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Post coronavirus-disease-vaccination immune reconstitution inflammatory syndrome in tuberculosis treatment: a case report

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Abstract

Background Tuberculosis immune reconstitution inflammatory syndrome is an uncommon condition caused by excessive immune response against *Mycobacterium tuberculosis*. We report on a case which may have been precipitated by coronavirus disease messenger ribonucleic acid vaccine booster.

Case presentation A 47-year old Indian man developed reactivation tuberculosis in the cervical lymph nodes in the setting of immune suppression caused by tumor necrosis factor inhibitor adalimumab. The symptoms improved with starting antituberculous therapy, but 5 days after receiving a coronavirus disease booster messenger ribonucleic acid vaccine, he had recurrence of severe constitutional symptoms. After a detailed evaluation, he was diagnosed with immune reconstitution inflammatory syndrome and was successfully treated with high-dose steroid therapy, which was weaned off over several weeks.

Conclusion Immune reconstitution inflammatory syndrome should be considered as a differential in patients who develop paradoxical worsening of symptoms with antitubercular therapy in the setting of immune reconstitution. Hyperactive immune response after infection or messenger ribonucleic acid vaccine booster may have contributed to the development of immune reconstitution inflammatory syndrome syndrome in this patient.

Keywords Tuberculosis immune reconstitution inflammatory syndrome, mRNA COVID vaccination, Adalimumab, Case report

Background

Tuberculosis (TB) immune reconstitution inflammatory syndrome (IRIS) is an abnormal, excessive immune response against living or dead *Mycobacterium tuberculosis*. Paradoxical worsening of tuberculosis has been described after introduction of antituberculosis drugs. We report on an unusual presentation of TB IRIS in the setting of antitumor necrosis factor (TNF) therapy and messenger ribonucleic acid (mRNA) coronavirus disease 2019 (COVID-19) vaccination. We also review pertinent management issues.

Case report

A 47-year-old Indian man with no past medical history from India developed pain and weakness in his interphalangeal and metacarpal-phalangeal joints. On the basis of his symptoms, laboratory testing, and imaging of his hands, he was diagnosed with seronegative rheumatoid arthritis. He was started on biologic treatment with anti-TNF agent adalimumab and methotrexate. Before starting treatment, he had a chest X-ray, which was normal and a test for *M. tuberculosis* using an interferon gamma release assay, which was also negative. He received two doses of Pfizer mRNA vaccine 4 weeks apart

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without any complications. Then, 6 months after starting adalimumab, he developed constitutional symptoms including headaches, nocturnal sweats, and low-grade fever. He then developed neck pain and was noted to have bilateral cervical adenopathy noted on exam. Computed tomography (CT) scan of the neck confirmed bilateral cervical adenopathy (Fig. 1). His immunosuppressive therapy was stopped. A cervical lymph node biopsy was performed. The histology results were strongly positive for acid-fast bacilli. A diagnosis of tuberculous lymphadenitis was made, and he was started on a four-drug regimen with Isoniazid, Rifampin, Pyrazinamide and Ethambutol. Within 5 days of starting the regimen, he noted a significant improvement in his symptoms. The mycobacterial cultures revealed that the bacillus was susceptible to all the antituberculous drugs. About 2 weeks after starting his antitubercular therapy, he received a dose of previously scheduled COVID mRNA vaccine (third dose of Pfizer mRNA), and 5 days after receiving the vaccine, he developed severe constitutional symptoms including fever, chills, and excessive diaphoresis. He was admitted to the hospital for further evaluation. His exam was unremarkable for any new finding. He was ruled out for sepsis with negative blood cultures and serological testing. Inflammatory markers including ESR and C-reactive protein (CRP) were elevated at 35 mm/hour and 5.33 mg/l. He was diagnosed with antitumor-necrosis-factor-alpha-induced tuberculosis-associated IRIS. Treatment was started with intravenous methylprednisolone 80 mg every 8 hours, with resolution of his symptoms. He was transitioned to oral prednisolone 100 mg twice a day and discharged home 5 days later. His oral steroids were gradually weaned off over the next 3 months. He finished a 12-month course of antitubercular therapy. He had had no recurrent symptoms at 18-month follow-up and was discharged from the infectious disease clinic. He was able to resume therapy with adalimumab after 4 months of antitubercular therapy.

The diagnosis of TB-IRIS is based on initial improvement of TB-related symptoms with initiation of TB therapy, paradoxical deterioration of TB related symptoms during TB therapy, and exclusion of other possible causes of clinical deterioration [1]. This patient fulfilled all these criteria. His immune response after receiving COVID vaccine booster may have further contributed to activation of his immune system, resulting in presentation with IRIS.

