

CASE REPORT



A case of Loeffler's endocarditis after initiation of adalimumab

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ABSTRACT

Tumor necrosis factor antagonists (anti-TNF) are increasingly prescribed as maintenance therapy for a variety of autoimmune conditions. Therefore, frequent monitoring and awareness of side effects are of the utmost importance. Adalimumab is known to cause peripheral eosinophilia, but there are few reports of more severe adverse events. Loeffler's endocarditis is a rare and fatal disease characterized by eosinophilic infiltration of the endomyocardium leading to fibrosis and restrictive cardiomyopathy. Herein we describe a 72 year old female on adalimumab therapy for two years for rheumatoid arthritis presenting with Loeffler's endocarditis. This case represents a rare case of Loeffler's endocarditis diagnosed rapidly and without myocardial biopsy. Early intervention is crucial in the prevention of permanent fibrosis and mortality in Loeffler's endocarditis. This case demonstrates the need for close monitoring and early recognition in patients on anti-TNF therapy.

Abbreviations: tumor necrosis factor (TNF), hypereosinophilic syndrome (HES)

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KEYWORDS

Adalimumab; Loeffler's endocarditis; tumor necrosis factor; peripheral eosinophilia; hypereosinophilic syndrome



1. Introduction

Hypereosinophilic syndrome (HES) is a rare blood disorder with the dysregulation and overproduction of eosinophils that ultimately leads to end-organ damage. The systemic response of HES includes skin, pulmonary, gastrointestinal, hematologic, and cardiac involvement and infiltration [1]. Cardiac involvement in HES, also known as Loeffler's endocarditis, is of utmost concern as it is the most common cause of morbidity and mortality in these patients [2]. Loeffler's endocarditis is characterized by eosinophilic infiltration of the endomyocardium (Figure 1), leading to fibrosis and restrictive cardiomyopathy (Figure 2). HES is reported to be a result of adverse drug reactions, parasitic infections, connective tissue diseases, lymphomas, and certain solid tumors [3]. We present a case of Loeffler's endocarditis in a patient recently started on tumor necrosis factor (TNF) antagonist therapy.

2. Case presentation

A 72 year-old female with rheumatoid arthritis on adalimumab (a TNF- α inhibitor) for two years presented with a three-week history of progressive dyspnea on exertion and intermittent low-grade fevers. Her fevers did not resolve after recent outpatient antibiotic therapy for community acquired pneumonia. Her last dose of adalimumab was two

weeks prior to onset of symptoms. Initial chest x-ray showed right middle and basilar lower lobe consolidation accompanied by a small right sided pleural effusion. Initial blood work revealed leukocytosis with profound eosinophilia of 65% with an absolute eosinophil count of 21. She was treated with broad spectrum antibiotics, including vancomycin, cefepime, and azithromycin. Her troponin I trended up slightly. This prompted an echocardiogram which revealed a normal ejection fraction with no wall motion abnormalities, but a small pericardial effusion (Figure 3). She continued to worsen on appropriate therapy, and a CT scan of the chest was obtained. This showed a moderate to large right pleural effusion with right basilar atelectasis and findings consistent with a laminar thrombus within the left ventricular apex. A repeat echocardiogram showed a filling defect in the apex, confirming left ventricular thrombus and findings suspicious for eosinophilic heart disease (as seen in Figure 4). She underwent thoracentesis and pleural fluid studies showed significant eosinophilia and an exudative effusion. A bronchoscopy with bronchoalveolar lavage revealed 88% eosinophilia without signs of infection. Fungal, parasitic, bacterial, and autoimmune workup were all negative. After a negative bone marrow biopsy and flow cytometry, she was diagnosed with adalimumab-induced eosinophilia leading to Loeffler's endocarditis. She was started

