CASE REPORT

Reactivation of Tuberculosis in Patients with Ankylosing Spondylitis on Tofacitinib Therapy

Parminder Singh[1], Manavdeep Kaur[2], Dinesh Kumar[3], Harsimran Kaur[4]

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Abstract

Ankylosing spondylitis (AS) is an inflammatory disorder affecting the axial skeleton and peripheral joints. It is immune-mediated common in the second and third decades having symptoms such as sacroiliitis, synovitis, and difficulty in movement of the spine. It is treated with non-steroidal anti-inflammatory drugs (NSAIDs), JAK 2 inhibitors, and other biologicals such as infliximab and etanercept. This is the case report of a 24-year-old male student who presented with lower backache, and morning stiffness which improved with activity. On investigation, his HLA B 27 was positive and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were raised. He was treated with tofacitinib for 1 year, later he developed pott's spine as its side effect. This case report represents the rare side effect of tofacitinib as pott's spine.

Keywords: Ankylosing spondylitis, Pott's spine, Tofacitinib.

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Case Description

A 24-year-old male, student by profession, presented with a complaint of lower back pain from 1 year, insidious in onset, the pain was moderate-to-severe in intensity, and morning stiffness was present, which improves with activity but reoccurs again when the patient was not working. He often experienced pain during night. He also had a loss of spinal mobility and limitation of anterior and lateral flexion and extension of the lumbar spine, along with bony tenderness and left eye pain, photophobia, and lacrimation. Magnetic resonance imaging (MRI) lumbosacral spine was done which showed bone marrow edema, enthesitis and sacroiliitis. Also, HLA B27 was found to be positive and ESR and CRP were raised. Rheumatoid factor, anti-CCP and ANA were negative. He was started on tofacitinib therapy 5 mg twice a day, after which he started improving and got relief from severe pain and improved symptomatically. However, after 1 year of therapy, he started complaining of lower back pain again. The MRI 2D spine was done and findings were suggestive of pott's spine [Tuberculosis (TB) of spine] and Montoux test was also positive. No other symptom of TB was there such as cough, fever, and weight loss. Tofacitinib was discontinued and anti-tubercular treatment (ATT) was started which was given for 6 months and he started improving gradually. Then, instead of any other biologicals, he was started on NSAIDs (Fig. 1).

Discussion

Ankylosing spondylitis is an inflammatory disorder of unknown cause which affects axial skeleton, peripheral joints, and extra-articular structures. It shows correlation with HLA B27. Sacroiliitis is an early manifestation of AS. In AS, synovitis and myxoid marrow represent the earliest changes followed by pannus and subchondral granulation tissue.[1,2] Marrow edema, enthesitis, synovitis, and chondroid differentiation are also found (Table 1).

In pathogenesis of AS, immune-mediated evidence is there, which is suggestive of autoinflammatory pathogenesis. Tumor necrosis factor-α (TNF-α) or interleukin 17 (IL-17) plays central

[1–4]Department of Medicine, Sri Guru Ram Das University of Health Sciences, Amritsar, Punjab, India

Corresponding Author: Manavdeep Kaur, Department of Medicine, Sri Guru Ram Das University of Health Sciences, Amritsar, Punjab, India, Phone: +91 9464823105, e-mail: mdeep2k7@gmail.com

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Fig. 1: The T2-weighted MRI dorsal spine shows pott's spine at D12 vertebrae

Table 1: The AS criteria for classification of axial spondyloarthritis

Sacroiliitis on or imaging plus ≥1 SpA feature	*HLA-B27 plus ≥1 SpA features*
Sacroiliitis on imaging • Active (acute) inflammation on MRI highly suggestive of SpA-associated sacroiliitis and/or • Definite radiographic sacroiliitis according to modified New York criteria	SpA features • Inflammatory back pain • Arthritis • Enthesitis (heel) • Anterior uveitis • Dactylitis • Psoriasis • Crohn's disease or ulcerative colitis • Good response to NSAIDs • Family history of SpA • HLA-B27 • Elevated CRP

