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Case Report

Treatment of Arthropathic Psoriasis Vulgaris by Plasmapheresis - A Forgotten Treatment Option?

Rauno J. Harvima[1]*, Julia Barantseva[2], Heli Koukkunen[3], Anne Lumiaho[3], Susanna Kinnunen[3] and Ilkka T. Harvima[1]

[1]Department of Dermatology, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland

[2]Department of Rheumatology, Kuopio University Hospital, Kuopio, Finland

[3]Department of Nephrology, Kuopio University Hospital, Kuopio, Finland

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***Corresponding author:** Dr. Rauno J. Harvima, MD, PhD, DSc, Department of Dermatology, Kuopio University Hospital, FIN-70210 Kuopio, Finland, Fax: +358-17-174420, Email: rauno.harvima@kuh.fi

ABSTRACT

After numerous conventional oral, topical, targeted synthetic DMARDs and biologic medications for arthropathic psoriasis vulgaris failed due to lack of efficiency or severe side effects, the patient was finally treated with plasmapheresis giving a clear and marked response within a few plasmapheresis sessions.

Keywords: Targeted synthetic DMARDs; Plasmapheresis; Arthropathic psoriasis vulgaris; Biologics; Adverse reactions

Introduction

Psoriasis is an inflammatory disease affecting skin and joints. The treatments for skin psoriasis include topical emollients, corticosteroids, calcipotriol, light therapies by UVB and PUVA. The "old" conventional oral medications include methotrexate (MTX), acitretin and cyclosporin (CsA). Recently oral apremilast and numerous biologic medications targeted to TNF-alpha, IL 12/23, IL17, IL 23 have been developed and used successfully.

The medications for arthropathic psoriasis include MTX, CsA, leflunomide, hydroxychloroquine, sulfasalazine, azathioprine and also many biologics that are used also for skin psoriasis.

Therapeutic plasmapheresis as extracorporeal therapy allows the removal of pathogens from plasma used in immune-mediated diseases and toxic conditions for decades as reviewed recently by Altobelli et al[1]. In dermatology, plasmapheresis is mainly used in severe pemphigus vulgaris, systemic scleroderma and toxic epidermal necrolysis[1].

Decades ago, in the 1970s to 1980s, there were publications of use of plasmapheresis for skin and arthropathic psoriasis. After 1991, no articles have been published by PubMed. However, in Russia, plasmapheresis is advertised to be rather freely available outside public hospitals.

Six patients with psoriasis vulgaris were treated once weekly for 7 weeks with either plasmapheresis or sham-plasmapheresis; no difference was found between active treatment or placebo[2].

Four patients with psoriasis vulgaris treated with plasma exchange got a surprising clinical improvement during the initial phase of therapy but the final results were not satisfactory[3].

Treatment-resistant psoriasis of 5 patients were treated 10 times with plasmapheresis over a 4-weeks period and all experienced improvement after 3 exchanges. Relapses occurred

in 2 to 4 weeks and one patient with erythrodermic psoriasis relapsed 2 days after the treatment. Circulating immune complexes were elevated before treatment and fell after each exchange by 20% to 70% of the former values[4].

Nine patients with psoriasis vulgaris were treated with plasmapheresis by 2 to 6 times. Three patients after 4 to 6 sessions showed no demonstrable psoriatic lesions. However, this improvement was transient[5].

Psoriasis vulgaris treated with plasma exchange showed no convincing signs of improvement in 9 patients[6].

In a study of 18 patients[7], 8 had psoriasis vulgaris, 6 had exudative psoriasis, 1 pustular psoriasis and 3 erythrodermic psoriasis. Plasmapheresis was conducted 5 to 8 times with 3-day intervals. Clinical remission was in 10 patients, a marked improvement in 5 patients and a moderate improvement in 3 patients, thus a positive response in all 18 patients. However, there was not mentioned the follow-up time. Later by the same group[8], a pronounced therapeutic effect of plasmapheresis was recorded in 21 patients with psoriasis.

In an Italian study, 10 patients with psoriatic arthritis received plasmapheresis treatments 3 times in the 1st week, then twice a week for the next 2 weeks, thereafter once a week for 2 weeks followed by one session after 15 days. Thereafter clinical controls after every 15 days up to 3 months. All of the patients had obtained complete remission by the 4th control and at the end of the treatment, everyone's function ability was improved[9].