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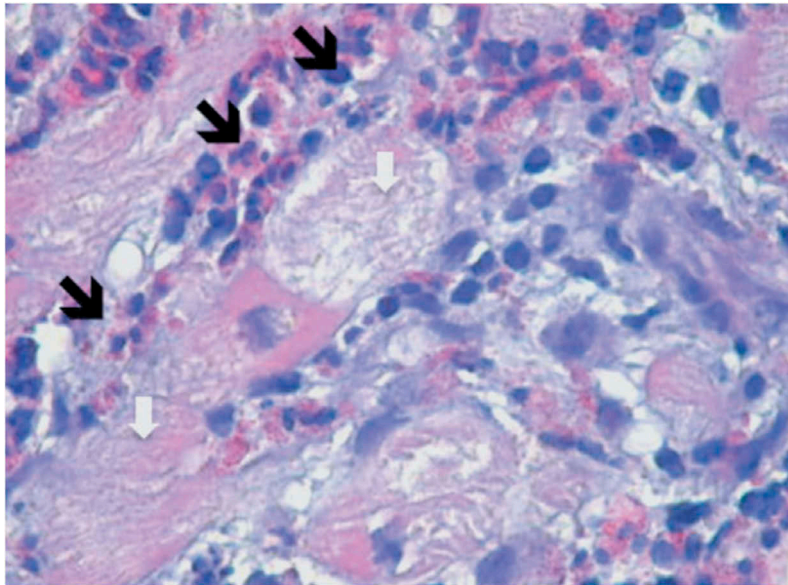


Figure 1. H&E staining of endomyocardial biopsy (acute disease) with diffuse interstitial eosinophilic infiltrate (black arrows) and areas of necrosis (white arrows).

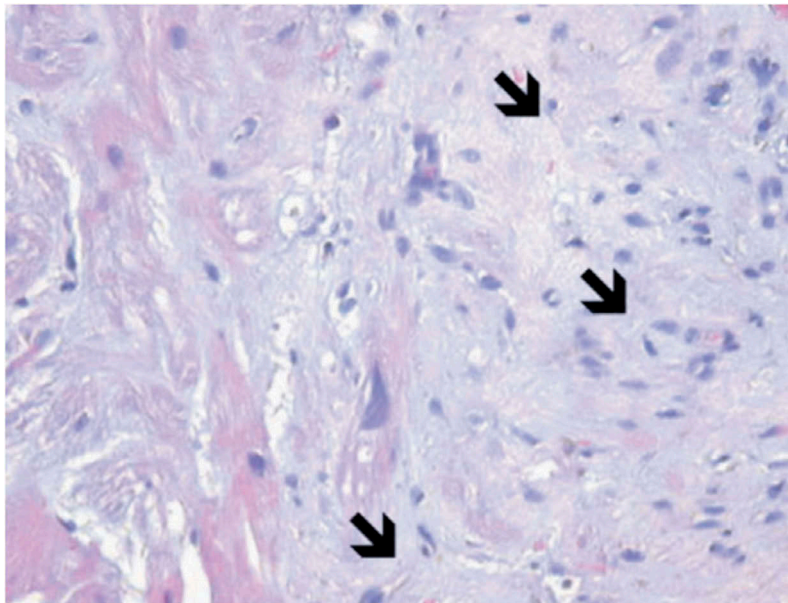


Figure 2. H&E staining of endomyocardial biopsy (end stage disease) with fibrosis.

on therapeutic heparin and high-dose prednisone for treatment of her thrombus and eosinophilic heart disease respectively.

3. Discussion

Due to the dysregulation of eosinophils in HES, there is an increased propensity for end-organ damage. This damage is mediated by proteins, such as major basic protein and eosinophilic cationic protein, that lead to endothelial damage, direct cytotoxicity, and a thromboembolic phenomenon [1]. Cytokines such as interleukins and tumor necrosis factor-beta are also thought to be involved in HES.

In Loeffler's endocarditis, cardiac involvement progresses from the acute necrotic stage to chronic damage. Chronic changes include the progression of damaged endocardium and thrombus formation to fibrotic changes in the heart. The hallmark of the final stage is the progression to restrictive cardiomyopathy [1]. As in our patient, cardiac involvement can present as acute decompensated heart failure. The diagnostic process has yet to be standardized for this disease. While endomyocardial biopsy is the gold standard, cardiovascular magnetic resonance imaging (CMR) and trans-thoracic echocardiography have also been used.

Tumor necrosis factor alpha is a proinflammatory cytokine and is active in the systemic immune response.

