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Case Report

Leukopenia successfully treated by Ustekinumab in patients with psoriatic arthritis

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Abstract:

Introduction:

Psoriatic Arthritis (PsA) is an immune-mediated disease. The effectiveness of biologics has changed therapeutic strategies for psoriasis. We report a case of leukopenia in a patient with psoriatic arthritis (PsA) who was treated with Ustekinumab.

Case presentation:

A 36-year-old Syrian female presented for a follow-up concerning the treatment of psoriatic arthritis. She was diagnosed with psoriatic arthritis according to the CASPAR criteria.

She was treated with Methotrexate, then Sulfasalazine. On presentation, the physical examination revealed tenderness in the metacarpals, proximal interphalangeal joints, and distal interphalangeal joints of both hands.

Laboratory analysis showed: white blood cells (WBC):3500 /mm^3, (Neut:23% n = 40-65%, Lymp:65% n= 25-40%), erythrocyte sedimentation rate (ESR): 40 mm/h1, and C-reactive protein (CRP): 9.3 mg/L. Given the patient's ongoing disease activity and the presence of leukopenia, we started with Ustekinumab 45 mg subcutaneously. After the third dose of Ustekinumab, the evaluation showed improvement in her peripheral arthritis and normal laboratory findings.

Discussion:

Patients with psoriasis had higher total white blood cells and neutrophils. Ustekinumab has good efficacy against disease activity as well as a favorable safety profile. In the literature, we found a case of myelodysplastic syndrome associated with inflammatory bowel disease treated with Ustekinumab. Another case of constitutional neutropenia and psoriasis vulgaris was treated with Ustekinumab.

Conclusion:

This is the first case of leukopenia associated with PsA successfully treated with Ustekinumab. UST treatment might be recommended for leukopenia associated with PsA, but further researches are recommended.

Keywords: Biologics; Ustekinumab; PsA; cDMARDS; disease activity.

Introduction:

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis found in about 20% of patients with psoriasis (1). It has been estimated to have a prevalence of 0.05% to 0.25% in the general population and around 6% to 41% in psoriasis patients, usually in the 30s and 40s in both sexes (2).

The goal of PsA treatment is to achieve remission or minimal/low disease activity. Nonsteroidal anti-inflammatory drugs are commonly used as first-line treatment for pain, meanwhile, conventional synthetic disease-modifying antirheumatic drugs: csDMARDs (e.g., methotrexate, sulfasalazine) are commonly used to treat peripheral arthritis and skin disease (3).

Biologic agents are recommended for the treatment of active moderate-severe PsA in adults with inadequate response to previous non-biologic DMARDs (4).

Biologic disease-modifying antirheumatic drugs (bDMARDs) target various cytokines involved in the pathogenesis of PsA and have been shown to improve symptoms and inhibit the progression of structural damage(3).

Ustekinumab (UST) is a fully human IgG1 monoclonal antibody that binds with high affinity to the shared p40 subunit of human IL-12 and IL-23, inhibiting their binding to the IL-12Rβ1 receptor on the surface of T cells, NK cells, and antigen-presenting cells (APCs) (5). Ustekinumab was approved for adults with moderate to severe plaque psoriasis and psoriatic arthritis (5,6). The therapeutic benefit of Ustekinumab appears to be independent of concomitant methotrexate use or previous anti-TNF exposure (6).

Case Presentation:

A 36-year-old Syrian female presented to the outpatient clinic at Almouasat University Hospital in November 2022 for a follow-up concerning her treatment of psoriatic arthritis.

Three years before our evaluation, she was diagnosed with psoriatic arthritis according to the CASPAR criteria (7), as arthralgia in her hands, feet, and knees, psoriasis, and negative rheumatic factor. She was treated with Methotrexate 10 mg/ week for two years, then Sulfasalazine 2 g per day for one year, and folic acid 5 mg/week, the patient was never treated with systemic steroids.

