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Treatment of severe atopic dermatitis with extracorporeal photopheresis

Received: 29 June 1994

Abstract Extracorporeal photopheresis using UVA irradiation of enriched lymphocytes in the presence of 8-methoxypsoralen (8-MOP) as a photoactivatable substrate has been employed for the treatment of several immunologically mediated disorders. We report on the first three patients subjected to extracorporeal photopheresis for severe atopic dermatitis. All patients had a lifelong history of atopic skin inflammation, and their disease had finally become resistant to well-established therapeutic regimes. Extracorporeal photopheresis resulted in a marked clinical improvement in the skin lesions of all patients. The decrease in cutaneous inflammatory activity became evident by the end of the second photopheresis cycle. In two patients skin lesions had virtually disappeared after the fifth treatment cycle, while in the third patient a lasting and substantial improvement in pruritus and erythema was achieved. Clinical remission was stable under maintenance therapy with prolonged intervals between photopheresis sessions. Therapeutic efficacy was reflected by a marked reduction in IgE serum levels in all three patients, while serum concentration of IgG, IgM and IgA as well as the profile of circulating lymphocytes remained essentially unchanged. No clinical signs of immunosuppression or other severe adverse events became evident. Collectively, our preliminary results indicate that extracorporeal photopheresis may interfere with the pathomechanisms leading to atopic dermatitis and therefore should be considered as a treatment modality for severe forms of this recalcitrant disorder.

Key words Atopic dermatitis · Extracorporeal photopheresis

Introduction

Atopic dermatitis is a common, multifactorial, chronic and often relapsing inflammatory skin disease. It is characterized by cutaneous erythema, induration and severe pruritus [5]. The clinical manifestations of the disease are representative of a certain type of immune reaction that includes an excessive overproduction of IgE antibodies as well as an exaggerated activation of a distinct T-cell subset in the skin producing a particular pattern of inflammatory mediators [2, 7, 14, 15]. These two events are considered as pivotal for disease manifestation. Therefore, it was decided to explore whether a causal treatment of atopic dermatitis is capable of controlling both lymphocyte activation and IgE synthesis.

Recently, extracorporeal photopheresis has evolved as an effective treatment for several immunologically mediated disorders such as T-cell lymphoma, scleroderma, lupus erythematosus and pemphigus vulgaris [3, 6, 11, 12]. It consists of the passage of freshly drawn blood that contains photoactivatable 8-MOP through an extracorporeal UVA exposure system. UVA irradiation activates the pharmacologically inactive 8-MOP which then reacts with the lymphocytes within the blood preparation, which is then reinfused into the patient. This treatment is clearly capable of downregulating exaggerated immune functions [10]. In order to explore whether the immunomodulatory capacity of extracorporeal photopheresis works in atopic dermatitis, three patients suffering from long-lasting severe and finally intractable manifestations of this disease were enrolled in a pilot study. The aim of this trial was to obtain data on the safety and efficacy of photopheresis treatment in patients with atopic dermatitis.

Patients and methods

Patients

Three patients with longstanding atopic dermatitis were treated with extracorporeal photopheresis at 4-week intervals. All patients had been suffering from erythrodermic eczema that finally had be-
come unresponsive to standard treatment regimens. They were tested negatively for the presence of hepatitis B antigen and pregnancy as exclusion criteria for the study.

**Patient 1**

A 52-year-old woman had a lifelong history of severe atopic dermatitis, perennial rhinoconjunctivitis and asthma bronchiale. She had been treated with topical corticosteroids, systemic prednisone, antihistamines, and a 3-month course of PUVA therapy in 1992. The latest exacerbation had failed to respond to the PUVA therapy.

Physical examination showed a diffuse exfoliative erythroderma, generalized scaling and itching with lichenification in the antecubital and popliteal areas. The patient presented with several typical signs of atopy, such as palmar hyperlinearity, Dennie-Morgan infraorbital folds, the Hertoghe sign and white dermographism.

**Patient 2**

A 33-year-old man had a disease duration of 30 years. Former treatment included topical corticosteroids, UV irradiation and prednisone systemically. The disease characteristically flared during winter months.

Physical examination showed a severe generalized erythroderma with excoriations and flexural lichenification. Characteristic signs of atopy included palmar hyperlinearity, recurrent conjunctivitis, orbital darkening and white dermographism.

**Patient 3**

A 32-year-old woman had longstanding atopic dermatitis. The patient's history contained multiple episodes of generalized erythroderma with impetiginization requiring hospitalization on several occasions.

Physical examination showed a diffuse scaling and itching erythroderma with distinct flexural lichenification. Other characteristic findings included xerosis, lichenification, keratosis pilaris, palmar and plantar hyperlinearity, cheilitis, infraorbital folds, orbital darkening and white dermographism.

**Photopheresis procedure**

Photopheresis was performed as described previously [3] using a UVAR II system (Therakos, Johnson & Johnson, USA). The treatment was initiated 2 h after the patient had ingested 0.6 mg/kg 8-methoxypsoralen (8-MOP) (Meladinine, Basotherm, Germany). The patient's blood was collected via a 17-gauge antecubital cannula and separated by continuous centrifugation in six cycles to obtain 240 ml of leucocyte-enriched blood and 300 ml of plasma. The total volume was then exposed to UVA (range 334–346 mm) within the photopheresis device to obtain a final level of photoenergy delivery of 2 J/cm² to the white blood cell DNA. The entire volume of leucocyte-enriched plasma was then reinfused into the patient. This procedure was performed on 2 consecutive days at 4-week intervals. After twelve cycles the intervals were prolonged to 6 weeks.

**Concomitant therapy**

External use of topical steroids (prednicarbat), by itself insufficient to control disease activity, was allowed in all patients.

**Assessment of treatment response**

The objective response to treatment was assessed by regular physical examinations that measured disease activity using a standardized protocol that had formerly been used for the evaluation of lymphoma patients [3]. It scored the affected body areas according to a scale of five severity criteria (0 = no lesions; 1 = minimal erythema; 2 = substantial erythema, scaling; 3 = submaximal erythema, plaques, excoriation; 4 = maximal erythema, vesicles, exudation). Each of the following areas was evaluated: face and neck (9% body area), anterior trunk (18%), posterior trunk (18%), perineum (1%) arms (7% each), hands (2% each), legs (16% each) and feet (2% each). A final score was derived from the sum of the severity criteria multiplied by the percentage of body surface affected. It ranged from 0 to 400.

In addition, patients were asked to score their erythema, desquamation, crusts, pruritus, general well-being, fitness for work, social activity, and sleeplessness on a scale of 0 (none) to 10 (severe). The self-assessment scores ranged from 0 to 80.

**Laboratory evaluations**

Laboratory evaluations included CBC and differential count, platelet count, blood electrolytes, glucose, liver and kidney functions, serum immunoglobulin levels (IgG, IgM, IgA, IgE), ANAs, and C3 and C4 components of complement. Blood lymphocyte subsets were determined by flow cytometry on a FACScan (Becton & Dickinson, Heidelberg, Germany) using fluoresceinated monoclonal antibodies.

**Fig. 1** Changes in IgE serum levels during treatment