Discussion

Antitumor-necrosis-factor-alpha-induced tuberculosis IRIS was first described in 2005 [2]. The pathogenic mechanism of anti-TNF-alpha-induced IRIS is not known for certain. However, it may occur as a result of reconstituted immune response against *M. tuberculosis*, causing an uncontrolled inflammatory reaction [3]. Appropriate treatment of anti-TNF alpha TB IRIS is controversial. Previous case reports have shown that this condition may respond to treatment with high-dose

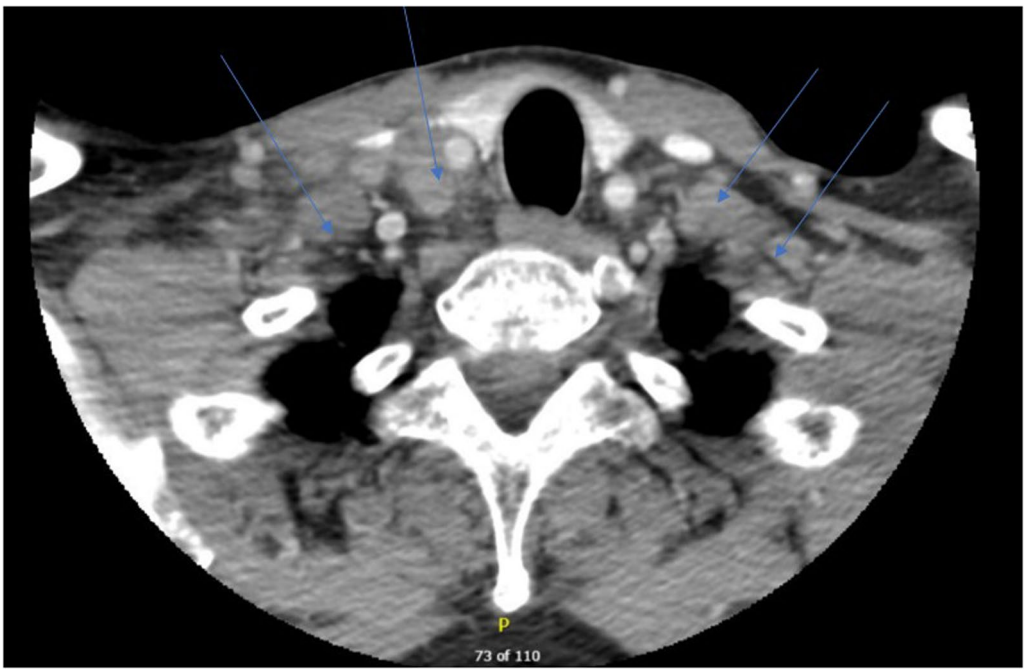

Fig. 1 Arrows pointing to enlarged cervical lymph nodes

steroids [4]. However, there is currently a lack of consensus regarding the use and dosage of steroid therapy for the treatment of anti-TNF-induced TB IRIS [5]. This patient was managed successfully with use of steroid therapy, which was tapered off over a period of 3 months. Other reports have suggested using TNF alpha agonists with satisfactory antitubercular therapy to attenuate the inflammatory response with IRIS [6]. A total of 4 months after initiating antitubercular therapy, the patient was able to restart his treatment with TNF alpha inhibitor for rheumatoid arthritis without any significant sequela until 1 year of follow-up after initial presentation. Vaccination with mRNA vaccine for COVID may have stimulated his immune system. There are several reports of mRNA vaccine causing autoimmune disease or flare ups of autoimmune disease [7]. There are also reports of mRNA vaccines precipitating immune-response-related rejection phenomenon in transplant recipients by stimulating the natural immune responses [8]. We strongly suspect that the immune response precipitated by the mRNA booster vaccine may have resulted in the development of the IRIS syndrome in this patient.

Conclusion

IRIS should be considered as a differential in patients who develop paradoxical worsening of symptoms with antitubercular therapy in the setting of immune reconstitution. Hyperactive immune response after mRNA vaccine booster may have contributed to the development of IRIS syndrome in this patient.

Patients initiating antitubercular therapy should be monitored closely during the initial period of therapy, as they may be at an increased risk of developing IRIS in response to any inflammatory event such as a vaccination or an infection.

Abbreviations

TB	Tuberculosis
IRIS	Immune reconstitution inflammatory syndrome
TNF	Tumor necrosis factor
mRNA	Messenger ribonucleic acid

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Author contributions

AM completed the manuscript for the case report. AP was a major contributor to the manuscript. Both authors have read and approve the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval and consent to participate

Ethical approval is not required for this type of study. A written consent was obtained from the patient.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal.

Competing interests

The authors declare they have no competing interests.

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