Journal of Enterocolitis

Case Report

Tuberculous Pericarditis in a Patient with Crohn's Disease After Anti-tumor Necrosis Factor-Alpha Therapy

Mehmet Oğuzcan Alada[1], Aslı Çiftcibaşı Örmeci[2], Ayşenur Yılmaz[1], Bilger Çavuş[2], Aysun Yakut[2], Filiz Akyüz[2], Sabahattin Kaymakoğlu[2]

[1]Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul, Turkey
[2]Department of Gastroenterology, İstanbul University, İstanbul Faculty of Medicine, İstanbul, Turkey

Cite this article as: Alada MO, Çiftcibaşı Örmeci A, Yılmaz A, et al. Tuberculous pericarditis in a patient with crohn's disease after anti-tumor necrosis factor-alpha therapy. *J Enterocolitis.* 2022;1(1):23-25.

Corresponding author: Aslı Çiftcibaşı Örmeci, e-mail: aslic79@yahoo.com.tr

Received: April 11, 2022 **Accepted:** April 28, 2022

DOI:10.5152/Jenterocolitis.2022.220507

Abstract

This report describes a 54-year-old female, who experiences tuberculous pericarditis after using tumor necrosis factor-alpha blocker for her diagnosis of Crohn's disease. Following the diagnostic work-up, anti-tbc treatment was started and she had a very good response after 1 month. This case emphasizes the importance of considering the diagnosis of tuberculous pericarditis in patients who use tumor necrosis factor-alpha antagonists, even though the latent tuberculosis infection screening was negative at the beginning.

Keywords: Crohn's disease, infliximab, pericarditis, tuberculous, tuberculosis, tumor necrosis factor inhibitors

INTRODUCTION

The incidence of opportunistic infections has increased with the use of tumor necrosis factor-alpha (TNF-α) blocking agents in various immune-mediated diseases such as rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, and psoriasis.

Mycobacterium tuberculosis is one of the most important opportunistic microbial agents. Therefore, tuberculosis (TB) screening is mandatory before starting TNF-α antagonists due to the risk of reactivation of latent TB during anti-TNF treatment use. Recent studies have shown that some inflammatory bowel disease patients (1.65%) may still develop TB even after latent tuberculosis infection (LTBI) screening before the use of TNF-α antagonists.[1] Aside from the classic pulmonary TB, patients who use TNF-α antagonists are also prone to develop extra-pulmonary TB.

Pericarditis is one of the important extra-pulmonary presentations of the TB infection. Because of its late diagnosis rate, it may result in complications such as constrictive pericarditis, cardiac tamponade, and increased mortality.

In this report, we will discuss a case who was diagnosed with tuberculosis pericarditis after TNF-α antagonist use.

CASE PRESENTATION

A 54-year-old woman, a housewife, was diagnosed with ileocolonic-type Crohn's disease in April 2008, and treatment was started. Initially, she was treated with budesonide for remission induction, followed by azathioprine 2 mg/kg therapy. She was in remission for 12 years. In 2020, the patient had abdominal pain and subileus attacks. In abdominal computerized tomography (CT), we detected an increase in wall thickness along the ileum starting from the terminal ileum.

The decision to start anti-TNF therapy was made considering active disease with abdominal pain, subileus attacks, and the CT findings. Comprehensive history, tuberculin skin test (TST), chest x-ray, and quantiferon test were evaluated before starting anti-TNF therapy. Tuberculin skin test was negative, chest x-ray was normal, and quantiferon-TB gold test was negative. Before starting anti-TNF therapy, there was no need for isoniazid (INH) prophylaxis. We started infliximab (IFX) therapy with the dose of 5 mg/kg.

At the fifth month of IFX treatment, she was admitted to the emergency department with poor appetite, malaise, fever, 10 kg weight loss, and night sweats. She also had progressive exertional dyspnea and anterior chest pain for 2 days. On physical examination, she was afebrile, arterial pressure was 90/60 mmHg, and heart rate was 100/min. Pulsus paradoxus and jugular vein engorgement were seen in inspection, and soft heart sounds were heard in cardiac auscultation. Her oxygen saturation was 92%, the respiratory rate per minute was 20-22, and the respiratory sounds were decreased, more prominently on the right. Gastrointestinal system examination was normal. Laboratory tests revealed hemoglobin of 12.4 g/dL,

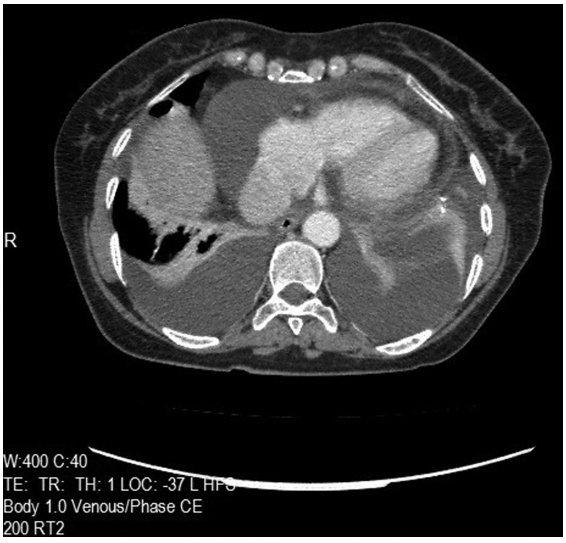

Figure 1. Thorax computerized tomography shows bilateral pleural effusion and pericardial effusion.

