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Severe psoriatic arthritis in an HIV/AIDS patient treated with several TNF blockers switching: a case-based review

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ABSTRACT:

— ***Objective:*** This case-based review aims to describe the clinical findings, treatment, and outcome of an HIV/AIDS patient with psoriatic arthritis (PsA) who received four anti-TNF agents and review case reports concerning this rare clinical association.

— ***Case report:*** A 51-year-old man was diagnosed in 2008 with psoriatic arthritis. He was initially treated with methotrexate 17.5 mg/week and had a partial response. Next, he received various anti-TNF agents, with inadequate or no response, including etanercept, infliximab, adalimumab, and finally golimumab, when he experienced good response. He received the HIV diagnosis in 1998, initially treated with lamivudine, zidovudine, and efavirenz. Other comorbidities were systemic hypertension, diabetes mellitus type 2, dyslipidemia, and acute myocardial infarct in 2016 treated with a revascularization surgery, heart arrhythmia, and depression. He is currently treated with golimumab, methotrexate, antiretroviral agents (lamivudine, zidovudine, and dolutegravir), vitamin D, and adequate PsA control.

— ***Conclusions:*** The present article describes a unique case of an HIV patient who received four different TNF blockers to obtain clinical control of PsA. It seems that TNF-α inhibitors are a viable option for psoriasis/PsA patients with HIV without advanced disease.

— ***Keywords:*** Psoriasis, Psoriatic arthritis, Anti-tumor necrosis factor, Adalimumab, Infliximab, Etanercept, Golimumab, Spondyloarthritis.

INTRODUCTION

Anti-tumor necrosis factor (anti-TNF) drugs have emerged as a potential alternative for treating various rheumatic conditions, including rheumatoid arthritis, and ankylosing spondylitis play a prominent role in inflammation[1,2]. The pathophysiological mechanism of psoriasis also includes TNF-α action, and thus, blocking TNF-α with biological agents is an effective treatment[3]. Psoriatic arthritis (PsA) which clinically consists of psoriasis and associated arthritis is also effectively treated with anti-TNF[4].

With the spread of anti-TNF use, specific groups of patients need this biological therapy, such as people living with HIV (PLWHIV) or people with Acquired Immune deficiency syndrome (AIDS). Knowledge about their safety and efficacy is limited to case reports, case series, and small clinical studies[5-11]. Therefore, their use has not been routinely used. Further studies are needed to determine if immunosuppressive drugs can be safely and effectively used in PLWHIV affected by psoriasis and other autoimmune disorders. There are few cases in the literature reporting HIV patients with psoriatic arthritis treated with anti-TNF[5-10].

This study's objective was to describe the clinical findings, treatment, and outcome of a patient with PsA and concomitant HIV/AIDS infection who received several anti-TNF drugs and review case reports concerning this rare clinical association.

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CASE REPORT

A 51-year-old man was diagnosed in 2008 with psoriatic arthritis, with psoriasis and arthritis's simultaneous onset. He was initially treated with methotrexate 17.5 mg/week and had a partial response. Etanercept 50 mg/week was associated, and he experienced a partial improvement mainly of the psoriatic lesions, although arthritis remained. After 6 months, etanercept was switched to infliximab 500 mg every 8 weeks for 4 months, but no improvement was detected. Then, this drug was changed to adalimumab 40 mg every 15 days for 5 months. He felt no difference, and at last, golimumab 50 mg monthly was started with an improvement of skin and arthritis. This patient received HIV diagnosis in 1998, and he was treated initially with lamivudine 150 mg/day, zidovudine 300 mg/day and efavirenz 600 mg/day. He also had many comorbidities such as systemic hypertension, treated with losartan 50 mg/day, diabetes mellitus under pioglitazone and alogliptin, dyslipidemia under rosuvastatin 20 mg/day, and evolocumab every 15 days, acute myocardial infarct in 2016 treated with a revascularization surgery, heart arrhythmia under amiodarone 100 mg/day, and depression treated with sertraline 100 mg/day.

