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CASE REPORT

Cardiac sarcoidosis responding to monotherapy with infliximab

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Abstract Cardiac involvement is a rare and potentially life-threatening complication of sarcoidosis. We report the case of a young previously healthy woman who presented with complete atrioventricular heart block. Further evaluation revealed non-caseating granulomas in the hilar and mediastinal regions. A pacemaker was inserted, and she was treated with four doses of infliximab after she refused treatment with steroids. Rapid resolution of the pulmonary lymph nodes was documented and repeated interrogations of the pacemaker 1 year after her last infliximab infusion documented that she was in sinus rhythm. Infliximab may be considered as an alternative first-line therapy in sarcoidosis with serious organ involvement.

Keywords Heart block · Infliximab · Sarcoidosis · Tumor necrosis factor

Introduction

Cardiac involvement is a rare and potentially life-threatening complication of sarcoidosis. In very rare instances, it may be the presenting feature of the disease [1]. We present the case of a young woman who presented with complete atrioventricular heart block. She refused steroid therapy and was successfully treated with infliximab only.

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Case report

A 37-year-old woman presented to the emergency room with gradual onset of generalized weakness, shortness of breath, and easy fatigability of 1 month duration. Her evaluation revealed bradycardia with a heart rate of 39 beats per minute. Electrocardiogram showed Mobitz type II atrioventricular (AV) block, left anterior hemiblock, and right bundle branch block. Echocardiography revealed no signs of heart failure with normal size and good contractility of both cardiac ventricles. She was admitted to the coronary care unit. A computerized tomography (CT) of the chest and abdomen revealed enlarged hilar and mediastinal lymph nodes in the paratracheal, precarinal spaces, and in the paraortic space near the take-off of the superior mesenteric arteries. A bronchoscopy was done and multiple lung biopsies were taken that revealed small non-caseating granulomas. Acid fast and fungal stains were negative, and no evidence of malignancy was detected. Magnetic resonance imaging of the brain was negative. Based on the above findings, the diagnosis of sarcoidosis was made, and a trichamber pacemaker was inserted.

The patient refused to be treated with corticosteroids. Subsequently, we decided to initiate treatment with infliximab 200 mg intravenous (IV) as a monotherapy for her disease. She received 4 injections at times 0, 2, and 6 weeks, and 1 additional injection 12 weeks after the third injection. A repeat CT scan of the chest and abdomen showed a significant decrease in the size of the mediastinal and hilar lymphadenopathy. She received her last dose of infliximab 1 year ago. On her last evaluation, she was asymptomatic and pacemaker interrogation on several occasions showed that she was pacing on her own.

Discussion

We have described the first patient with cardiac sarcoidosis who presented with Mobitz type II AV block who was treated with infliximab alone with rapid resolution of the pulmonary lymphadenopathy and reversion to sinus rhythm.

Although cardiac involvement is a rare manifestation of sarcoidosis, it is one of the potentially life-threatening manifestations of this disease [1–3]. Cardiac sarcoidosis may proceed, follow or occur concurrently with involvement of the lungs or other organs. The diagnosis of myocardial involvement may be very difficult especially if cardiac dysfunction is the sole manifestation of the disease. The clinical manifestations of cardiac sarcoidosis depend on the location and extent of the granulomatous inflammation. The signs and symptoms range from benign arrhythmias, heart block, intractable heart failure, and intense chest pain to fatal ventricular fibrillation [3, 4].

In the majority of patients, the cardiac involvement may be subclinical. Silverman et al., in a clinicopathologic study of 84 unselected patients with systemic sarcoidosis, reported that myocardial granulomas were seen in 27% of these patients, moreover, 37% of the patients with cardiac involvement had no clinical signs or symptoms of heart disease [5]. Iwai et al. later reported that granulomatous lesions in the heart were found, on autopsy studies, in 24 of 123 patients (19.5%) with sarcoidosis [6]. In a more recent retrospective study on 41 cases with cardiac sarcoidosis, the average age at diagnosis was 38 years, and all patients had extra-cardiac histological proof of sarcoid tissue [1]. The presenting cardiac signs were clinical in 63% of cases and electrical in 22%. Thirty-nine patients received high dose steroid therapy, associated in 13 cases with another immunosuppressive treatment [1]. After an average follow-up of 58 months, 54% were cured from a clinical and laboratory point of view. Two patients worsened; one of them due to lack of treatment, except for a pacemaker. Based on these findings, Chapelon-Abric et al. recommended treating cardiac sarcoidosis with corticosteroids as soon as possible and to use another immunosuppressive treatment where there is an insufficient therapeutic response or where there are contraindications to corticosteroids [1].