white blood cell count of 17 000/mm^3 with polymorphs of 60% and lymphocytes of 37%, erythrocyte sedimentation rate of 38 mm/h, C-reactive protein level of 292 mg/L (normal <5 mg/L), and an elevated ferritin level of 900 ng/mL. Electrocardiography (ECG) showed low voltage complexes with sinus tachycardia. Thorax CT showed a large pericardial effusion with pericardium contrast enhancing but no pulmonary opacities (Figure 1). A transthoracic ECG confirmed pericardial tamponade. She proceeded to undergo pericardiocentesis with 2000 mL of blood-stained fluid removed from her pericardium. The results of effusion analysis were total protein=5.1 mg/dL, leukocytes/Ml=800 (90% lymphocytes), glucose=42 mg/dL, and an lactat dehydrogenase (LDH)=1100 mg/dL. Both pericardial and pleural fluids had exudative properties.

In the cardiology consultation, pericardiectomy was not advised as it was not anatomically suitable. In cardiac magnetic resonance imaging, thickened, fibrotic visceral and parietal pericardial layers were seen (Figure 2). Positron emission tomography (PET)-CT showed an fluorodeoxyglucose (FDG) uptake at the level of diffuse malignancy

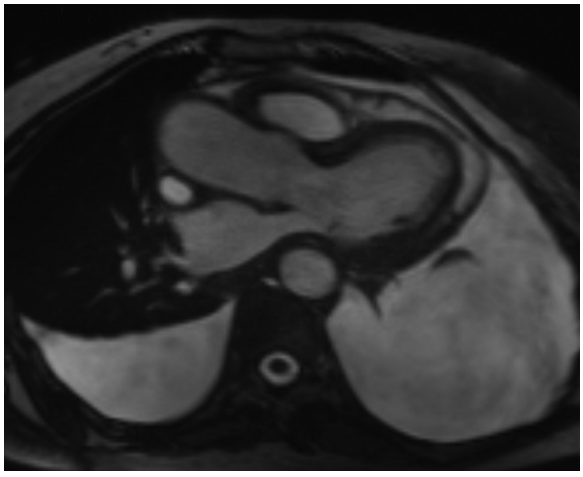

Figure 2. Cardiac magnetic resonance imaging shows 1 cm of pericardial effusion and thickened pericardial layers

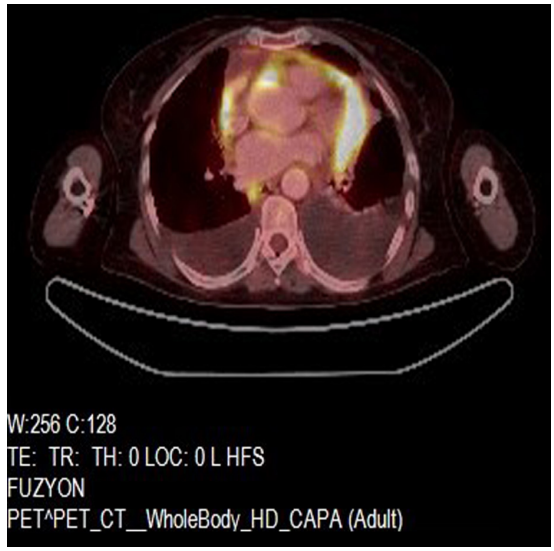

Figure 3. PET scan shows hypermetabolism starting from the base of the heart, continuous along the whole pericardium, reaching the mediastinum until the level of arcus of aorta (Standardized Uptake Value (SUV) max: 13.4).

throughout the pericardium (Figure 3). All cultures, including tbc culture, were negative. In the stains for gram, acid-fast bacillus, and fungi, no organisms were seen. The cytology to detect malignancy was negative. The blood cultures were negative. The rheumatological tests including rheumatoid factor, anti-cyclic citrullinated peptide antibody, and anti-histone antibody were negative. Adalimumab (ADA) level was 80 mg/dL in pleural effusion.

In contrast to the quantiferon test, which was performed before the initiation of anti-TNF therapy, we detected positive quantiferon test result in control. Considering the probable diagnosis of tuberculosis pericarditis, empirical tuberculosis treatment that consists of INH, rifampin, pyrazinamide, and ethambutol was started. In the follow-up after the first month of the treatment, all laboratory values became normal and the effusion was found to be regressed (Figure 4). For the patient who had tuberculosis pericarditis under anti-TNF therapy, we decided to start vedolizumab therapy.