In a Japanese study, 13 psoriatic patients treated with hemofiltration and/or direct hemoperfusion showed a complete remission in 5 patients, 5 experienced improvements and 3 remained unaffected[10]. Of these 3 patients, a complete remission was achieved after 2 sessions of plasmapheresis in a patient with pustular and arthropathic psoriasis. In the 2nd patient, both psoriasis vulgaris lesions and arthropathic psoriasis joint pain were markedly improved. The 3rd patient showed a marked improvement with only 2 session pf plasma exchange, but later follow-up was not described[10].

Here we describe a challenging treatment of psoriasis vulgaris with severe arthropathic symptoms, which were not sufficiently treated by oral, topical, synthetic DMRDS or biologics, either due to lack of efficacy or due to severe side effects. The patient was finally treated with plasmapheresis giving a response within a few plasmapheresis sessions.

Case Report

A non-atopic female patient born in 1974 (158 cm, 89 kg) had at age of 20 genital lichen sclerosus & atrophicus treated with topical class II corticosteroid and 1% pimecrolimus creams. At age of 23 sodium valproate was started for epilepsy which medication was stopped after symptomless 8-year-period due to ALAT-increase. She had at age of 31 pulmonary sarcoidosis treated successfully by oral prednisolone for 3 months. The radiologic contrast agent had caused a wide urticaria. Gout was also detected and treated with allopurinol.

At age of 32, she experienced a prolonged urticaria and dermographism treated with antihistamines and prednisolone. Helicobacter pylori was treated, and the basic Prick tests were negative.

At age of 35, psoriasis vulgaris diagnosis was established appearing at lower stomach-pubic area treated with topical class II-III steroids, D-vitamin, and pimecrolimus. Her grandmother had psoriasis.

Psoriasis exacerbated widely to face treated with 1% hydrocortisone and 1% pimecrolimus creams, and betamethasone-calcipotriol gel for scalp. Cyclosporine (CsA) was initiated giving a good response at 2 mg/kg, but psoriasis worsened with guttate-type lesion. CsA had no effect at 2.5 mg/kg and it also elevated her with serum creatinine.

Thus, in April 2011, CsA was changed to methotrexate (MTX) and arthropathic psoriasis was also diagnosed. MTX was gradually increased during 5 months to 15 mg/wk. One month later MTX was stopped after vaginal mucosa ulcers appeared, and only topical treatment by betamethasone-calcipotriol ointment and D-vitamin was continued, and dental infective focuses were treated.

Two months later, a shortened nbUVB was initiated for psoriasis, urticaria and dermographism, with oral prednisolone, antihistamines and standard topical steroids.

Since Feb 2013, for worsened psoriasis vulgaris with arthropathy, adalimumab was initiated with standard procedure. Even after 1st dose, a marked reduce in skin lesion was seen, but after a 2 months break, re-administration did show efficacy (PASI 10.8). Thus, her adalimumab treatment was changed to ustekinumab with standard protocol, with moderate effect about 6 months later (PASI 3.0). Ustekinumab was discontinued for 5 months due to orthopedic operation planned in spring 2014 but this was not performed due to heavy worsening of skin psoriasis. Ustekinumab was initiated again with good outcome. At control 3 months later, PASI was reduced to 5.6.

About 6 months later ustekinumab was discontinued due to stable psoriasis, 3 months later (PASI 5.1). Ustekinumab was again started in April 2015 with good outcome.

However, 6 months later, PASI increased to 9.5, and also joint symptoms increased treated with NSAIDs (etoricoxib, ibuprofen) and pregabaline. Sedimentation rate increased to 95 mm/h. Ustekinumab dose was increased to 90 mg in 12-week intervals. Salazopyrin was initiated in Jan 2016 but was not tolerated and discontinued fast. Gradually skin and joint symptoms relieved.

At March 2017, ustekinumab was discontinued due to slight loss of efficacy and fever, and changed to secukinumab, used intermittently due to cough symptoms from Aug 2017 to Dec 2017. Thereafter, due to repeated mouth labial herpes simplex episodes, and preventive oral medication by acyclovir was started at time of secukinumab dose.

In June 2018, skin and joint symptoms started to worsen. Thus, secukinumab was changed to ixekizumab with moderate to good response. However, it lost efficacy 10 months later. Rheumatologist prescribed tofasitinib with intra-articular steroids injections. Due to joint symptoms, the patient was on sick-leave. Topically earlier treatments were used.

