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CASE REPORT

A case report of a psoriatic arthritis patient on hemodialysis treated with tumor necrosis factor blocking agent and a literature review

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Abstract This report seeks to describe the clinical efficacy and safety of infliximab in a patient with psoriatic arthritis on hemodialysis and to review the literature on the topic. We present a patient with psoriatic arthritis on hemodialysis treated with infliximab and we review the literature. Our case includes a patient with severe psoriasis and dactylitis with chronic renal failure requiring regular hemodialysis. At presentation the patient had a psoriasis area and severity index (PASI) score of 35.1 and dactylitis affecting the right thumb. Evaluation of laboratory parameters revealed a slight increase of erythrocyte sedimentation rate (21 mm/h) and a mild normocytic anemia (Hct 36.4). The rest of the laboratory and imaging tests were within normal limits. Infliximab was initiated at the loading dose of 5 mg/kg body weight at weeks 0, 2, 6, and every 8 weeks thereafter. On retreatment at week 14 the PASI score was measured to 3.4. After the conclusion of 6 months of treatment, the reduction of PASI score was sustained reaching the point of 0.8. In addition, dactylitis, as well as laboratory parameters, showed a striking improvement. On the other hand, during the same period of time, no changes of renal functions were noted and no complications were reported and the patient continued his hemodialysis on a regular basis. Our case is in accordance with other reports supporting that infliximab treatment in patients undergoing hemodialysis can be safe, well tolerated, and effective. However, larger trials are needed to prove its use in these patients.

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Introduction

Chronic plaque psoriasis is a skin disease characterized by sharply demarcated, erythematous, scaly lesions. Twenty to thirty percent of patients with psoriasis develop psoriatic arthritis (PsA). With the advent of selective biologic modulators and particular of tumor necrosis factor (TNF)-α blockers, the therapeutic armamentarium against psoriasis and PsA has grown further [1, 2]. However, the management of a patient with severe psoriasis, dactylitis, and renal failure represents a therapeutic challenge. Special attention should be drawn to the increased risk of toxicity and to dose adjustments of the drugs used in this group of patients. We report our experience in treating such a patient with infliximab in our rheumatology clinic and we review the relevant literature.

Case report

A 52-year-old Caucasian male presented to us because of psoriatic arthritis according to the European Spondyloarthropathy Study Group [3]. On presentation, the patient had severe plaque psoriasis and pain and swelling of the right thumb. He had been diagnosed with psoriasis at the age of 16, which was initially mild and treated with topical agents. However, 2 years before presentation to our clinic he had been diagnosed with advanced renal failure due to chronic glomerulonephritis of no obvious cause, which in a few

weeks led to end-stage renal disease (ESRD) requiring regular hemodialysis. Since that time the patient described progressive worsening of psoriasis, which he partly related to the emotional stress associated with the renal disease. Topical treatments were of benefit no more. Moreover, 3 months before visiting our clinic, he experienced flares of very painful, swollen joints of the right thumb. However, the response of small doses of steroids and nonsteroidal anti-inflammatory drugs was inadequate. As for the rest of his history, 1 year before presenting to us, screening with a pure protein derivative skin test was positive and the patient was treated with rifampicin and isoniazid for 6 months (for unknown reason). His chronic drug treatment consisted of amlodipine, furosemide, clopidogrel, allopurinol, carvedilol, quinapril hydrochloride, sevelamer carbonate, pantoprazole, antacid, and erythropoietin injections.