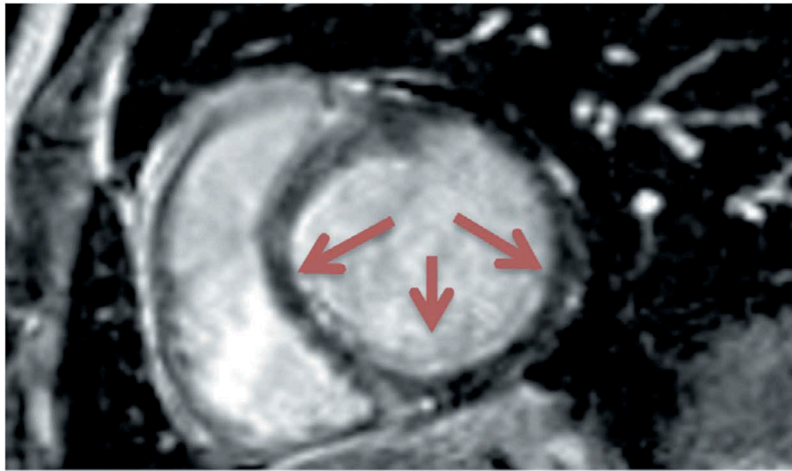


Figure 3. CMR showing endocardial involvement of inferior and inferolateral wall as well as inferior septum.

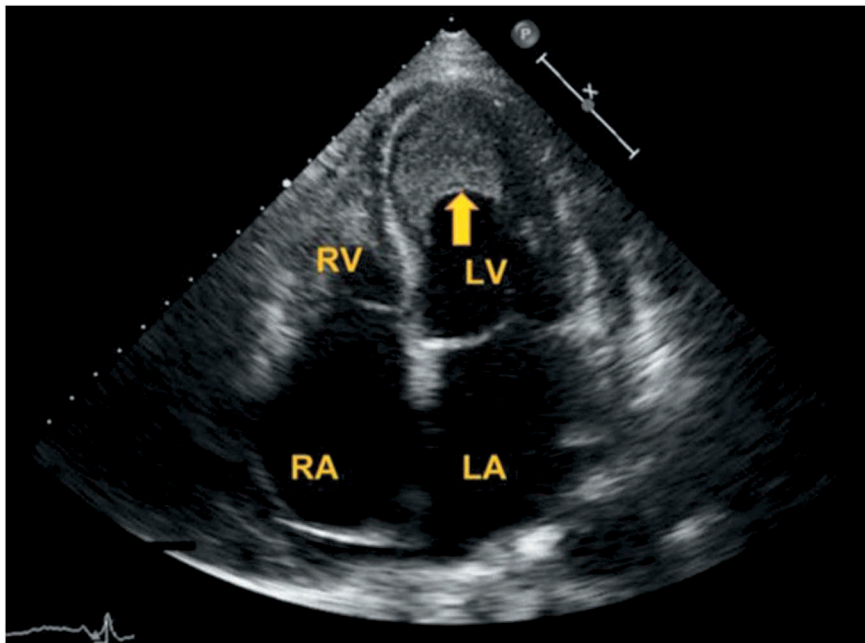


Figure 4. TTE, apical 4 chamber view with obliteration of apex of left ventricle from endocardium thickening and thrombus.

Anti-TNF therapy is used in diseases such as rheumatoid arthritis, ankylosing spondylitis, and inflammatory bowel disease. This therapy is known to be relatively safe, however reported side effects include infection, malignancy, and a variety of skin lesions [4]. Previous reports of Anti-TNF therapy associated with sarcoid-like granulomatosis have been reported with pulmonary, cutaneous, and interstitial nephritic involvement [4,5]. These findings were seen 10 to 18 months after onset of therapy with adalimumab or etanercept. Our patient began experiencing symptoms related to her cardiomyopathy almost two years after beginning therapy with adalimumab. While currently there are no consensus guidelines for treatment, prompt

administration of steroids and removal of the offending agent is recommended.

Due to the high mortality of Loeffler's endocarditis, most cases are only diagnosed on autopsy. This case represents a rare case of Loeffler's endocarditis diagnosed rapidly and without myocardial biopsy. In patient's taking adalimumab, the incidence of eosinophilia is 1%, and HES is less than 0.1% [6]. To our knowledge, this is the third report of Loeffler's endocarditis due to anti-TNF therapy. Early intervention is crucial in the prevention of permanent fibrosis and mortality. This case demonstrates the need for close monitoring and early recognition of HES, particularly with cardiac involvement, in patients on anti-TNF therapy.

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A version of manuscript has been presented as an abstract at ATS 2018: B47 (Critical Care Case Reports: Cardiovascular Diseases and Echocardiography).

Data Availability

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

Disclosure statement

No potential conflict of interest was reported by the authors.

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