In Sept 2019, the joint conditions were excellent, but situation for was skin moderate. tofasitinib was changed to oral apremilast. After 1.5 months, tofasitinib was again added to as combined medication. However, the efficacy with this combination was insufficient.

Infliximab-infusions were initiated but fast stopped due to side effects as tongue, throat, and skin reactions. Guselkumab was started in Feb 2020.

At control 4 months later, skin condition was good but efficacy to joint symptom insufficient. Rheumatologist initiated leflunomide in Sept 2020, but after a few weeks, it was stopped due to intestinal diarrhea. Previous guselkumab was used for a while in Oct-Nov 2020. Thereafter, mouth labial herpes simplex infection appeared again. At rheumatologist controls, steroid (triamsinolone hexacetonide) was injected to all symptomatic joints, subacromial bursas, and methylprednisolone acetate to tendon sheets by Ultrasound direction.

First dose of 210 mg brodalumab was given in Dec 2020, and within 30 minutes, itch and redness in face and upper extremities and upper back appeared, Thus, loratadine 10 mg and prednisolone 10 mg were given twice as well as salbutamol inhalations. The symptoms disappeared within 2 hours.

After the 1st dose of 150 mg risankizumab given in Jan 2021, within one hour a marked itch, cough, and urticaria appeared. When checking the content of these two latest biologics, the common was polysorbate 20 (also known as Tween 20). Structurally similar is polysorbate 80 (known also as Tween 80) that can be got by food stuff and was also challenged by adalimumab 8 years earlier. The patient's bacterial cultures from nose and throat were negative. Skin biopsy revealed lymphocyte-rich inflammation fitting to erythema and exanthema.

Next dose of risankizumab divided in 2 doses of 75 mg in 10 min intervals was given in March 2021 with previous 20 mg + 20 mg prednisolone. Similar symptoms appeared as with earlier risankizumab dose. The symptoms relieved fast with additional 20 mg loratadine and 20 mg prednisolone followed by decreasing prednisolone doses during 3 days.

In Nov 2021, pure polysorbate 20 diluted in 0.9% saline and filtered was administered at the same 0,34 mg dose and volume as is in brodalumab and risankizumab. Within 10 min, the same symptoms, i.e., facial redness, swelling, cough, wide itch, and redness in upper back appeared. 20 mg loratadine and 20 mg prednisolone were given and the symptoms gradually disappeared within 1 h 15 min.

In Feb 2022, etanercept 50 mg (Enbrel-Myclic pen) was administered into right thigh, and after 20 minutes, cough and hoarseness of voice appeared. Dermographism tested for upper back was clearly positive. Prednisolone 40 mg and 10 mg of desloratin (Kevenix) was given, and the symptoms disappeared gradually within 4 hours. This batch of etanercept contained as excipients: sucrose, NaCl, L-arginine-HCl, sodiumdihydrogen phosphate dihydrate, disodium phosphate dihydrate, water, but not any polysorbate. The etiology of this adverse event remained unknown.

At control with rheumatologist in March 2022, patient had been moving for months with a wheel chair, certolizumab pegol (Cimzia, not containing any polysorbate) for arthropathic psoriasis was initiated weekly with previous 40 mg prednisolone and 20 mg loratadine. Still, mild itch in throat and skin appeared. Personal sun-bathing vacation in Spain was performed just recently, thus, skin psoriasis was moderate treated with only previous topical treatments. After the 3rd certolizumab pegol dose, the symptoms became more pronounced with also labial swelling, in spite of protective prednisolone and loratadine, and this treatment was stopped in April 2022. The etiology of the adverse event remained unknown.

The skin psoriasis was wide in scalp, face, trunk, lower legs and soles, elbows and dorsal palms, Previous topical treatments were continued. UVB-light therapy was considered but long travel to hospital clinic did not make it reasonable.

In May 2022, due to serious joint symptoms, ustekinumab was initiated with protective 60 mg prednisolone and 20 mg cetirizine. After 8 minutes, the same facial and throat symptoms appeared that were treated with additional cetirizine 20 mg and the symptoms mostly disappeared in 20 minutes, and oral steroid was prescribed for additional 12 days starting from 20 mg/day with gradually decreasing the dose. Next ustekinumab doses were given after 4 weeks and thereafter 12 weeks later, with similar precautions by prednisolone and antihistamine. The patient felt similar ustekinumab-related symptoms, but the joint symptoms became better.