As mentioned above, on presentation to our clinic the patient had extensive plaque psoriasis of the trunk, upper and lower extremities, with an estimated psoriasis area and severity index (PASI) score of 35.1 (Fig. 1). He also had onychopsoriasis and dactylitis affecting the right thumb, but the rest of the physical examination was unremarkable. Laboratory evaluation revealed a mild normocytic anemia (hematocrit 36.4%, hemoglobin 9.7 g/dL), while C-reactive protein (CRP) was 2 mg/L (normal <6 mg/L) and the erythrocyte sedimentation rate (ESR) was 21 mm/h. Liver biochemistry was normal and serologic testing for hepatitis B and C virus and human immunodeficiency virus infection was negative. Chest X-ray was normal. The use of infliximab was discussed with the patient, and after he consented, the drug was initiated at the loading dose of 5 mg/kg body weight at weeks 0, 2, 6, and every 8 weeks thereafter. Initial as well as subsequent infusions were uncomplicated. At week 14, the PASI score was 3.4; and as we completed 6 months of treatment and follow-up, we noticed a sustained reduction in the PASI score as it reached the level of 0.8 (Fig. 2). In addition, dactylitis improved impressively. Laboratory parameters also improved. After 6 months of treatment, hematocrit and hemoglobin were 42.3 and 14.2, respectively. On the other hand, CRP and ESR values were normalized. The patient is maintained on infliximab infusions every 8 weeks. Furthermore, no clinical or immunological side effects have been detected, and he remains in clinical remission. On the other hand, during the same period of time, the patient continued his hemodialysis on a regular basis. More specifically, he presented to the renal department three times per week, and during this period of time, the renal function was stable, no electrolytic or cardiovascular complications were reported. In addition, no infections or blood abnormalities were noted. Since the hematocrit and hemoglobin were normalized, erythropoietin injections were discontinued.

Discussion

Psoriasis and PsA are chronic autoimmune diseases of unknown etiology for which MTX and CsA are often used in daily clinical practice. MTX, one of the most effective drugs in autoimmune diseases, such as rheumatoid arthritis

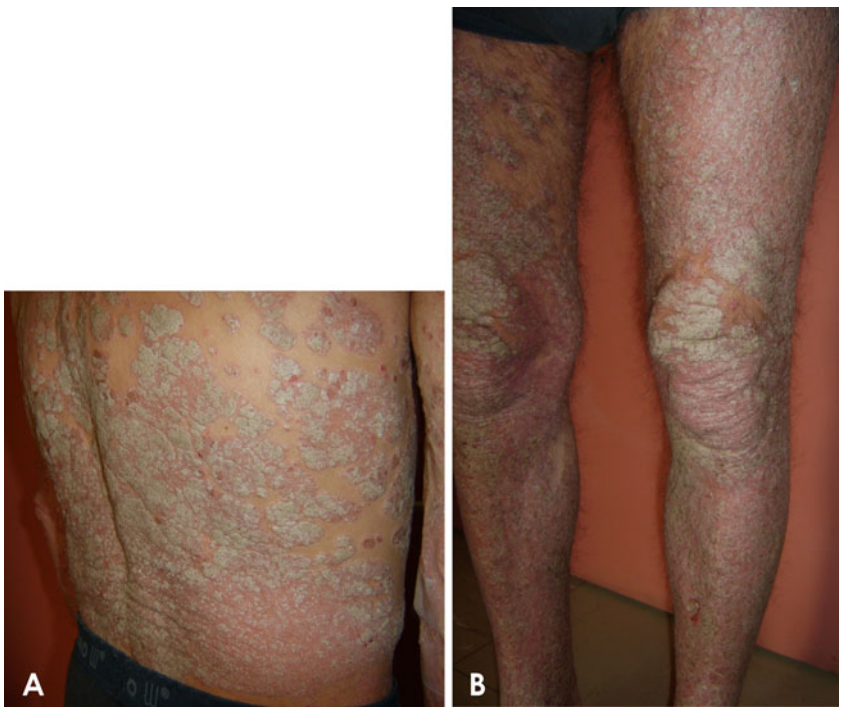

Fig. 1 Extensive plaques psoriasis of the trunk (**a**) and lower extremities (**b**) before infliximab treatment

