CASE REPORT

Secukinumab induced Behçet’s syndrome: a report of two cases

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Abstract

Secukinumab is a human monoclonal antibody against IL-17A that has been shown to be effective in psoriasis, psoriatic arthritis and ankylosing spondylitis (AS) [1–3]. On the other hand, in randomized controlled trials among patients with Crohn’s disease (CD) and uveitis due to Behçet’s syndrome (BS) treated with secukinumab, primary end points were not met and the drug caused more exacerbations compared to placebo. The drug fact sheet states that secukinumab should be used with caution in patients with CD; however, there are no warnings for those with BS. Here, we present two patients with AS treated with secukinumab; we observed exacerbation of BS in one and emergence of de novo BS in another. Although IL-17A is thought to contribute to the pathogenesis of BS, our observations suggest that it might have a protective role. Finally, we suggest caution is required with the inhibition of IL-17 in BS.

INTRODUCTION

Secukinumab, a fully human monoclonal antibody against IL-17A, has been shown to be effective in psoriasis, psoriatic arthritis and ankylosing spondylitis (AS) [1–3]. On the other hand, in a randomized controlled trial (RCT) among patients with moderate to severe Crohn’s disease (CD), primary end points were not met and secukinumab caused more exacerbations compared to placebo [4]. Emergence of inflammatory bowel disease in one patient with psoriasis and another with AS treated with secukinumab have also been reported [5]. Moreover, secukinumab was reported to be ineffective in controlling non-infectious uveitis as stated in a comprehensive review of three RCTs (ENDURE, INSURE and SHIELD) [6]. Of the three RCTs, only one enrolled patients with Behçet’s syndrome (BS) with posterior uveitis or panuveitis (SHIELD study), while non-BS patients with active (INSURE study) or inactive noninfectious uveitis (ENDURE study) were included in two. Secukinumab was ineffective to prevent ocular attacks and also BS-associated clinical manifestations have been observed in SHIELD [6]. After completion of the SHIELD trial, the INSURE trial was terminated early. The ENDURE trial also was terminated early because the primary efficacy end points were not met as shown in prespecified interim data analysis [6]. The licensed product specification states that secukinumab should be used with caution in patients with CD; however, there are no warnings for those with BS. We report here exacerbation of BS in one and emergence of de novo BS in another patient treated with secukinumab for AS.
extremity superficial thrombophlebitis and bilateral panuveitis. He was diagnosed with BS. Secukinumab was stopped; three pulses of methylprednisolone and infliximab 5 mg/kg were started. After 1 week of this treatment, he felt better and the acute phase response regressed (CRP: 5 mg/dl, ESR: 37 mm/hr). He is asymptomatic with normal acute phase reactants at fifth month of infliximab.

**DISCUSSION**

IL-17A is a proinflammatory cytokine mainly produced by Th17 cells [1]. Besides proinflammatory properties, it plays important role in the protection against bacterial and fungal infections at the mucosa [1]. Higher levels of IL-17A have been also found in the peripheral blood of patients with Behçet uveitis and as such it has been considered important in disease mechanisms. However, in the SHIELD study, not only secukinumab was ineffective in controlling uveitis, but the most frequently reported serious adverse events were non-ocular BS exacerbations, uveitis and papulopustular lesions in the secukinumab arm [6].

We observed—to the best of our knowledge for the first time—full blown BS in two patients with AS who were treated with secukinumab. There was exacerbation of BS in one and emergence of de novo BS in another patient. Only patient 1 was positive for HLA-B51, which suggested that the exacerbation with secukinumab was not associated with HLA-B51. Both patients presented with fever and high acute phase response, which were highly suggestive for gastrointestinal involvement. In patient 1, evidence for gastrointestinal involvement after secukinumab use was present. Unfortunately, although planned we failed to do a control colonoscopy in the second patient in whom acute phase response decreased immediately after steroids.

For decades, there has been a lumper’s attempt to cluster BS with seronegative spondyloarthritides [7]. More recently, the IL-17A pathway was also considered important to tie BS with this group of diseases [8]. Our observation of two patients, the unfruitful experience with secukinumab use in CD [4, 5], a condition with which BS has many shared features, and the findings from the SHIELD study [6] indicate that we should be more cautious in our conclusions about the role of IL-17A in the disease mechanisms of BS. After all, we might even consider it is somewhat protective in BS. BS has a very involved morbid entity, and we maintain splitting rather lumping should be the way forward in deciphering it [7].
CONFLICT OF INTEREST STATEMENT
None of the authors had any financial interest or any conflict of interest with regard to this work.

FUNDING
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ETHICAL APPROVAL
Ethical approval was not required because of the nature of data collection.

CONSENT
Informed patient consent was obtained from both patients and the documents are available from the authors.

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