

Therapeutic challenges of psoriasis in the HIV-infected patient: A case report

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Abstract. Psoriasis can be paradoxically associated with human immunodeficiency virus (HIV) infection, having a prevalence similar to the general population but with a more severe evolution. In the genetically predisposed patients with the CW*0602 haplotype, HIV infection can be a triggering factor and a first sign of infection, and lesions can spontaneously remit with immune reconstruction after antiretroviral therapy. Our patient is a 34 year-old male with recent HIV infection, in spite of being for over 10 years the partner of an HIV-positive patient with whom the patient has two HIV-positive children. The patient was diagnosed with psoriasis 7 years ago and was treated topically. The physical

examination at HIV diagnosis was overall favorable, with skin findings compatible with disseminated vulgar psoriasis. Following antiretroviral treatment with Triumeq the patient had a favorable viral response, with complete viral suppression after 12 weeks, but the pre-existent psoriasis lesions worsened. Methotrexate (MTX) treatment followed for 12 weeks, with partial improvement of psoriatic dermatitis. This medication was continued for 1 year, but the lesions reappeared, possibly due to treatment resistance. MTX treatment for psoriasis in the HIV-infected patient was beneficial, but limited to one year, leaving biologics as possible treatment following therapy under strict monitoring for adverse effects, T-lymphocyte CD4⁺ and viral levels.

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Abbreviations: HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome; IL2, interleukin-2; INF- γ , interferon- γ ; TNF- α , tumor necrosis factor- α ; UV, ultraviolet; MTX, methotrexate; BMI, body mass index; RNA-HIV, ribonucleic acid HIV; HBV, hepatitis B virus; HCV, hepatitis C virus; CMV, cytomegalovirus; PASI, Psoriasis Area and Severity Index; ALT, alanine aminotransferase; HAART, highly active antiretroviral therapy

Key words: psoriasis, HIV, methothrexate, triumeq, biologics

Introduction

Psoriasis is an autoimmune disease with chronic course, having relapse and remission periods and a variable European country prevalence from 1.3 to 11.4% (1-3).

Psoriasis may be associated with human immunodeficiency virus (HIV) infection, but the prevalence of the viral infection does not differ significantly from that of the general population. Although it is not a characteristic presentation of the acquired immunodeficiency syndrome (AIDS), the evolution of psoriasis can be more severe in patients with HIV (4-6).

HIV infection can be a triggering factor for psoriasis development and a first sign of infection in genetically predisposed patients having the CW*0602 haplotype (7). In these patients, psoriasis lesions could improve once immune reconstruction has taken place after antiretroviral therapy, reaching even spontaneous remission. That being said, some guttate and vulgar forms of psoriasis can worsen in the advanced stages of AIDS (4).

The pathogenesis of associating psoriasis to HIV-infected patients is paradoxical and is explained by the imbalance between immune cellular components. T lymphocytes have the main purpose of mediating the excessive inflammatory

Table I. Biologic outcome in an HIV-positive patient suffering from psoriasis, under MTX treatment.

Timeline	February 2019	May 2019	September 2019	September 2020
Hb (g/dl)	15.2	15.4	14.5	15.5
WBC (cells/mm ³)	8,110	6,310	9,600	11,000
ALT (UI/l)	24.2	31	24.6	96.3
AST (UI/l)	22	28.2	26.4	66.8
Creatinine (mg/dl)	0.82	0.79	0.74	0.75
T-lymphocyte CD4 (cells/mm ³)	466	581	450	500
ARN-HIV (copies/ml)	146,000	Undetectable	Undetectable	Undetectable
TRIUMEQ	√	√	√	√
MTX		√	√	√
PASI (%)	21.2	19	17	16.2

HIV, human immunodeficiency virus; ALT, alanine aminotransferase; AST, aspartate aminotransferase; MTX, methotrexate; PASI, Psoriasis Area and Severity Index. √ indicates that the patient was receiving treatment with the relevant agent during this time period.

response that takes place in psoriasis, while HIV infection is characterized by T-lymphocyte depletion (a state which renders the body susceptible to various opportunistic infections) (8). The cytokine profile of the two diseases is also different, psoriasis having a Th1 pattern [interleukin-2 (IL2), interferon- γ (INF- γ), tumor necrosis factor- α (TNF- α)], while HIV infection has a Th2 pattern (IL-2, IL-5, IL-10) (9-11).