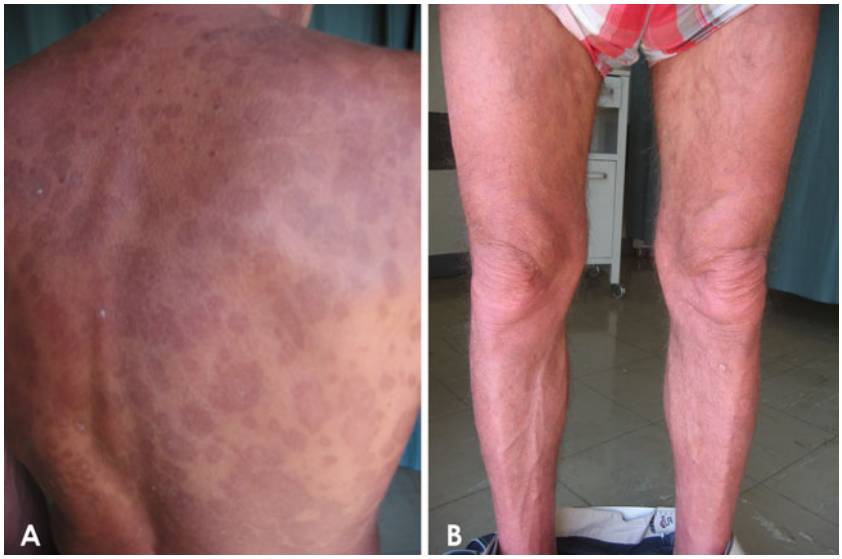

Fig. 2 Significant regression of psoriatic skin lesions after 6 months of infliximab therapy. The sites of former plaques are suggested by the areas of residual skin discoloration of the trunk (**a**), while a clearing of skin lesion is evident in the lower extremities (**b**)

(RA), PsA, and psoriasis, is eliminated primarily through the kidneys. Studies have shown that, while serum levels of MTX can be efficiently reduced by hemodialysis with high-flux dialyzers [4], peritoneal dialysis is ineffective for reducing MTX serum levels [5]. Moreover, dialysis of any type has little effect on the removal of the polyglutamated MTX metabolites within cells. Furthermore, there have been several reports of severe or fatal adverse events of MTX in patients with ESRD, such as pancytopenia [6–8]. Hence, given that the use of MTX in patients with ESRD may have irreversible or fatal complications even in the setting of regular hemodialysis, there is a need for new effective and safer therapeutic alternatives.

CsA, on the other hand, can be given to nontransplanted patients with ESRD at the same dose as in patients with normal renal function [9]. Evidence in the literature concerning its safety in this setting is scarce. There has been a report of a patient on hemodialysis with bone marrow aplasia who was successfully treated with CsA [10]. On the contrary, there have been reports implicating CsA in the development of chronic ischemic glomerulonephropathy and vasculopathy. There is a report of a systemic sclerosis patient on CsA who developed thrombocytopenia, acute renal failure, and hemolytic anemia [11].

As far as TNF-α inhibitors are concerned, very little is known about their use in patients with renal impairment, hemodialysis, or peritoneal dialysis because renal disease has been an exclusion criterion in all major clinical trials of these drugs. Three TNF-α antagonists are currently licensed for treatment of severe plaque psoriasis, etanercept, infliximab, and adalimumab. Infliximab is a chimeric human/murine anti-TNF-α monoclonal antibody and the only one administered intravenously. In patients with normal renal function, infliximab has the smallest volume of distribution among the three TNF-α antagonists [12] and its median terminal half life is 7.7–9.5 days. However, the exact pharmacokinetics of infliximab in patients with ESRD on hemodialysis is not known. Only few cases of renal adverse events during anti-TNF-α treatment have been reported. They usually include the development of nephritic syndrome, lupus nephritis, and immune complex renal vasculitis [13–15].

Singh et al. [16] described a RA patient on hemodialysis who responded immediately when treated with infliximab and after about 2 years of therapy, no side effects were observed. Hammoudeh et al. [17] also described a patient with RA undergoing hemodialysis who was treated with infliximab effectively and safely. Yee et al. [18] reported the successful treatment with infliximab of a patient with sarcoidosis. The patient during the disease progression developed acute anuric renal failure and hemodialysis was initiated. However, although the intestinal and muscular symptoms resolved with infliximab therapy, the patient developed a hypercoagulable state, and infliximab was ultimately discontinued. A summary of cases reported of anti-TNF-α therapy in patients with renal disease is illustrated in Table 1.