AS, ankylosing spondylitis

role in immune pathogenesis of AS. Other gene related to TNF pathway[3] shows association with AS, including TNFRSF1A, LTBR, and TBKBP1. At least five genes in IL-23/IL-17 pathway show association with AS, including IL-23R, PTER 4, IL-12B, CARD9, and TYK 2. Also, IL-23 and IL-17 are elevated in patients with AS. The HLA B27 plays direct role in pathogenesis of AS. In patient with AS, NSAID is a first line pharmacologic therapy. Patient with AS treated with Infliximab (chimeric human/mouse anti-TNF-α–monoclonal antibody), etanercept (soluble p75 TNF-α receptor–IgG fusion protein), adalimumab or golimumab (human anti-TNF–monoclonal antibody, or certolizumab pegol (humanized mouse anti TNF-α–monoclonal antibody) have shown rapid, profound, and sustained reduction. In all clinical and laboratory measures of disease activity, tofacitinib also shows great efficacy in treatment of AS. In our patient, tofacitinib was started in place of etanercept. Tofacitinib is Janus kinase 2 (JAK-2) inhibitor. Janus kinase and signal transducer and activator of transcription (STAT) molecules are central transmitters of pro- (IL-2, -7, -12, and -23) and anti-inflammatory (IL-10) signals in immune regulation. The IL-17 and IL-23 is important in pathogenesis of SpA and is partly controlled by JAK. Janus kinase enzymes are intracellular enzymes which consist of a group of intracellular tyrosine kinase that transmit signals from cytokine or growth factor receptor interactions on the cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylates and activators of transcription STAT which modulates intracellular activity including gene expression. It is also involved in synthesis of IL-23/IL-17 pathway. Tofacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. Inhibition of JAK reduces production of and modulates pro inflammatory cytokines. As Tofacitinib is immunomodulator, it has various side effects such as nasopharyngitis which is a primary side effect. Other less common side effects are angioedema, bone marrow suppression, gastrointestinal (GI) perforation, herpes zoster, hepatitis B reactivation, TB reactivation, interstitial Lung disease, lymphoma.[4] Our 24-year-old male patient was taking tofacitinib 5-mg twice a day from past 1 year, later he developed reactivation of TB as pott's spine, and tofacitinib was discontinued and ATT was started. He was started on NSAIDs instead of any other immunomodulator. After completion of ATT, patient's backpain got relieved and is now on NSAIDs for AS. Since AS is immune-mediated disease and biologicals are given, it can cause various side effects such as TB.[5] So, patient should be treated along with various side effects kept in mind after initiation of treatment.

Conclusion

Ankylosing spondylitis is immune-mediated disorder in which IL-23 and IL-17 are raised. Biologicals are given which has various side effects as it suppresses the immune system like reactivation of TB, herpes zoster, bone marrow suppression, and malignancy. Patient on these therapies should be on regular follow-up to avoid adverse effects or for detection of such side effects earlier, so that they can be treated and treatment will be modified if required.

References

1. Cantini F, Niccoli L, Goletti D. Adalimumab, etanercept, infliximab, and the risk of tuberculosis: data from clinical trials, national registries, and postmarketing surveillance. J Rheumatol Suppl 2014;91:47–55. DOI: 10.3899/jrheum.140102.
2. Souto A, Maneiro JR, Salgado E, et al. Risk of tuberculosis in patients with chronic immune-mediated inflammatory diseases treated with biologics and tofacitinib: A systematic review and meta-analysis of randomized controlled trials and long-term extension studies. Rheumatology 2014;53(10):1872–1885. DOI: 10.1093/rheumatology/keu172.
3. Cantini F, Niccoli L, Goletti D. Tuberculosis risk in patients treated with non-anti-tumor necrosis factor-α (TNF-α) targeted biologics and recently licensed TNF-α inhibitors: Data from clinical trials and national registries. J Rheumatol Suppl 2014;91:56–64. DOI: 10.3899/jrheum.140103.
4. McVeigh CM, Cairns AP. Diagnosis and management of ankylosing spondylitis. BMJ 2006;333(7568):581–585. DOI: 10.1136/bmj.38954.689583.DE.
5. Hammitzsch A, Lorenz G, Moog P. Impact of Janus kinase inhibition on the treatment of axial spondyloarthropathies. Front Immunol 2020;11:591176. DOI: 10.3389/fimmu.2020.591176.