Secukinumab for recalcitrant Psoriatic Arthritis cases

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Extended Abstract

Abstract:

In the pre-TNF inhibitors (TNFi) era, several recalcitrant, moderate-to-severe, psoriatic arthritis (PsA) cases have been reported [1, 2]. The available treatment options were glucocorticoids (GCs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), retinoids, and photochemotherapy, but the results were modest [3]. TNFi revolutionised the treatment for PSA, with a constant decline of the recalcitrant cases [4, 5]. TNFi are biologic disease-modifying antirheumatic drugs (bDMARDs) bearing a significant capacity to achieve low disease activity or remission having an appealing efficacy/safety profile [6, 7]. The first TNFi for moderate-to-severe PsA was etanercept [8]. Nowadays, several bDMARDs(adalimumab, infliximab, golimumab, certolizumabpegol, ustekinumab, secukinumab, ixekizumab) and targeted synthetic DMARDs are already available such astofacitinibandapremilast.

We present a case of recalcitrant PsA to two TNFi, which showed a remarkable improvement after administration of secukinumab, an IL-17A inhibitor.

Informed consent, for the publication for this case report and any additional related information was taken from the patient involved in the study.

CASE REPORT

A 37-year-old female suffering from severe plaque psoriasis and arthritis involving the large joints, mainly knees, left ankle, and left elbow visited our outpatient clinic. The diagnosis of psoriasis had been made at the age of 13. Topical therapy with some improvement was the first approach. She had no arthritis at that time and she developed asymmetrical polyarthritis 2 months prior to her visit to our department. Past medical and family history were unremarkable.After the appropriate screening test, methotrexate (MTX) (15 mg/week) and prednisone (7.5 mg/day) was given. Despite some clinical improvement, the patient developed hepatotoxicity after two months (AST 127IU/L, ALT 120IU/L), thus MTX was discontinued and cyclosporine-A (CSA) (200 mg/day) was added. Three months after the initiation of CSA skin manifestations had a significant improvement but there was no improvement of synovitis of both knees. In addition, the patient had high acute phase reactants. Then, and after the appropriate discussion with the patient, we started adalimumab (40 mg/14 days) subcutaneously. Although the significant clinical and laboratory improvementafter 8 months of adalimumab and CSA treatment, she had a disease flare-up with symmetrical synovitis, including both knees and ankles, as well as severe skin manifestations. At that point, both drugs were discontinued.Subcutaneous (sc)etanercept (50 mg/week) and leflunomide (20 mg/day) were two other drugs that were administered. At the

beginning and more specifically for the first three months, she had a significant clinical and laboratory response but she developed elevated liver enzymes once again. A workup for liver disease (ultrasonography, screening for hepatitis B and C) was negative. Leflunomide was discontinued and she carried on with etanercept (50 mg/week). She did quite well, but 7 months later, she developed a severe exacerbation involving the knees and the skin[disease activity score (DAS 28) 5.2, Psoriasis Area Severity Index (PASI) score 10.8] (Fig. 1a). After discussion with the patient, there was a switch from TNFi to secukinumab, an IL-17a inhibitor. She started on 300 mg s.c. on weeks 0, 1, 2, and 4 and monthly thereafter. On follow-up and re-evaluation, 4 weeks later, (Fig. 1b) the patient reported a rapid skin and musculoskeletal improvement. PASI score was 2 and DAS 28 was 2.3. Secukinumab showed a dramatic and rapid response in the reduction of pain, followed by improvement of laboratory and clinical signs of joint inflammation. Skin disease also responded well after a short period of time which had a positive impact on patients' psychology. After 36 months of treatment with secukinumab, she is now free of joint pain and her skin has a near-normal appearance (Fig. 1c).

DISCUSSION

PsA is a challenging diagnosis as far as it concerns the treatment options. Patients need to feel and see improvement of the musculoskeletal system but also the skin. PsA is a unique inflammatory arthritis due to the fact that these patients have to deal not only with pain but also with their skin appearance, which may have a detrimental effect on their everyday live and psychology [9]. PsA has been linked with anxiety and depression [9, 10], which may lead to flare-ups of the disease, and in fact there is a vicious circle between disease activity and psychological status of the patient.

Older guidelines propose the use of a second TNFi when the first TNFi fails to prove success regarding disease activity but currently, secukinumab is recommended alongside other biologics.Secukinumab is a new, promising biologic agent with rapid results and a good safety profile [11, 12]. This is a case of a moderate-to-severe PsA that showed significant improvement of synovitis and plaque psoriasis after failing in two TNFi and three csDMARDs. An interesting article from Kurosaki et al. describes a case of refractory psoriasis and pruritus, which became unresponsive to several biologics (ustekinumab, adalimumab, infliximab plus MTX). Treatment was switched to secukinumab, and after 32 weeks, PASI 100 was achieved [13].

Data from the clinical literature on switching bDMARD therapies in PsA are limited. In general, numerous bDMARDS have demonstrated efficacy in PsA, including the TNFi, the IL-12/23 inhibitor ustekinumab, and the IL-17A inhibitor secukinumab, but there are limited data on cases of recalcitrant PsA. The IL-17A inhibitor secukinumab is approved for the treatment of moderate-to-severe plaque psoriasis, ankylosing spondylitis, and PsA. Results of large-scale phase 3 studies indicate that secukinumab significantly improves the signs and symptoms of PsA in both TNFi-naive and TNFi-experienced patients.

Other studies such as those of Mease et al. [14] and McInnes et al. [15](FUTURE 1 and FUTURE 2 respectively) showed that secukinumab is superior to placebo both in TNFi-naïve and TNFi-experienced patients, regardless of concomitant MTX use.

CONCLUSIONS

Secukinumab seems to be a reasonable choice in cases of recalcitrant PsA patients. IL-17A is an important player in the pathogenesis of psoriatic lesions. In addition, downregulation of proinflammatory cytokines such as IL-1, IL-6, and TNFa, possibly augment the therapeutic potency of secukinumab [16]. Improvement of skin manifestations also encourage PsA patients and improves their psychological status [17].

Figures

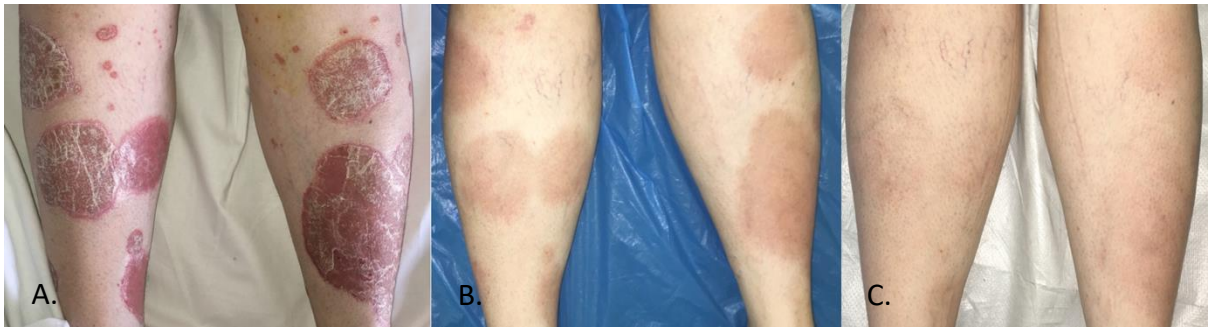

Figure 1. A: skin involvement while on etanercept; B: marked improvement on week 4 of secukinumab; C: significant improvement on week 36 of secukinumab.

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