Hueber et al. [19] analyzed retrospectively 11 patients who had increased serum creatinine levels before or during treatment with TNF-α antagonists and concluded that the use of TNF-α inhibitors has no adverse effects on renal function of patients with kidney disease.

Gottenberg et al. [20] examined the safety and tolerance of anti-TNF-α agents in 15 patients with histologically proven amyloidosis and renal involvement. After treatment with anti-TNF-α agents (ten patients received infliximab, four received etanercept, and one received both drugs), the rate of proteinuria sharply decreased in three patients and their renal function subsequently improved. Moreover, the renal function parameters in five other patients were

Table 1 Summary of cases reported of anti-TNF-α therapy in patients with renal disease

Author (years)	No of patients	Age	Sex (Male/Female)	Underlying disease	Renal impairment at the time of diagnosis	Drug	Duration of follow-up	Serious adverse events	Concomitant drugs	Discontinuation of anti-TNF
Hueber et al. [19]	11	62.3 (mean)	4/7	9 RA, 1 PsA 1 JRA	Yes	5 ETA, 4 INF 2 ADA/ETA/INF	24 months (mean)	No	NR	No
Hammoudeh [17]	1	45	Female	RA	Yes	INF	NR	No	NR	No
Yee and Pochapin [18]	1	72	Female	Sarcoidosis	No	INF	6 weeks	Hypercoagulable state	NR	Yes
Singh et al. [16]	1	60	Female	RA	No	INF	2 years	No	NR	No
Gottenberg et al. [20]	15	49.5 (mean)	10/5	5 RA, 6 AS 1 aSD, 1 PsA 1 CINCA, 1 JIA	Yes	4 ETA, 10 INF 1 ETA+INF	10.4 months (mean)	No	2 CS, 3 NSAIDS 1 MTX, 2 AZA 3 MTX+CS	3 INF (a) 1 ETA (b)
Ortiz-Santamaria et al. [21]	6	59.3 (mean)	3/3	5 RA, 1 AS	Yes	INF	18 months (mean)	1 transient pancytopenia	NR	2 (c) 1 anaphylactoid reaction
Our case (2009)	1	52	Male	PsA	No	INF	6 months	No	No	No

a inefficacy, *b* lost from follow-up, *c* initiation of hemodialysis, *ETA* etanercept, *INF* infliximab, *NR* not reported, *JRA* juvenile rheumatoid arthritis, *ADA* adalimumab, *AS* ankylosing spondylitis, *CS* corticosteroid (prednisone), *NSAIDs* nonsteroid anti-inflammatory drugs, *aSD* adult Still disease, *AZA* azathioprine, *CINCA* chronic infantile neurologic cutaneous and articular syndrome, *JIA* juvenile idiopathic arthritis.

stabilized. Ortiz-Santamaria et al. [21] reported the use of infliximab in six patients with amyloidosis (five related to RA and one to ankylosing spondylitis). Two out of six withdrew from infliximab therapy because they required hemodialysis. One of them withdrew after he had developed transient pancytopenia alongside with renal function impairment. The other patient developed no adverse events but discontinued because at that time it was not known whether such a therapy could be administered to patients undergoing hemodialysis.

Our patient presented to us while already on hemodialysis since about 3 years before. He suffered from severe psoriasis and dactylitis which had a major impact on his quality of life. The patient responded rapidly and satisfactorily to infliximab infusions, as this was reflected on the dramatic decrease of the PASI score, improvement of anemia, and reduction of acute phase reactants. On the other hand, no changes of renal function were noted and the patient continued hemodialysis treatment on regular basis. Up to now, the drug has been well tolerated and he has shown no adverse events. This further supports evidence from other case reports that infliximab treatment in patients undergoing hemodialysis can be safe, well tolerated, and effective. However, larger trials are needed to support its use in these patients.

Disclosures None

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