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A Case of Autoimmune Myocarditis Treated with IL-17 Inhibition

Atieh Jibbe, M.D.[1], Brett C. Neill, M.D.[1], Anand Rajpara, M.D.[1], Jacob Whitsitt, M.D.[2], Mark Hamblin, M.D.[1]
[1]University of Kansas Medical Center, Kansas City, KS
Department of Internal Medicine, Division of Dermatology
[2]UCHealth Cherry Creek Medical Center, Denver, CO

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INTRODUCTION

Myocarditis is an inflammatory process affecting the heart muscle.[1] Myocarditis, however, occurs because of an external antigen exposure, such as viruses, bacteria, fungi, parasites, toxins, or drugs, with viruses being the most common, or internal triggers.[2,3] Autoimmune myocarditis can occur as an isolated entity in which the primary targeted organ is the heart, as is seen in giant cell myocarditis and eosinophilic myocarditis, or as part of a systemic autoimmune disease which can affect heart tissues, generating myocarditis in the context of a broader autoimmune phenomenon.[1] These diseases include systemic lupus erythematosus, rheumatoid arthritis, sarcoidosis, Sjogren's syndrome, vasculitis, polymyositis, and psoriasis as seen in our case.[1,4,5] There is a surplus of literature detailing the specific immune mechanism targets in autoimmune myocarditis including that of the Th17 and IL-17 mediated pathways. A case of a patient diagnosed with autoimmune myocarditis in the setting of psoriasis was treated successfully with the IL-17 inhibitor, secukinumab, thus directly targeting the immune mechanisms found to be involved in autoimmune myocarditis and its progression.

CASE REPORT

A 35-year-old woman presented with heart palpitations and excessive fatigue. She had frequent premature ventricular contractions (PVCs) with no apparent cause which eventually self-resolved. One year later, she developed new onset shortness of breath and had a recurrence of heart palpitations with Holter monitoring revealing occasional to frequent single, unifocal PVCs. She was started on flecainide 50 mg twice daily, which controlled her PVCs. Symptomatic PVCs recurred anytime flecainide was held.

She underwent an electrophysiologic study which mapped PVCs to the anteroseptal right ventricular outflow tract region. This area was ablated with symptoms controlled, and flecainide was discontinued.

A few months after the ablation, the patient experienced recurrent palpitations. Holter monitoring showed frequent monomorphic PVCs and a PVC burden at 20%. The patient was re-started on flecainide 50 mg twice daily. At this time, she underwent advanced imaging studies to evaluate the possibility of myocarditis. A fluorine-18, fluoro-deoxyglucose (18f-FDG) PET-CT scan showed diffuse heterogeneous increased FDG uptake involving the left ventricular myocardium, involving the mid-basal inferolateral wall of the left ventricle with a standardized uptake value (SUV) max of 12.83. The max SUV at basal septal wall was 8.8 and apex was 10.24 (Figure 1).

Given the presence of myocarditis on PET imaging, she underwent a comprehensive workup to rule out alternative causes of myocarditis. Cardiac biomarkers were unremarkable with a troponin of 0 ng/mL and a brain natriuretic peptide less than 15 pg/ml. Extensive workup for viral etiologies was unremarkable.

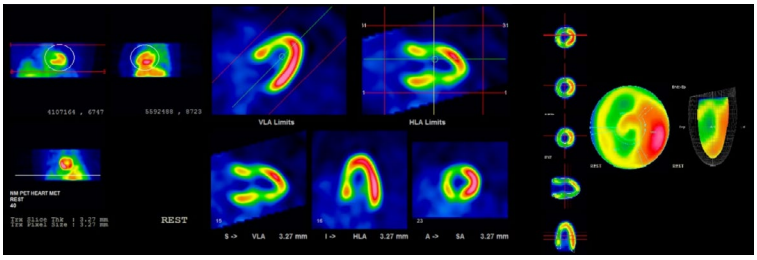

Figure 1. Increased diffuse heterogeneous increased fluoro-deoxyglucose uptake involving the left ventricular myocardium which was consistent with moderate acute myocarditis. No metabolically active mediastinal or hilar nodes, or pulmonary nodules noted.

The patient's autoimmune serologies revealed only a mildly elevated antinuclear antibody panel of 80. CT imaging of the chest, abdomen, and pelvis was within normal limits. A stress test was negative for ischemia and showed left ventricular volume decrease and systolic function that improved with exercise. PVCs only were noted at rest but did not appear during exercise. A 2D Doppler echocardiogram showed normal left ventricular function with an ejection fraction of 55%. Of note, she had a past medical history of psoriasis since early childhood and was being treated with apremilast and narrowband ultraviolet phototherapy at that time.