On presentation, the physical examination revealed tenderness in the metacarpals, proximal interphalangeal joints, and distal interphalangeal joints of both hands.

There was no finger pitting. There were two erythematous psoriatic plaques in her legs, the first one was about 5 *3 cm on the front side of the right leg, and the second one was about 2*1 cm on the front side of the left leg. The psoriasis area and severity index (PASI) (8) was 2.8.

The patient had moderate disease activity up to DAPSA (disease activity index) (9). The remainder of the physical examination was normal.

The laboratory findings are shown in Table (1):

TABLE (1):

WBC	3500 /mm^2 (n=4000-1000mm^3)	**Erythrocyte sedimentation rate: (ESR)**	40 mm/h1 (normal range for female 0-20 mm/h1)
Neutrophils	23% n=40-65 %	**C-reactive protein: (CRP)**	9.3 mg/L (n= 0 -6 mg/L)
Lymphocytes	65% n=25-40%	**Rheumatoid factor: (RF)**	Negative
Hemoglobin	12.2 g/dl The normal range for female	**Anti-cyclic citrullinated peptide**	Negative

	(12-16 g/dl)	**antibody: (ANTI-CCP)**	
Platelet count	$300*10^3/mm^3$ (n =150 - 450 $10^3/mm^3$)	**Antinuclear antibody: (ANA)**	Negative

Peripheral blood smear revealed:

red blood cells within the normal limits of size and pigmentation, platelets within normal limits of number and distribution. Leukocytes appear below the normal range with neutropenia (Figure 1-2-3). The hematology consultation recommended bone marrow aspiration, but the patient refused this procedure.

Figure 1-2-3: leukopenia presented in blood smear

Figure1

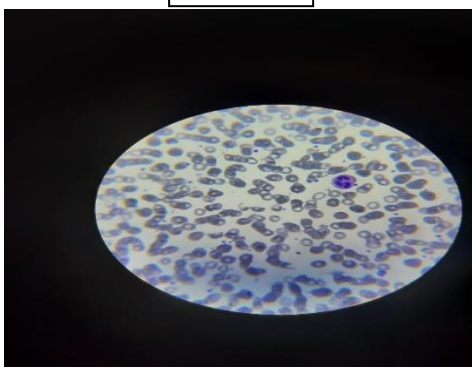


Figure2

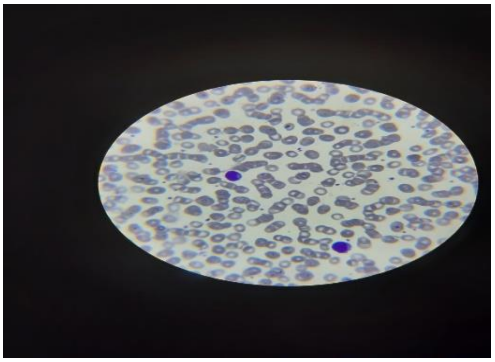
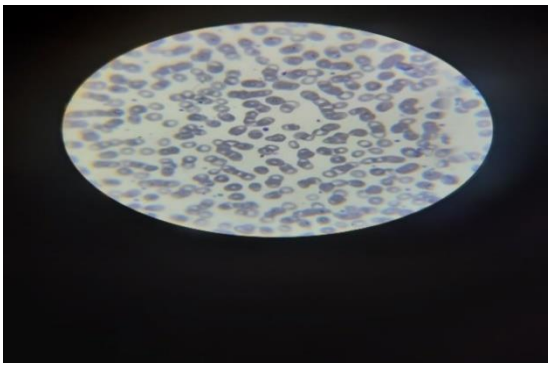


Figure 3



Given the patient's ongoing disease activity, and the presence of leukopenia, we started with Ustekinumab 45 mg subcutaneously, followed by another dose after four weeks, then 45mg every twelve weeks. Re-evaluation after the first and second doses showed no improvement in clinical and laboratory findings, and the patient still had arthralgia, leukopenia, and elevated erythrocyte sedimentation rate.

