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A case of psoriasis successfully treated by extracorporeal photopheresis during COVID-19 pandemic

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ABSTRACT

Psoriasis is a chronic inflammatory skin disease that is characterized by well-demarcated erythematous plaques with a silver scale. Although many new and emerging therapeutic agents are often sufficient to control the disease, there is still a need for alternative treatment options in challenging cases. Extracorporeal photopheresis (ECP) has been applied to many T-cell-mediated diseases to restore immune homeostasis and treat psoriasis effectively. In this paper, we present a psoriasis patient who did not respond to methotrexate, narrowband ultraviolet B, or acitretin. Because of a diagnosis of non-Hodgkin lymphoma, the patient had contraindications for cyclosporine, fumaric acid esters, and biologics but achieved remission with a total of 12 sessions of ECP in two and a half months. Although exacerbation was recorded after polymerase chain reaction (PCR) confirmed coronavirus 2019 (COVID-19) disease infection at the end of the first month, scores from the psoriasis area severity index (PASI) and dermatological life quality index (DLQI) were regressed significantly within two and a half months. ECP seems to provide an effective and rapid response for psoriasis and should be considered for psoriasis patients who fail to respond or have contraindications to existing treatments.

1. Introduction

Psoriasis is a chronic inflammatory skin disease involving multiple organ systems and affects approximately 2% of the world's population. The disease is primarily known as an epidermal hyperproliferation disorder and is characterized by inflammatory plaques on the skin. Besides, with a complex pathophysiology of a genetic predisposition, the disease triggers environmental factors and abnormal immune activity of T cells, dendritic cells, and neutrophils following proinflammatory cytokine release [1].

Topical medications, such as corticosteroids, vitamin D analogs, calcineurin inhibitors, keratolytics, and emollients, provide sufficient benefit to many patients. As the disease worsens, numerous traditional agents, such as methotrexate, acitretin, cyclosporine, and apremilast, are recommended [2]. Owing to the growing understanding of the pathogenesis of psoriasis, biologics that target the specific immunologic signaling pathways are considered first-line treatments for moderate to severe psoriasis. Although they show excellent long-term efficacy and tolerability, possible risks of systemic side effects and immunosuppression have led to the consideration of other targeted treatment

alternatives, such as extracorporeal photopheresis (ECP), for the restoration of immunotolerance in cases of patients who have contraindications to immunosuppressive therapies [3].

ECP was originally used to manage cutaneous malignant T-cell lymphoma, but it also seems to be a potential therapeutic option in many T-cell-mediated diseases by downregulating activated T cells. The procedure of ECP consists of ultraviolet A (UVA) irradiation of peripheral lymphocytes incubated with 8-methoxy psoralen and reinfusion back to the patient [4]. Although the mechanism of action is not fully understood, it is thought to provide its effect through lymphocyte apoptosis and normalizing the immune system. Successful outcomes of ECP were investigated in many autoimmune dermatological conditions, such as atopic dermatitis, pemphigus vulgaris, erosive lichen planus, nephrogenic fibrosing dermopathy, cutaneous mucinosis, scleromyxedema, eosinophilic fasciitis, and psoriasis [5,6].

In this paper, we present a case of psoriasis in which the patient was unresponsive to conventional systemic medications, had a high risk of immunosuppression, which possibly arose from biologics and cyclosporine, and achieved remission following a two and a half month course of ECP.

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2. Case presentation

A 51-year-old man was referred to our outpatient clinic with a diagnosis of recalcitrant and severe psoriasis. The patient was diagnosed with psoriasis and non-Hodgkin lymphoma following histopathological confirmation four and three years ago, respectively. He also had psoriatic arthritis and asthma. Dermatological examination of the patient revealed results that were consistent with thick, scaly plaques on the elbows, knees, dorsum of the feet and hands, posterior and anterior trunk. There were prominent signs of psoriatic nail involvement on fingers and toes. Owing to the severity of psoriasis, topical agents alone were not considered. The patient did not obtain any additional benefit from 25 mg/day of acitretin. Methotrexate was administered two separate times but had to be stopped owing to severe liver impairment. The patient was unresponsive to long sessions (62 sessions) of narrow-band ultraviolet B (UVB). Because patients with a history of systemic malignancy in the last five years should avoid cyclosporine and biological agents, fumaric acid was considered for off-label use. However, it was not approved owing to the risk of progression of non-Hodgkin lymphoma.

ECP was considered for the patient in the present research in order to avoid systemic side effects during the selective restoration of the immune system. The central venous access, considered a clean skin area from the psoriasis plaques, was used with a double-needle and a total blood volume of 1500 mL. To prevent occlusion of the catheters, heparin was administered in an amount (approximately 1.2 and 1.4 mL) to fill the catheter lumens at the end of each treatment session. The patient had received a total of 12 ECP sessions within 2.5 months, as depicted in Fig. 1. However, the ECP had to be interrupted for 15 days at the end of the first month because he had coronavirus disease 2019 (COVID-19) disease confirmed by polymerase chain reaction. The patient described only flu-like symptoms and did not have severe symptoms that required hospitalization. While exacerbation was recorded during this period, the patient improved significantly after two and a half months on the basis of two objective scores. The PASI score, which is calculated for the extent of involved body surface area and the intensity of redness, scaling, and plaque thickness, was significantly regressed from 17.5 to 2.8 (Figs. 2 and 3). The dermatological life quality index (DLQI), which is the tool most frequently used to measure the impact of skin disease on the quality of life, improved from 19 to 6. Considerable improvement was also observed in psoriatic nail findings, such as distal onycholysis, oil spots, and splinter hemorrhage, according to the records of dermatoscopic photographs taken two and a half months apart (Fig. 4). The patient tolerated ECP well without any evidence of side effects.