His physical examination in 2008 showed erythematous-desquamative plaques over the extensor face of elbows and no arthritis. The laboratory tests revealed low platelets of 139,000/mm^2, erythrocyte sedimentation rate of 2 mm/1st hour, C-reactive protein of 0.5 mg/dL, vitamin D of 10 ng/mL [normal range (nr): > 30 ng/mL], positive HIV serology with undetectable viral load and CD4 count of 1592 cells/mm^3 (nr: 456-1492 cell/mm^3) and CD8 of 1437 (nr: 272-1144cell/mm^3). AST was 93 U/L, ALT 157 U/L, alkaline phosphatase, and gamma-glutamyl transpeptidase were normal. Total cholesterol of 69 mg/dL, HDL-c 30 mg/dL, LDL-c of 1 mg/dL and triglycerides of 362 mg/dL (nr: < 100 mg/dL), TSH 6.18, free T4 1.35, with negative anti-thyroperoxidase and anti-thyroglobulin. Antinuclear antibodies, anti-Ro/SS-A, anti-La/SS-B, anti-dsDNA, anti-Sm, anti-U1RNP antibodies were all negative HLA-B27 was absent. Serology for infectious diseases, including hepatitis B and C, HTLV I and II, cytomegalovirus, toxoplasmosis, rubella, mononucleosis, syphilis, were all negative. Vitamin D 20,000 IU/day was prescribed, and a hypocaloric and hypolipemic diet was suggested. He is currently treated with golimumab, methotrexate 20 mg/week, antiretroviral agents, vitamin D, and adequate PsA control.

DISCUSSION

To our knowledge, this is the first study that describes a case of severe PsA treated with several anti-TNF therapies in a patient with a background of positive HIV, and, additionally, we review case reports concerning this clinical association.

One of the advantages of this study was reviewing the case reports that restricted the evaluation of patients with HIV/AIDS and PsA, without concomitant chronic infections such as hepatitis B and C. The inclusion of a homogeneous PsA and HIV group of patients is essential since other chronic diseases might hamper data interpretation, and the underlying disease pathophysiology (hepatitis B and C) can worsen the patients' clinical status.

HIV-infected patients with psoriasis are more prone to more severe and persistent skin lesions with erythrodermic, guttate, and inverse and psoriasis subtypes[12]. Similarly, those with PsA may have a more severe, deforming, erosive arthropathy commonly refractory to standard therapy[13]. In addition, the onset of psoriatic arthritis in HIV patients frequently communicates the development of opportunistic infections in this viral infection[14]. The most common clinical presentation is an asymmetrical oligo- or polyarthritis of the lower limbs, but arthritis *mutilans* involving the distal interphalangeal joints may also occur[15]. Notably, the number of joints affected tends to increase with time[8].

Treatment is further complicated since most systemic therapies commonly used for refractory cases involve immunosuppressive agents, which can cause severe complications in HIV-positive patients. A retrospective open-label case series of 8 patients demonstrated that TNF blockers' use seems safe and effective in PLWHIV with rheumatic diseases even on the follow-up of 28 months[16]. Studies[17-19] have recently demonstrated the safe use of ustekinumab and secukinumab in uncomplicated PLWHIV and psoriasis, and these agents seem to be an alternative biological therapy for them.

Furthermore, a retrospective multicenter study evaluated the safety and effectiveness of conventional and biologic immunosuppressive drugs in treating patients with psoriasis and concomitant HIV infection. It concluded that biologic drugs, both anti-TNF alpha agents and ustekinumab, seem to have an acceptable safety profile and high effectiveness in PLWHIV (76.5% of the patients had achieved a Psoriasis area and severity index (PASI 75) on the follow-up of six months[11].

