CASE REPORT

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A Case of Psoriatic Arthritis Using Anti-Tumor Necrosis Factor-Alpha Diagnosed with Tuberculosis Lymphadenitis Under Preventive Treatment

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ABSTRACT Psoriatic arthritis (PsA) is a multisystemic inflammatory condition that can lead to disability and impaired quality of life. Anti-tumor necrosis factors (TNFs) are approved drugs for PsA with good control of symptoms and inhibition of disease progression. Latent tuberculosis infection reactivation is one of the important complications observed after treatment with TNF-α inhibitors. Here we present a case of PsA that was treated with 2 different types of anti-TNF drugs who was diagnosed with tuberculosis lymphadenitis even though receiving a 9-month preventive therapy. This case report emphasizes the importance of close follow-up and careful examination of the patients with rheumatological diseases using anti-TNF treatment.

Keywords: Psoriatic arthritis; tuberculosis; tumor necrosis factor inhibitors

Psoriatic arthritis (PsA) is inflammatory arthritis belonging to a group of rheumatological diseases classified as spondyloarthritis. PsA possesses a wide spectrum of clinical manifestations and is shown to be associated with various comorbidities.[1] It is well known that PsA may manifest by peripheral articular and periarticular involvement (arthritis, tenosynovitis, dactylitis, enthesitis), axial involvement (spondylitis), skin and nail psoriasis.[2]

There are different therapeutic approaches including biological therapies that target specific molecules linked to the pathogenesis of psoriasis and PsA. Currently, biological therapies directed against tumor necrosis factor-alpha (TNF-α) have significantly improved the treatment of psoriasis and PsA.[2]

On the other hand, latent tuberculosis infection (LTBI) reactivation is one of the important complications observed after biological treatments, especially TNF-α inhibitors. Therefore, various guidelines have been published to be followed in the screening of LTBI before usage of biological treatments.[3]

Here we present a case of PsA who was diagnosed with tuberculosis (TB) lymphadenitis after anti-TNF treatment even though receiving a 9-month preventive therapy for LTBI.

CASE REPORT

A 68-year-old female patient, who had a diagnosis of psoriasis for 30 years, was admitted to the department of rheumatology with complaints of back, waist and hip pain. She described the morning stiffness lasted for 2-3 hours. On physical examination, shoulders, elbows, vertebrae, sacroiliac joints, wrists and ankles were sensitive, hip range of motion was severely restricted. Both wrists were tender, hot, and swollen. Her laboratory results showed elevated acute phase

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reactants [erythrocyte sedimentation rate (ESR): 79 mm/h and C-reactive protein (CRP): 43.2 mg/L], anemia (Hgb: 11.3 g/dL) and bilateral Stage III sacroiliitis was detected on sacroiliac joint radiography confirming the diagnosis of PsA (Figure 1).

The patient was given glucocorticosteroid (4 mg/day), methotrexate 15 mg/week, sulfasalazine 2 g/day and non-steroidal anti-inflammatory drugs and followed up accordingly. In the follow-up period, leflunomide 20 mg/day was started because of sulfasalazine intolerance. In the 6th month of the treatment, anti-TNF was planned because of lack of disease control. In the family history of the patient, her mother had had TB and since the patient's image-guided radiation therapy test was positive, isoniazid (INH) therapy (300 mg/day) was initiated and at the end of the 4th week of treatment, certolizumab treatment was started. Joint and skin findings regressed remarkably and ESR, CRP levels decreased to normal. She started to have arthritis attacks again and ESR, CRP values increased at the end of the second year of the certolizumab treatment. No reason could be found to explain the exacerbation, such as infection, incorrect storage or administration of the drug or any pathological finding in physical examination. Infliximab treatment was started, considering the secondary unresponsiveness and tolerance to the drug.

The patient was evaluated by a pulmonologist and no lung pathology was detected in computed tomography of thorax. The patient, who responded rapidly and very well to infliximab, was still in clinical and laboratory remission after 3 months, but a palpable lymph node was detected in the right epitrochlear region on physical examination, and she was examined further for other enlarged lymph nodes by ultrasonography (Figure 2). Pathological lymph nodes in the bilateral cervical, left epithrochlear and right inguinal region were noted. Epitrochlear lymph node excisional biopsy was performed, first considering lymphoproliferative disease and then tuberculous lymphadenitis. The pathology was reported as necrotizing granulomatous lymphadenitis. The patient was evaluated by a pulmonologist and regarding the fact that she recieved anti-TNF treatment and other immunosuppresive drugs, she was started anti-TB treatment. After 2 months of quadruple therapy, dual (INH, RIF), therapy was continued for another 4 months. The lymphadenopathies were totally regressed as confirmed by ultrasonography. The patient did not experience joint problems until the 4th month of anti-TB treatment, but after that, the morning stiffness that lasted for one hour and the increase in the number of sensitive joints were the reasons to re-start the infliximab treatment. Currently, 300 mg infliximab treatment is continued every 8 weeks and patient is in remission as she has no complaint and laboratory findings are within normal limits.