Psoriasis biological therapies which target lymphocyte Th1 contribute to the severity of HIV infection progression, while antiretroviral therapy has the capacity to improve psoriatic lesions. However, some case reports have revealed that antiretroviral therapy initiation in severe immune-suppressed patients, especially when T-lymphocyte CD4⁺ levels are below 50 cells/mm³, could be associated with a temporary exacerbation of psoriasis, within the immune reconstruction inflammatory syndrome (12).

Available therapies for HIV-associated psoriasis are classified into 3 categories, producing results that vary from complete remission to lack of any response. Local therapy uses tar products, emollients, salicylic acid, corticosteroids and retinoids. Ultraviolet (UV) phototherapy is controversial. Systemic therapy is based on acitretin, methotrexate (MTX) and cyclosporine, anti-TNF- α biologic therapy. MTX is rarely used in HIV patients due to its immune-modulating effect, renal toxicity or the folate metabolism (13-16).

Previous studies have revealed that the purpose of Th17 lymphocytes in natural and adaptive immunity in skin and mucous membranes, is their involvement in the pathogenesis of autoimmune, neoplastic and infectious processes at this level. Th17 lymphocytes are a Th-lymphocyte subset, which produce cytokines that act on epithelial cells, thus becoming a target for research in patients with both psoriasis and HIV infection, in the hopes of finding new therapies (13-15).

Case report

The case of a 34-year-old male, unqualified construction worker from a rural environment with a primary school education level, is presented, who addressed the 'Sf. Cuvioasa Parascheva' Clinical Hospital of Infectious Diseases (Galati,

Romania) for the evaluation, monitoring and treatment of his recent HIV infection. For over 10 years the patient has been the partner of a positive HIV patient, with whom the patient has two seropositive HIV children, systematically breaching the safe sex measures. His last HIV testing, two years ago, was negative. The patient was a chronic smoker (23 pack-years) and alcohol consumer (4 units/day). A total of 18 years ago, the patient suffered multiple trauma involving cranial-cerebral injuries and coma, being hospitalized for over a month. A total of 7 years prior to the HIV diagnosis (when the patient was 28), the patient received the clinical diagnosis of psoriasis and followed various topical treatments. The family history is negative for psoriasis and the patient suffers from low self-image with poor quality of life due to the appearance and discomfort of the psoriatic lesions.

Upon initial clinical examination, when the patient was diagnosed as being HIV-positive, his general health status was favorable, the patient was afebrile with a body mass index (BMI) of 21.2 kg/m² and blood pressure of 150/100 mmHg, with rhythmic heartbeats and no additional heart sounds; the lung sounds were normal, as was the neurologic examination. Mucosal examination revealed candidiasis lesions. Onychomycosis and squamous scalp lesions were also identified, and the skin examination revealed disseminated vulgar psoriasis lesions. Laboratory data revealed an CD4⁺ T-lymphocyte number of 466 cells/mm³, a ribonucleic acid (RNA)-HIV viral load of 146,000 copies/ml, with negative serologic examination for hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), toxoplasma and syphilis. The remaining hematological and biochemical investigations were in the normal ranges, while no significant lesions were found on the thoracic X-ray.

The patient received antiretroviral treatment with Triumeq (dolutegravir + lamivudine + abacavir), registering a favorable viral response with complete viral suppression after 12 weeks. The treatment was well tolerated, but the pre-existent psoriatic lesions treated with topical medication became more extended and accentuated the inflammatory response with a Psoriasis Area and Severity Index (PASI) score of 21.2. The patient then received systemic treatment with MTX as 15 mg/week,



Figure 1. Clinical outcome of psoriasis under MTX treatment in an HIV-positive patient. (A) At the beginning of treatment. (B) After 4 months of treatment. (C) After 1 year of treatment.

for 12 weeks, with major improvement of lesions and partial remission. Under strict biologic monitoring, MTX treatment was continued with the same dosage for a year, but the lesions reappeared, coinciding with a three-fold increase in alanine

aminotransferase (ALT) levels. The laboratory changes during MTX treatment (from May 2019 to September 2020) are highlighted in Table I, along with the evolution of hand skin lesions in Fig. 1.

Discussion

MTX is an immune suppressive drug frequently used in autoimmune and inflammatory dermatological diseases (17,18).

Current treatment guidelines recommend MTX as first-line systemic treatment in any form of psoriasis which cannot be controlled by topical therapy, which significantly affects the quality of life of the patient and fulfills one of the following conditions: is extensive (PASI >10%); is localized, but is associated with significant functional deterioration; or phototherapy cannot be used, is inefficient or has led to a fast relapse. Concerning severity scores after MTX use for 12-24 weeks, randomized prospective studies conducted on large cohorts of patients suffering from psoriasis, proved to have similar efficacy as biological therapies with adalimumab, briakinumab, infliximab, but also as with cyclosporine (17).