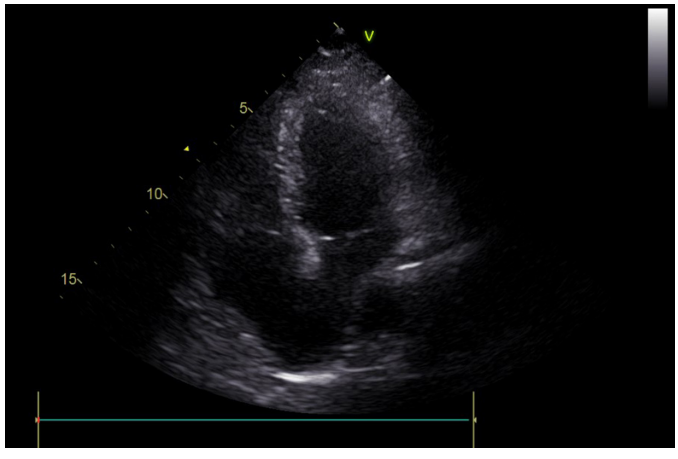

Figure 4. After 1 month of tbc treatment, cardiac echocardiography shows no effusion.

DISCUSSION

Tumor necrosis factor-alpha is a molecule that is very important in defense against many bacterial infections, including intracellular bacteria. As a result of its mechanism of action, anti-TNF treatment is suggested to increase predisposition to infectious diseases, especially TB where it would play a critical role in the host response, including granuloma integrity and control of the disease. To detect latent tbc before starting anti-TNF therapy, a physician may use a combination of patient history, chest x-ray, TST, and interferon-gamma release assays (IGRA) according to the local prevalence and national recommendations. In case of any positive result, INH prophylaxis should be started. Tuberculin skin test was negative at the beginning, but our patient was under azathioprine treatment during the tests. Past researches say that TST may be false negative in patients on corticosteroids for 1 month or thiopurines or methotrexate for 3 months.[2] The efficacy of IGRAs in the diagnosis of LTBI is better than the TST, but it also should be kept in mind that the sensitivity of IGRAs to detect LTBI is 80%.

There is a risk of TB even in patients who receive INH prophylaxis. In a case series, 175 patients who received anti-TNF in terms of latent tuberculosis reactivation were evaluated. Of these 175 patients, 60 had pretreatment testing showing latent TB infection and therefore were treated concomitantly with INH for 9 months in addition to their anti-TNF treatment. Tuberculosis reactivation occurred in 4 of these 60 co-INH/anti-TNF treated patients.[3] Therefore, we know that there is a risk of TB reactivation even if prophylaxis is used.

The diagnosis of definite tuberculous pericarditis (TP) can only be made by showing the tubercle bacilli in stained smear or culture of pericardial fluid. On the other hand, the diagnosis of probable TP can be made by showing evidence of TB in a patient with pericarditis or examining the pericardial exudate for high ADA levels or detecting good response after the use of anti-tbc drugs in a patient with pericarditis.[4] High ADA levels have been shown to be related to TP.[5]

Because that TP may result in serious complications and the early onset of anti-TB treatment can possibly prevent, it is important to consider the diagnosis of TP in patients who use anti-TNF therapy. According to previous research, it is advised that the treatment can be given empirically in the presence of strong clinical suspicion, especially in endemic regions. Although we did not show the TB bacillus in our case, with the clinical and laboratory findings (positive quantiferon testing, high ADA level in pleural fluid, etc.), we considered our patient as probable TP. The positive quantiferon test in our case, which was negative at the beginning, supported us in the diagnosis. Furthermore, we received a clinical and biochemical response to the TB treatment.

In conclusion, in the patients with pericarditis and/or cardiac tamponade who use anti-TNF and live in endemic areas, even if *Mycobacterium tuberculosis* bacilli cannot be shown with the cultures, the diagnosis of TP and empirical treatment should be considered early.

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.C.Ö., F.A., S.K.; Design – A.C.Ö., F.A., S.K.; Supervision – A.C.Ö.; Materials – M.O.A.; Data Collection and/or Processing – A.C.Ö., A.Y., B.C.; Analysis and/or Interpretation – B.C., A.Y.; Literature Review – A.C.Ö., B.C.; Writing – A.C.Ö., M.O.A.; Critical Review – F.A., S.K.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Jauregui-Amezaga A, Turon F, Ordás I, et al. Risk of developing tuberculosis under anti-TNF treatment despite latent infection screening. *J Crohns Colitis*. 2013;7(3):208-212. [CrossRef]
2. Rahier JF, Magro F, Abreu C, et al. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. *J Crohns Colitis*. 2014;8(6):443-468. [CrossRef]
3. Akyuz F, Cavus B, Iliaz Raim, et al. Inflammatory bowel disease and mycobacteria: how much can we trust isoniazid prophylaxis during anti-tumor necrosis factor therapy? *Eur J Gastroenterol Hepatol*. 2019;31(7):777-780. [CrossRef]
4. Isiguzo G, Du Bruyn E, Howlett P, Ntsekhe M. Diagnosis and management of tuberculous pericarditis: what is new? *Curr Cardiol Rep*. 2020;22(1):2. [CrossRef]
5. Chau E, Sarkarati M, Spellberg B. Adenosine deaminase diagnostic testing in pericardial fluid. *JAMA*. 2019;322(2) :163-164. [CrossRef]