Infliximab, a chimeric, monoclonal antibody directed against tumor necrosis factor (TNF)-α, has been approved for use in patients with rheumatoid arthritis and Crohn's disease. TNF-α is critical in the genesis and maintenance of granulomatous inflammation. In experimental models [7, 8], TNF-α had an important role in the recruitment of T cells and granuloma formation in response to mycobacterial antigens, and TNF-α reduction may prevent sarcoid granuloma formation.

Several previous case reports have described the success of infliximab in patients with sarcoidosis who are refractory to conventional therapy [9–13]. However, in all of these reports, it was used after failure of other immunosuppressive therapies. In a recent multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy of infliximab in sarcoidosis, 138 patients with chronic pulmonary sarcoidosis were randomized to receive intravenous infusions of infliximab (3 or 5 mg/kg) or placebo at weeks 0, 2, 6, 12, 18, and 24 and were followed-up through week 52. Infliximab therapy resulted in a statistically significant improvement in predicted forced vital capacity at week 24, suggesting a potential beneficial role for anti-TNF-α therapy in severe, chronic, and symptomatic sarcoidosis [14].

Infliximab, however, should be used cautiously or may be contraindicated in patients with signs of heart failure. Although initial observations suggested that inhibition of TNF-α may favorably modify the course of heart failure, a later study by Chung et al. to evaluate the efficacy and safety of infliximab in 150 patients with moderate-to-severe heart failure showed that TNF-α inhibition adversely affected the clinical condition of these patients [15].

Conclusion

We have described a patient with multisystem sarcoidosis involving the myocardium who presented with complete heart block and responded to monotherapy with infliximab. The resolution of the heart block and the regression of the pulmonary granulomas in our patient further support the use of anti-TNF-α therapies in sarcoidosis, and possibly as an alternative to steroid or other immunosuppressive treatments.

References

1. Chapelon-Abric C, de Zuttere D, Duhaut P, Veyssier P, Wechsler B, Huong DL et al (2004) Cardiac sarcoidosis: a retrospective study of 41 cases. Medicine (Baltimore) 83:315–334
2. Veinot JP, Johnston B (1998) Cardiac sarcoidosis—an occult cause of sudden death: a case report and literature review. J Forensic Sci 43:715–717
3. Sharma OP (2003) Diagnosis of cardiac sarcoidosis: an imperfect science, a hesitant art. Chest 123:18–19
4. Shabetai R (2000) Sarcoidosis and the heart. Curr Treat Options Cardiovasc Med 2:385–398
5. Silverman KJ, Hutchins GM, Bulkley BH (1978) Cardiac sarcoid: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. Circulation 58:1204–1211
6. Iwai K, Sekiguti M, Hosoda Y, DeRemee RA, Tazelaar HD, Sharma OP et al (1994) Racial difference in cardiac sarcoidosis incidence observed at autopsy. Sarcoidosis 11:26–31
7. Prior C, Knight RA, Herold M, Ott G, Spiteri MA (1996) Pulmonary sarcoidosis: patterns of cytokine release in vitro. Eur Respir J 9:47–53
8. Roach DR, Bean AG, Demangel C, France MP, Briscoe H, Britton WJ (2002) TNF regulates chemokine induction essential for cell

recruitment, granuloma formation, and clearance of mycobacterial infection. J Immunol 168:4620–4627
9. Baughman RP, Lower EE (2001) Infliximab for refractory sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 18:70–74
10. Ulbricht KU, Stoll M, Bierwirth J, Witte T, Schmidt RE (2003) Successful tumor necrosis factor alpha blockade treatment in therapy-resistant sarcoidosis. Arthritis Rheum 48:3542–3543
11. Doty JD, Mazur JE, Judson MA (2005) Treatment of sarcoidosis with infliximab. Chest 127:1064–1071
12. Carter JD, Valeriano J, Vasey FB, Bognar B (2004) Refractory neurosarcoidosis: a dramatic response to infliximab. Am J Med 117:277–279
13. Yee AM, Pochapin MB (2001) Treatment of complicated sarcoidosis with infliximab anti-tumor necrosis factor-alpha therapy. Ann Intern Med 135:27–31
14. Baughman RP, Drent M, Kavuru M, Judson MA, Costabel U, du Bois R et al (2006) Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. Am J Respir Crit Care Med 174:795–802
15. Chung ES, Packer M, Lo KH, Fasanmade AA, Willerson JT (2003) Randomized, double-blind, placebo-controlled, pilot trial of infliximab, a chimeric monoclonal antibody to tumor necrosis factor-alpha, in patients with moderate-to-severe heart failure: results of the anti-TNF therapy against congestive heart failure (ATTACH) trial. Circulation 107:3133–3140