our patient was 82 kg and his haematocrit was 40% = 0.40. Thus the patient's plasma volume was approximately 3.5 l ($82 \times 70 \times 0.60 = 3444$ ml). Replacement fluids were 1000 ml of 5% or 3.5% albumin solution and 1000–1200 ml 0.9% saline. In 1987, we started to use 5% albumin solutions, but after a few years, as the interval between treatments was prolonged, we changed to 3.5% albumin. No plasma was used as substitute. The patient's blood albumin and immunoglobulins (IgG, IgA and IgM) were always normal. During the observation period C3, haemoglobin and thrombocyte count were slightly below the reference values but were not associated with clinical symptoms. No adverse reactions occurred during the plasma exchanges.

COMMENT

This case demonstrates the beneficial effect of regular plasma exchange in a case of pemphigus foliaceous, a treatment which has controlled the disease for over 10 years and kept the patient in full-time employment. Plasma exchange is now his only treatment. This contrasts with what most authors advocate, i.e. plasma exchange as an adjuvant therapy when all other treatments have failed (4). The presence of circulating antibodies has been ascribed a role in the pathogenesis of pemphigus and it is thought to be useful for monitoring the patient and predicting the relapses (1). Intensive plasma exchanges are a treatment for reducing the titre of circulating autoantibodies which is correlated with clinical improvement (5). In our case, no specific autoantibodies could be identified until 11 years after the disease was diagnosed and their presence gave us no information about the activity of the disease. Clinical evaluation was used instead to monitor the frequency of treatments. Furthermore, the development of antibodies might be a rebound phenomenon which has been discussed elsewhere in the context of pemphigus and plasma

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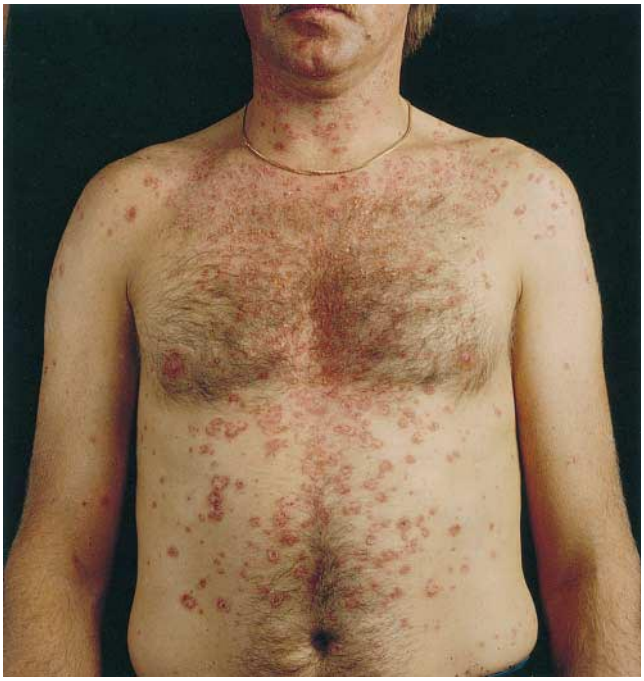

Fig. 1. The patient at time of diagnosis.

exchange treatment (6). No effort was made to start medical treatment, e.g. with cyclophosphamide, azathioprine or cyclosporine to suppress proliferating B-cells and thus reduce specific antibody production. At what stage of the pathogenesis the apheresis might interfere is at present unknown. A pathogenic factor may have been removed or reduced in concentration, or else the plasma exchange has induced some kind of immunomodulation. There could be several such plausible explanations for the excellent control of the disease, but since active lesions reappear when the intervals between treatments are increased the supportive underlying process is probably active. The steroid saving effect of apheresis has been shown in three studies (7–9). However, our case has been off steroids for over 10 years apart from topical steroid preparations.

In this patient, no adverse effects of the plasma exchanges have occurred. Mild complications are common, however. The Canadian Apheresis Study Group reported that 40% of patients experienced at least one complication during treatments (10). The commonest reactions were fever, chills, urticaria, hypotension, muscle cramps and paresthesias. Severe complications, including cardiac arrest, ischaemic chest pain and cardiac arrhythmias, have been noted (10). Despite its relative safety, therapeutic apheresis cannot be recommended as a first-line treatment, because deaths have been directly or indirectly ascribed to its use (11).

It can be debated whether the favourable course of the disease in our patient is due to the fact that pemphigus foliaceus is a mild variant of pemphigus. A retrospective study by Dehen et al. (12) showed that relapses were commoner in pemphigus foliacous than in the vulgaris type, whereas remissions, mean duration of the disease and iatrogenic complications were the same.

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