Reactivation of latent tuberculosis associated with methotrexate therapy: A Case Report

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ABSTRACT Tuberculosis is highly prevalent in developing the world. Post-primary tuberculosis occurs in the setting of depressed immunity commonly affecting the lungs. Reactivation of tuberculosis concomitantly at different non-pulmonary sites is very uncommon. Here we report an immunocompetent male with rheumatoid arthritis presented with reactivation of cutaneous and meningeal tuberculosis while on low dose methotrexate therapy. The case report highlights the fact that the treating clinician should be vigilant enough to suspect reactivation of latent tuberculosis even with non-biological disease-modifying anti-rheumatoid drugs therapy in the tropical world.

KEYWORDS Tuberculosis, rheumatoid arthritis, methotrexate, cutaneous abscess

Introduction

Tuberculosis (TB), an ancient infectious disease is characterized by caseating granuloma formation in response to mycobacterial infection in the pulmonary and the extrapulmonary organs. Methotrexate is the first line non-biological disease-modifying anti-rheumatoid drug (DMARD) which has an extremely rare association with the activation of latent TB. This case report illustrates a rare association of concomitant culture positive cutaneous and meningeal TB in a patient with seropositive rheumatoid arthritis receiving low dose methotrexate monotherapy for a period three years duration.

Case presentation

A 28-year-old farmer presented with inflammatory type, polyarthritis involving large and small joints of hands and upper limb for two months duration. He had high inflammatory markers (ESR-100mm/1st hour, C-reactive protein 75mg/dL) and positive rheumatoid factor and Anti-cyclic citrullinated peptide (ACCP) level with the negative antinuclear factor. His hand x-ray showed erosive arthritis suggestive of rheumatoid arthritis. His screening for tuberculosis including chest X-ray, sputum acid-fast bacilli and Mantoux test was negative. Subsequently, he was diagnosed with seropositive rheumatoid arthritis and was treated with methotrexate and was in remission for the last three years. While in good compliance and clinic follow up, he developed an abscess in the dorsum of first interdigital space of the right hand which responded poorly to routine antibiotic treatment.

He had high inflammatory markers (ESR-90mm/1st hour, C-reactive protein 85mg/dL). The prompted a TB screening including chest X-ray, Mantoux (8mm), and sputum for acid-fast bacilli which were negative. His high resolution computed tomography of the chest was not significant. Her vasculitic and autoimmune screening were negative. A sample of pus was sent for bacterial and mycobacterial culture. After a couple of weeks of the above presentation, he was readmitted with an altered level of consciousness, fever and photophobia. On examination, he had significant neck stiffness; however, he did not have any focal neurological signs. His magnetic resonance imaging (Figure 1) was favoured the diagnosis of tuberculosis meningitis and subsequently confirmed by analysis of cerebrospinal fluid including high titre of Adenosine Deaminase (60 IU/L), positive polymerase chain reaction and a positive mycobacterium acid-fast bacilli culture. The mycobacterium cultures of skin swabs were also positive. He received combined therapy category I antituberculosis therapy for six months with steroids for six weeks duration. He improved clinically and recovered without any neurological deficit and followed up at the medical clinic.

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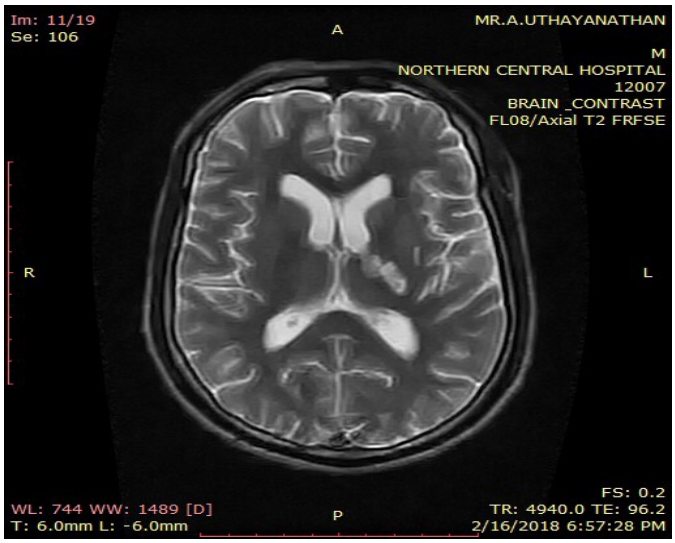

Figure 1: The magnetic resonance imaging showed the basal meningeal enhancement and vasculitic infarction of thalamus, basal ganglia in favoured the diagnosis of tuberculosis meningitis.

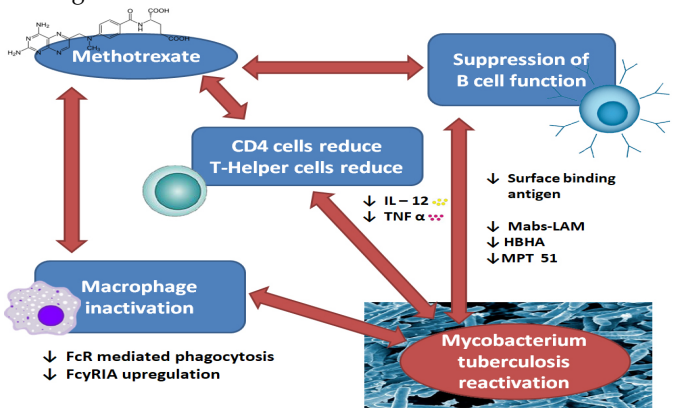

Figure 2: Mechanism of reactivation of latent tuberculosis associated with methotrexate therapy..

Discussion

TB is a global epidemic burden with a high prevalence among developing countries. Pulmonary TB (90%) is common than extrapulmonary TB (10%). Extrapulmonary TB commonly affects lymph nodes (35%), pleura (20%), bone and joints(10%), genitor-urinary tract(9%), meninges (5%), abdomen (3%,) and rarely skin[1]. The cutaneous TB can be acquired endogenously or exogenously [2]. Diabetes mellitus, retroviral infection, malignancy and immunosuppressive therapy are identified risk factors for cutaneous reactivation.

The incidence of extrapulmonary tuberculosis is rising due to impaired immunity and multidrug-resistant organisms. Immunocompromised patients have high mortality and diagnostic challenges related to TB. Immunosuppression caused by drugs is a well-known cause of latent TB reactivation. Immunomodulators used in the treatment of rheumatoid arthritis is one of the examples [3]. It is a well-known fact that biological therapy has significantly associated with reactivation of latent TB. Methotrexate monotherapy, the conventional initial choice of DMARD at lower dosage rarely associated with reactivation of latent TB [4].

Methotrexate, a structural analogue of folate which competitively inhibits dihydrofolate reductase enzyme and increases the concentration of extracellular adenosine which is a strong anti-inflammatory molecule. It also reduces the proinflammatory cytokines, intracellular adhesion from T Cells and repression the clonal growth of B and T cells (Figure 2). However, it has little effect on CD4/CD8 ratio [5]. This patient with seropositive rheumatoid arthritis had concomitant culture positive cutaneous and meningeal TB who was treated with methotrexate for three years duration. This case emphasizes that a strong clinical suspicion of any disseminated infection needs to be considered in any patient with immunosuppression either due to disease or medications.

Competing Interests

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