Consent was obtained from the patient for the publication.

DISCUSSION

In our patient, the recommended treatment algorithms were followed appropriately and anti-TNF was given to the patient because low disease activity could not be achieved and the patient showed a good response

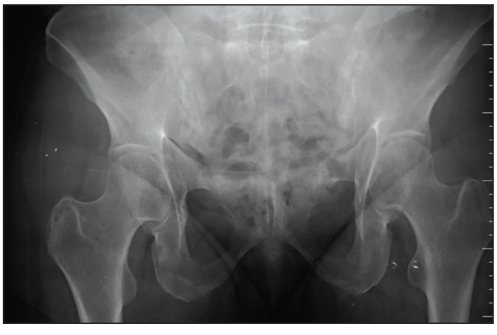

FIGURE 1: Bilateral Stage III spondyloarthritis was detected on sacroiliac joint radiography.

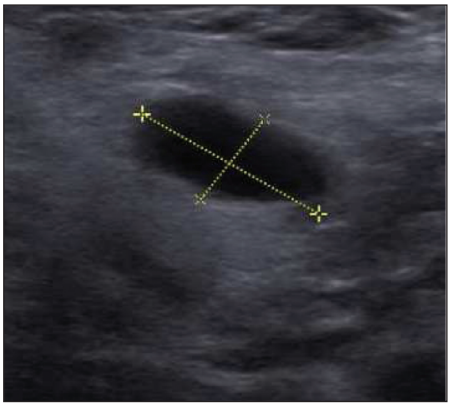

FIGURE 2: The ultrasonography imaging of the enlarged right epitrochlear lymphadenopathy.

to both biological drugs for a long time. Because of the risk of TB infection while using anti-TNF treatments, the patient was evaluated by the chest diseases department before anti-TNF treatment was started and before each prescription was renewed including the switch made to a new biological drug.

The presence of necrotizing granulomas in the pathological evaluation might be seen in other diseases like sarcoidosis and Kikuchi disease as well, but the pathologist especially pointed out that the patient should be searched for TB and regarding the fact that Turkey has still active TB cases, treatment was started immediately. The response to treatment supports the approach and since immunosuppressives were already given to the patient when the lymphodenopathies occured, sarcoidosis was ruled out.

Treatment of LTBI before anti-TNF-α therapy sometimes might not be enough to prevent TB occurrence. There are some reports from different countries including Turkey that have shown active TB cases even after receiving INH prophylaxis treatment.[4-6] Behçet`s disease patients were shown to be at a higher risk for both pulmonary and extrapulmonary TB and usage of infliximab together with inappropriate or insufficient INH treatment were independent risk factors for TB development.[6,7]

There are different types of anti-TNF treatments including infliximab, adalimumab, etanercept, golimumab and certolizumab.[8] There have been studies reporting different degrees of risk regarding TB among the anti-TNF agents, mainly infliximab and it has been shown that especially a higher risk is seen in infliximab usually at the early period of the treatment.[9] The switch of anti-TNF agent might have added a higher risk for TB development in our case.

Another reason for TB infection even though receiving INH for 9 months might be explained by possible resistance of the mycobacteria against INH which we could not examine as the specimen was not sent for culture but only for the pathological examination. Yet the patient could give a good response to the anti-TB treatment and remission of the findings were noted even though infliximab treatment was restarted.

An important factor that might have a role in increasing the risk of TB infection in patients receiving the anti-TNF treatment is the combination of these drugs with other immunosuppressives like methotrexate, azathioprine or corticosteroids as in our case.[10] Another possible cause might be a de-novo infection which can not be prevented with INH prophylaxis received before.

Studies have shown that anti-TNF re-initiation is safe and that can be started as soon as after 2 months of anti-TB treatment and the recurrence of TB is very low.[10,11] In accordance with the literature, the case presented also did not show recurrence of TB and the anti-TNF treatment was started after a 4-month period.

Taking into consideration the incidence of TB infection in specific regions, especially in countries such as Turkey where TB is still a public health problem, this case is important and emphasizes that the patients should be very closely followed up and carefully examined during the whole time of anti-TNF treatment.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Günay Şahin Dalgıç;* ***Control/Supervision:*** *Günay Şahin Dalgıç, Dorina Esendağlı, Şule Akçay, Ahmet Eftal Yüce;* ***Data Collection and/or Processing:*** *Günay Şahin Dalgıç;* ***Analysis and/or Interpretation:*** *Günay Şahin Dalgıç, Dorina Esendağlı;* ***Writing the Article:*** *Günay Şahin Dalgıç, Dorina Esendağlı;* ***Critical Review:*** *Şule Akçay, Ahmet Eftal Yüce.*

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