Pemphigus Foliaceus Successfully Controlled with Plasma Exchange During 10 Years

J. A. MARCUSON1, B. BJARNASON2 and A. SHANWELL3
1,2 Departments of Dermatology of Karolinska Hospital and Huddinge University Hospital and 3 Department of Transfusion Medicine, Huddinge University Hospital, Stockholm and Huddinge, Sweden

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

(Accepted January 2, 1998.)


Jan A. Marcusson, Department of Dermatology, Huddinge University Hospital, SE-141 86 Huddinge, Sweden.

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 macroscopically described as round erosions, 0.5–2 cm in diameter, with vesicles. 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 foliaceus 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 6th 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 ± SD; 2008 ± 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 × 70 ml × (1.0–haematocrit, as a decimal). The weight of our patient was 82 kg and his haematocrit was 40%. Thus the patient’s plasma volume was approximately 35.1 (82 × 70 × 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 foliaceus, 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
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 treat-
ments (10). The commonest reactions were fever, chills, urti-
caria, hypotension, muscle cramps and paresthesias. Severe
complications, including cardiac arrest, ischaemic chest pain
and cardiac arrhythmias, have been noted (10). Despite its rela-
tive safety, therapeutic apheresis cannot be recommended as a
first-line treatment, because deaths have been directly or indi-
rectly ascribed to its use (11).

It can be debated whether the favourable course of the dis-
ease 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
foliaceus than in the vulgaris type, whereas remissions, mean
duration of the disease and iatrogenic complications were the
same.

REFERENCES
1. Huigol SC, Black MM. Management of the immunobullous
2. Bystyn JC. Plasmapheresis therapy of pemphigus. Arch Dermatol
3. Guillaume JC, Roujeau JC, Morel P, Doute MS, Guillot B, Lam-
5. Kiprov DD, Strauss RG, Ciavarella D, Gilcher RO, Kasprisun
DO, Klein HG, Medele BC. Management of autoimmune disor-
6. Euler HH, Löffler H, Christophers E. Synchronization of plasma-
pheresis and pulse cyclophosphamide therapy in pemphigus vul-
et al. Plasma exchange in pemphigus. Arch Dermatol 1989; 119:
215–221.
8. Guillot B, Donadio D, Guilhou JJ, Meynadier J. Long-term
plasma exchange therapy in bullous pemphigoid. Acta Derm
Venereol (Stockh) 1986; 66: 73–75.
9. Sondergaard K, Carstens J, Jorgensen J, Zachariae H. The
steroid-sparing effect of long-term plasmapheresis in pemphigus.
10. Sutton DMC, Nair RC, Rock G. Complications of plasma
11. Klein HG. Therapeutic hemapheresis. In: Petz LD, Swisher SN,
Kleinman S, Spence RK, Strauss RD, eds. Clinical practice of
transfusion medicine. 3rd ed. New York: Churchill Livingstone,
Évolution et du pronostic du pemphigus vulgar et du pemphigus