Arthrosis was also diagnosed. However, the treatment response of wide skin psoriasis was insufficient (PASI 10.2), in spite of adequately used topical treatments by class II-IV steroids, calcipotriol and pimecrolimus. At the 4th ustekinumab injection in Oct 2022, the patient had taken the previous day 40 mg prednisolone with 30 mg/day cetirizine, and the same symptom as earlier became within 4 minutes.

By neurologist consultation, bisoprolol, used for migraine prophylaxis without any attacks for years, was also stopped but had no effect on skin psoriasis, thus was later added to the medication.

To exclude the steroid allergy, epicutaneous tests were done with appropriate positive-interpreted result for clobetasol and a similar milder reaction for betamethasone-dipropionate. Betamethasone-valerate and all other steroids tested were negative. To exclude atopy from background of facial redness, serum IgE was 46 kU/ml (range 0-100 kU/ml), and specific IgE for Malassezia (i.e., Pityrosporum) was 0.0 kU/L, and blood eosinophils were at normal range. Later in 10/2023 as control, serum IgE was 12.6. Patient did not get light therapy nor did not stay in the sunshine nor used any light-sensitive cosmetics.

At control in Jan 2023, 45 mg ustekinumab was given s.c., with precaution of 3 mg dexamethasone (equals to 20 mg Prednisolone) the previous day and in the morning of clinic visit together with antihistamines. This time the ustekinumab-related reactions were very mild. However, the next day the patient felt severe nausea lasting for several days with prolonged skin itch.

At control with rheumatologist in April 2023, the patient accepted to test MTX that had caused about 10 years earlier nausea and abdominal pain, also as i.m. form. However, the patient did not tolerate even 2.5 mg MTX dose even with help of 10 mg metoclopramide.

At rheumatologist control in Aug 2023, it was found that out that the patient had had a Covid-infection with 3 weeks of fever, and skin psoriasis was worsened markedly up to 10% of BSA. For swollen psoriatic arthropathy, 5 mg dexamethasone was administered with reducing doses for 4 weeks, since methylprednisolone (Medrol) seemed to produce itch. In Nov 2023, CsA was tried for treatment, but even 25 mg/day dose caused increased blood pressure in a few days. Topically,

momethasone furoate cream was prescribed together with remaining calcipotriol ungt and betamethasone valerate scalp solution. Thereafter, patient used dexamethasone with various doses until Sept 2023.

In Jan 2024, the patient was diagnosed type 2 diabetes and treated with 1 g metformin tablets because 500 mg and 750 mg strength tablets contain polysorbate 80.

At control with rheumatologist in Feb 2024, skin psoriasis was now in a fairly good condition. However, joint symptoms were severe making it necessary to move with a wheel chair.

At this stage, treatment options were very limited. Conventional medications and all biologics were ineffective or caused adverse events. Also etanercept as a polysorbate-free biologic drug was evaluated but it gave earlier insufficient efficacy. Thus, seeking for the old literature, some articles for the treatment for skin and joints psoriasis by plasmapheresis were published mainly in the 1980s, with very variable results, favoring arthropathic psoriasis. Thus, this treatment modality was chosen in a multiprofessional meeting for this special case. Plasmapheresis has never been reported to have been used in Finland earlier for psoriasis.

Plasmapheris Treatment

Plasmapheresis by using a MultifiltratePro (Fresenius Medical Care Ag&Co KGaA, Bad Homburg, Germany) was initiated in April 2024 via a tunneled dialysis catheter placed on the patient's neck. Plasmapheresis was performed by using standard protocol for treatment of autoimmune diseases, and albumin 40 g/L was used as compensatory solution. Filtration rate was 20 ml/min, and blood flow was 100 ml/min. Actilyse was used to keep catheter open.

In the beginning, 3,600 ml albumin was later decreased gradually during months of treatments to 2,800 ml, due to repeated hypotensive episodes during and after plasmapheresis.

During the 1st week, the treatment was performed daily for 3 days. Thereafter, treatments were performed 2 -3 times weekly. From week 7, the frequency of treatments was reduced to once a week due to nausea, slight hypotension and tiredness. Also, 1000 mg of i.v. ferric carboxymaltose (Ferinject) was administered once. A 2-week brake due to personal reasons led to exacerbation of skin symptoms.