As observed in our patient, refractory PsA patients are commonly managed by switching from one anti-TNF to another. Several case reports[6,8-10,20,21] describe the successful anti-TNF therapy, most commonly etanercept and infliximab, in patients with chronic HIV infection and PsA. Moreover, there were no significant adverse events or changes in CD4+ lymphocyte and viral load throughout the treatment in most of the studies[6,8-10,20,21]. Additionally, a systematic review[22] of the literature included 18 studies conducted and included studies assessing real-world effectiveness outcomes in patients who switched TNF blockers[22] (Table 1). Interestingly, first-line therapy produced better results than second-line therapy and between the second compared to the third-line anti-TNF treatments. They also noted that PsA patients were less likely to respond to a second anti-TNF course if safety, rather than lack of effect, caused them to switch. Moreover, subsequent treatment lines may be associated with less response in some measures[22]. Interestingly, our patient had a good response only after the fourth anti-TNF drug.

Table 1. Case reports describing the use of TNF-α antagonists on HIV-positive psoriasis arthritis patients and their outcomes.

Authors	Patient age, y/sex	Clinical Presentation	Treatment (n)	Therapy duration	Outcome
Aboulafia et al[8], 2000	45/M	Psoriatic arthritis and HIV on HAART	Etanercept	5 months	His psoriasis and joint deformities improved
Mikhail et al[20], 2008		Psoriatic arthritis, pustular psoriasis, and HIV on HAART	Etanercept	5 months (ongoing)	Therapy was discontinued due to recurrent infections Arthritis improved but has had some recurrence of the plaque psoriasis
Bartke et al[10], 2004		Psoriasis, psoriatic arthritis, AIDS on HAART	Infliximab	6 weeks (ongoing)	The patient's skin lesions and joint inflammation improved
Sellam et al[9], 2007	27/M NA/M	Psoriasis, psoriatic arthritis, HIV on HAART/	Infliximab/ Infliximab	22months/ 45months	Dramatic improvements in the skin and joint manifestations occurred in both patients No opportunistic infections occurred
Lindsey et al[6], 2014	49/M	Severe psoriasis and psoriatic arthritis in an HIV-positive patient	Adalimumab	30 months	The patient was successfully treated with no adverse events related to treatment
Barco et al[19], 2010	49/M	Psoriasis, psoriatic arthritis, AIDS on HAART	Etanercept	27 months (ongoing)	He responded successfully to treatment. There were no adverse events or changes in CD4+ lymphocyte and viral load all long the treatment.
Current study, 2021	51/M	Psoriatic arthritis, AIDS on HAART HAART	Etanercept/ infliximab/ Adalimumab/ Golimumab	6 months/ 4 months/ 5 months/ (ongoing)	Patient experienced complete joint remission after the golimumab use

HAART – Highly Active Antiretroviral Therapy, HIV – Human immunodeficiency virus.

CONCLUSIONS

This report describes an interesting case of an HIV patient with PsA who received several anti-TNF and found a good response after combining golimumab, methotrexate, and vitamin D supplementation. Thus, it seems that TNF-α inhibitors are a viable option for psoriasis/PsA patients with HIV who have no concomitant acute infections, cancers, latent tuberculosis, or chronic hepatitis B. Future studies with a larger number of PLWHIV and PsA treated with TNF-blockers, and novel biologicals are desired.

HIGHLIGHTS

- There are few cases in the literature reporting HIV patients with psoriatic arthritis treated with anti-TNF.
- We described in this paper a patient with psoriatic arthritis and HIV who received four different anti-tumor necrosis factor antagonists.
- A systematic review of the literature found 18 articles, and first-line anti-TNF produced better results than second-line therapy.

Conflict of Interest:
The authors declare that they have no conflict of interests.

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JFC: Conception, analysis, writing, interpretation, revision, submission.
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Ethical Statement:
The authors declare that they followed the World Medical Association Declaration of Helsinki in this study. Informed consent was obtained from the patient for publication of his case.

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