After the third dose of Ustekinumab, she had no pain in her hands, feet, and knees. DAPSA showed

low disease activity. The laboratory evaluation showed: white blood cells(WBC):7100 $/mm^2$ (Neut:66%, Lymp:30%), erythrocyte sedimentation rate ESR:20 mm/h1, and C-reactive protein (CRP): 4 mg/L.

Discussion:

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis (PsO). The onset of psoriatic arthritis is usually in the 30s and 40s and occurs about equally in males and females (10). Our patient is a 36-year-old female.

Diagnosis of psoriatic arthritis is made by CASPAR criteria, it consists of established inflammatory articular disease with at least 3 points from the following features: current psoriasis, a personal or a family history of psoriasis, dactylitis, typical psoriatic nail dystrophy, negative rheumatoid factor, juxta-articular new bone formation on hand or foot radiographs(7). Our patient had 3 points by criteria: arthralgia in her hands, feet, and knees, psoriasis, and negative rheumatic factor.

Many studies found that patients with psoriasis had higher total white blood cells and neutrophils (11). Our patient had leukopenia and low neutrophil.

The primary goals in the treatment of PsA are reduction of pain; improvement in the other signs and symptoms of disease, optimization of functional capacity and quality of life. The main medicines used to treat psoriatic arthritis include nonsteroidal anti-inflammatory drugs, traditional disease-modifying anti-rheumatic drugs, and biological agents that resulted in dramatic improvements in patients with PsA (12), as we did.

Ustekinumab is a fully human immunoglobulin G1 monoclonal antibody to the p40 subunit of IL-12 and IL-23 and was the first licensed non-TNFi biologic disease-modifying antirheumatic drug (bDMARDs) therapy in psoriasis and PsA. Additionally, ustekinumab has good efficacy against disease activity in joints and skin as well as a favorable safety profile (13). Our patient had responded well to Ustekinumab

Common adverse effects of ustekinumab include respiratory tract infections, nasopharyngitis, headache, and injection site reactions. Fortunately, severe long-term infections or significant cardiovascular adverse events rarely occur (6). Our patient didn't have any side effects.

We found a case in the medical literature talking about the role of Ustekinumab in the treatment of myelodysplastic syndrome (MDS) associated with inflammatory bowel disease in a 63-year-old male who was unresponded to anti-TNF-α agent, infliximab and azacytidine. After the initiation of UST, an endoscopic examination showed the shrinkage of ulcers 6 months after UST started, a marked reduction in the serum CRP level was observed 10 months after the initiation of UST, a decrease in the white blood cell and platelet counts after UST therapy led to an improvement of intestinal inflammation.

They explained that Elevated IL-17 levels and IL-17-induced interferon (IFN)-γ and TNF-α overproduction may be involved in the pathogenesis of MDS and the number of CD3+ CD4+ IL-17 producing T cells (Th17) has been shown to markedly increase in low-risk MDS, UST inhibits the IL12/23 signaling pathway, leading to reduced Th17 responses (14).

We found another case of a 44-year-old male with a year's history of psoriasis vulgaris with constitutional neutropenia. He had a previous diagnosis of familial constitutional leukopenia 17 years ago, with a mean leukocyte count of 2600 mm^3 and neutrophil count of 770 mm^3. He had been previously treated with many drugs with the persistence of erythematous-desquamative plaques with progressive worsening, considering the constitutional neutropenia. The use of ustekinumab was initiated and the patient showed significant lesion improvement after 12 weeks without any adverse effects during the 3 years of use (15).

Conclusion:

This is the first case of leukopenia associated with (PsA) successfully treated with UST.

UST treatment might be recommended for leukopenia associated with (PsA), but further researches are demanded.

Authorship List:

Author Contributions

S Dumirieh described the case and collected the clinical data. M Kudsi reviewed and edited the manuscript.

All authors have read and agreed to the published version of the manuscript

Consent Statement

Written informed consent was obtained from the patient to publish this report by the journal's patient consent policy"

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