MTX use in HIV patients is associated with a high risk for opportunistic infections. Medical literature data has reported a case of toxic encephalopathy which improved after cessation of MTX (19). In another study, 2 out of the 4 patients treated with MTX suffered from pneumocystis pneumonia, although they received prophylaxis for opportunistic infections prior to starting treatment (19). Having associated infections with HBV, HCV or latent tuberculosis are absolute contraindications for MTX use (19,20), but in our case the serologic markers of the patients for these infections were negative.

The medical literature has few data concerning the efficacy of systemic therapies in HIV-positive patients suffering from psoriasis, most recommendations exerting caution in their use. However, the American Academy of Dermatology collected data on the use of TNF- α inhibitors (etanercept, adalimumab and infliximab) in HIV-positive patients suffering from psoriatic arthritis who did not respond to the combination treatment with MTX and cyclosporine, adherent to the antiretroviral therapy with encouraging results (20,21). Ustekinumab is a p40-IL 12/23 inhibitor that was used for refractory forms of HIV-associated psoriasis, without registering any adverse effects in the first months of treatment (20,22).

Concerning certolizumab, a TNF- α inhibitor and an approved biologic drug for plaque psoriasis and for psoriatic arthritis, this is an agent that could be used as systemic treatment in HIV-positive patients suffering from psoriasis, having an undetectable viral load and under highly active antiretroviral therapy (HAART) (23,24). Risankizumab and guselkumab are both biologicals approved for targeting the p19 subunit of IL-23 (IL23/p19 inhibitors), used in moderate to severe plaque psoriasis. The advantage of using these two drugs would be an improved safety profile (as compared with TNF- α inhibitors) (23,25). Although guselkumab is reported to be safe and effective in HIV-positive patients suffering from psoriasis, on condition of close monitoring, there remains insufficient data for guselkumab and risankizumab use in these particular patients. These three agents could have positive effects on the T-lymphocyte CD4⁺ counts and on the viral load (17,23,25).

The case features were as follows: i) In spite of repeated unprotected sexual contact, the patient suffering from psoriasis was not infected with HIV for a long time, suggesting a strong immune response with a particular genetic determinism; ii) psoriasis was diagnosed prior to HIV and its onset was at

a young age, corresponding most probably to type I psoriasis; iii) the genetic profile CW*0602 remained uninvestigated, having no family links to other cases of psoriasis; iv) the evolution of psoriasis could be favored by external factors including alcohol, smoking, excessive sun exposure, hygiene deficit, which were not corrected during therapy; v) anti-retroviral treatment was followed by immune recovery and complete viral suppression; vi) psoriasis exacerbation after the first weeks of efficient antiviral treatment could correspond to a rare paradoxical inflammatory syndrome of immune reconstruction; vii) topical therapy resistance and controversies regarding the efficacy and safety of phototherapy in the HIV-positive patient justified the decision of using MTX as first-line systemic treatment; viii) MTX use in the patient with antiviral therapy-controlled HIV infection, was well tolerated and efficient, with a partial remission of psoriasis lesions in the first 12 weeks; and ix) re-emergence of lesions after one year of continuation of MTX could be explained by the development of treatment resistance, making it necessary to apply or associate other therapeutic options.

In conclusion, in the context of HIV infection, progression of psoriasis may be an expression of specific viral pathogenic immune deficiency, but also of inflammatory processes which accompany immune reconstruction after antiretroviral therapy. MTX use for severe psoriasis treatment was an efficient and safe solution for dermatological lesion control in the HIV-infected patient, but the benefits were limited to only one year. Biological therapies are the future options for psoriasis treatment after MTX failure, but they require rigorous monitoring for adverse effects, CD4⁺ lymphocytes and viral levels.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MA and AAA confirm the authenticity of all the raw data. MA, AAA, EN, SF, LA and ALT were major contributors in writing the manuscript, were involved in all the stages of the study, contributed to the conception and design of the work, as well as revising it and have also contributed in analyzing the data for the study. MA, AAA, EN, SF, LA and ALT revised it for important intellectual content. MA, AAA, EN, SF, LA and ALT approved the final version to be published. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

Ethics approval was granted by the Ethics Committee of the 'Sf. Cuvioasa Parascheva' Clinical Hospital of Infectious Diseases (Galati, Romania), with the decision no. 31 from 16.03.2021. The patient also provided written informed consent for participation in the study.

Patient consent for publication

The patient provided written informed consent for the publication of any associated data and accompanying figure.

Competing interests

The authors declare that they have no competing interests.

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