No other patients had symptoms or signs of COVID-19 during ECP procedures thanks possibly to strict hospital measures (increased sanitation intervals, periodic ventilation, and disinfection of rooms, adequate social distance between treatment beds, use of masks and hand sanitizers by hospital staff and patients, temperature monitoring before and after treatment sessions) against COVID-19. The PCR test was taken on the 14th day according to the national guideline of the Ministry of Health (Turkey). After confirmation of PCR negativity and symptom

resolution, treatment was re-started on the 15th day.

3. Discussion

Psoriasis is a chronic immune-mediated skin disease with important impacts on patients' quality of life. It is much more than a skin disease. Several medical comorbidities, especially joint involvement, may accompany psoriasis in patients [7]. While advances in pathophysiology continue to increase, as of today, the pathogenesis of psoriasis can be summarized as alterations or dysregulation in innate and acquired immune response. Interferon-alpha, tumor necrosis factor-alpha, interleukin 12 and 23, produced by plasmacytoid dendritic cells, and myeloid dendritic cells play a central role in the disease pathogenesis but also has led to a tremendous improvement in therapeutic efficacy through selective blockade [7,8]. Although it is known that CD4-positive T cells and less prominently CD8-positive T cells are observed in inflammatory infiltrates, the discovery of T helper 17 cells has led to important insights in this era [9].

ECP has been used to treat cutaneous T-cell lymphoma, graft versus host disease, transplant rejection, and many autoimmune diseases for more than 25 years [5,6]. It is thought to mimic the physiological process of peripheral tolerance through the immature dendritic cells and apoptotic leukocytes—the two key elements of peripheral immune tolerance—also suppressing effector T cell responses and upregulating T regulator cells, which is the 3rd key player of peripheral immune tolerance [5]. Although it restores immunotolerance, it does not cause an increase in the risk of infection or malignancy as in conventional immunosuppressive therapies. Therefore, it has been used to treat a broad spectrum of autoimmune dermatological diseases, including scleroderma, systemic lupus erythematosus, atopic dermatitis, epidermolysis bullosa acquisita, cutaneous mucinosis, lichen planus, pemphigus, and psoriasis [5,6,10]. In a study conducted with a group of eight patients with psoriasis and seronegative arthritis, it was reported that the effectiveness of treatment lasted more than one year in half of the patients who responded very well [11]. In addition to selective immunosuppression, the long duration of the therapeutic effect after cessation of the treatment makes ECP a unique alternative in autoimmune diseases. [5].

Several months, usually five–six months, are required to observe the maximal clinical outcomes in classical autoimmune diseases with ECP. While in a case series of four psoriasis patients—a period of 6–13 months was reported as a required period for clinical efficacy (10)—we observed an almost complete significant clearance of psoriatic plaques and marked improvement on nails at the end of the two and a half months of ECP treatment.

4. Conclusion

Although ECP is time-consuming and only available in specialized centers, it has many advantages for autoimmune dermatological diseases, including psoriasis. Our experience leads us to recommend ECP to manage challenging psoriasis cases.

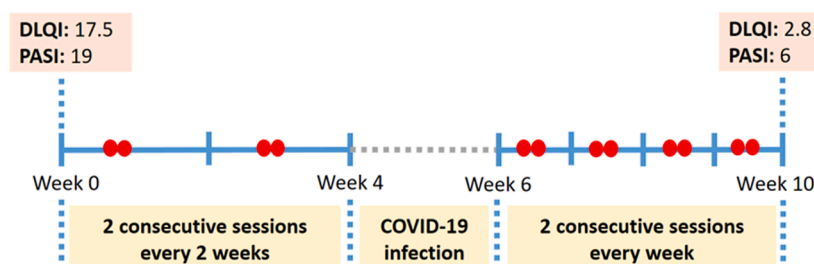


Fig. 1. Flowchart of the treatment and significant reduction in disease severity scores (DLQI and PASI) compared to baseline. During the first month, the patient received four sessions of ECP treatment, two consecutive sessions every two weeks. After a 15-day break due to COVID-19 infection, the patient received a total of eight sessions of ECP treatment, two consecutive sessions per week, for the second month. (Red dots represent each treatment session of ECP) At the end of a total of 12 sessions of ECP treatment, a remarkable decrease was observed in disease activity scores. (DLQI: dermatology life quality index, PASI: psoriasis area severity index) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).



Fig. 2. Significant regression of thick scaly plaques on the back, scalp, knees, and elbows and marked fading of accompanying erythema on plaques (top row: pre-treatment photos, bottom row: 2.5 months after ECP).



Fig. 3. Severe improvement of the dorsum of the hand and fingers and toenails (top row: pre-treatment photos, bottom row: two and a half months after ECP).

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Data availability statement

Data available on request from the authors

CRedit authorship contribution statement

Pelin Esme for conception or design of the work; the acquisition, analysis, interpretation of data for the work, and approval of the final version of the manuscript. **Semanur Coban** for conception or design of the work; the acquisition, analysis, interpretation of data for the work. **Bilge Ugur** for conception or design of the work; the acquisition, analysis, interpretation of data for the work. **Meltem Ayli** for conception or design of the work; the acquisition, analysis, interpretation of data for the work. **Ercan Caliskan** for conception or design of the work; the acquisition, analysis, drafting the work and revising it critically for important intellectual content.



Fig. 4. Regression of the psoriatic nail findings, such as distal onycholysis, oil spots, and splinter hemorrhage, are shown here (top row: pre-treatment photos, bottom row: two and a half months after ECP).

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Declaration of Competing Interest

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