After the 2nd plasmapheresis treatment, a clear response was obtained for joint and skin symptom. The patient could walk on her feet and reduce the use of the wheel chair.

Nausea and tiredness symptoms were experienced often after the plasmapheresis treatment lasting 2 to 3 days.

Later, treatment interval was reduced to 3 weeks. The catheter was changed due material failure and the second catheter after 6 months due to infection. Hypotensive episodes were treated by infusing saline intravenously and by reducing the amount of albumin as compensatory fluid. During the plasmapheresis treatments, 1 gram of calcium was administered at the start, 1 gram in the middle and 1 gram at the end of plasmapheresis. In addition, the patient takes orally 1 gram of potassium chloride (Kaleorid).

There was a 5-week break in Jun-July 2024, and skin psoriasis started to worsen. Skin psoriasis has remained at moderate to severe stage during the plasmapheresis treatment period up to Dec 2024. PASI level was at 15.6 to 22.6, but decreased gradually to 10.6 in Jan 2025.

Discussion

The treatment of the patient's skin and joint psoriasis was challenging. The conventional treatments by acithretin, MTX and CsA failed due to low efficacy or side effects or practical challenges with regard to light therapy. Etanercept and adalimumab gave efficacy in the beginning for both skin and joint symptoms, but gradually became ineffective. Thereafter, newer biologic treatments gave efficacy, but caused adverse events.

Thus, the treatment options were very limited. Therefore, we decided to use plasmapheresis that was used decades ago in the 1980s with variable results according to the literature. Our patient got already after 2nd plasmapheresis given in 3 consecutive days a clear response for both joint and skin symptoms. The treatment intervals were gradually prolonged to 3 weeks during the months. The efficacy for skin was moderate, and the 5-week brake in treatments caused worsening of skin psoriasis. Although the patient felt side effects as nausea and tiredness, she felt effects of reduced joint symptoms very positive even after 2nd plasmapheresis treatment, to give motivation to continue treatments, and in spite of the need to travel from home to hospital.

The mechanism of action of plasmapheresis treatment is not well understood in psoriasis. However, small molecules including immunoglobulins, are removed. The treatment has lasted now for 9 months and joint psoriatic symptoms are not present, but slight arthrosis was diagnosed in ankles.

The newer biologics gave efficacy, but caused facial swelling and redness, throat symptoms, cough, and hoarseness of voice within about 10 minutes after subcutaneous drug administration into the abdominal skin. The common factor for all these biologics was polysorbate 80 or 20, the latter was tested as a pure substance diluted in 0.9% saline solution at the equivalent amount and volume given similarly subcutaneously into the abdominal skin, causing the same facial and throat symptoms.

Of the biologics used for psoriasis, only etanercept and certolizumab pegol do not contain either polysorbate 20 or 80, but both these lost their efficacy for skin. The patient was challenged for polysorbate 80 already since 2013 by the use of adalimumab, and likely during years as food emulgator by dietary supplement code E433.

Interestingly, even some tablet-form medications can contain polysorbate 80 like metformin as 500 mg and 750 mg strengths but not as 1,000 mg strength leading to scrutinized checking of all medication used. It was also discovered that many paracetamol and ibuprofen tablet products used by the patient as pain killer contain polysorbate. This might explain the odd reactions with polysorbate-free etanercept and certolizumab pegol. And finally, Actilyse used in plasmapheresis sessions to keep the cannula open contains polysorbate.

The efficacy of plasmapheresis for arthropathic psoriasis is marked in this case, but for skin psoriasis at low level, as also published in the literature in the 1980s in many articles. In the future, plasmapheresis treatments are planned to give in

intervals of 3 weeks, but the total number of treatment sessions cannot be determined at this moment, when this case is the first reported in Finland's history, and thus, there are no reference patients available for comparison. Plasmapheresis treatment has caused a few times hypotensive episodes; thus, it has not been complication-free. It would be an interesting question whether plasmapheresis treatments could be discontinued and return to biologic treatments by, e.g., by etanercept, even though previously with low response to skin, to be continued with sufficient efficacy.

Ethical Approval

The patient has given her written consent for this case report.

Conflicts of Interests

Authors declare no conflicts of interests.

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