The negative laboratory evaluation and lack of other clinical signs and symptoms led to the diagnosis of an autoimmune myocarditis secondary to psoriasis. She was started on 30 mg prednisone. PVCs improved, but due to weight gain and hyperglycemia, methotrexate was added a few months later. Repeat cardiac 18f-FDG PET-CT showed persistent disease with a similar uptake pattern. The max SUV in the left basal lateral ventricular myocardium improved from 12.83 to 7.20 (Figure 2).

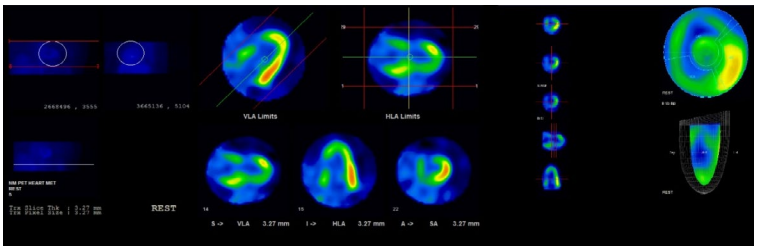

Figure 2. Continued heterogeneous uptake throughout the left ventricular myocardium suggestive of myocarditis.

Despite six months of treatment with methotrexate, the patient's PVC burden increased anytime her prednisone was decreased below 20 mg daily. Our multidisciplinary team attempted biologic therapy to treat the myocarditis. She was treated initially with adalimumab, but she could not tolerate it after two months, developing chest pain, shortness of breath, headache, and dizziness. Adalimumab and methotrexate were discontinued, and she was started on secukinumab 150 mg every two weeks. Within a month of therapy, the patient noticed significant improvement in her psoriasis and PVC burden. She was able to taper prednisone, but palpitations recurred when prednisone was tapered below 10 mg daily. Methotrexate was restarted two months after start-

ing secukinumab, and she was able to taper prednisone further. She had repeat cardiac PET imaging, which showed near complete resolution of the myocarditis (Figure 3). A repeat Holter monitor showed near complete resolution of PVC burden.

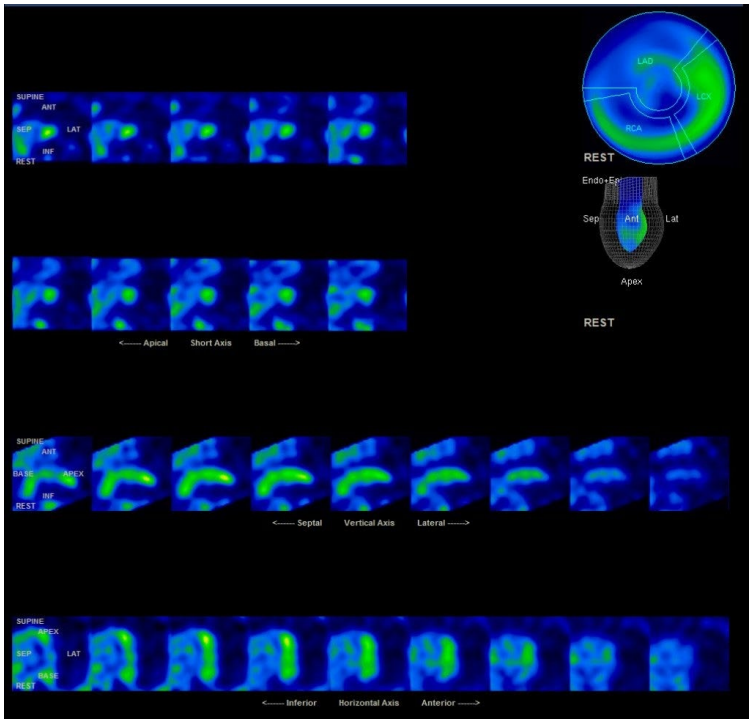

Figure 3. Near complete resolution of increased uptake in the left ventricular myocardium reflective of favorable response to therapy.

DISCUSSION

The PET imaging consistent with acute myocarditis along with an extensive negative workup (negative autoimmune and viral serologies) led to a diagnosis of autoimmune myocarditis secondary to psoriasis. The possibility of a viral myocarditis cannot be ruled out, though it is unlikely as there was no acute episode at onset of symptoms, and the symptoms were progressive and developed insidiously.

Psoriasis is an inflammatory disease with IL-17 as the major effector cytokine in its pathogenesis.[6] Similarly, the Th17 arm of the immune system is linked to the pathogenesis of myocarditis and dilated cardiomyopathy (DCM), which would explain both the likely etiology of the autoimmune myocarditis, and the success of treatment with secukinumab, an IL-17 inhibitor.

Several studies have utilized a mouse model, experimental autoimmune myocarditis (EAM), to establish the connection between Th17 cells and IL-17 cytokines in the development of autoimmune myocarditis and its progression to DCM.[1,7-11] Targeting of IL-17 and subsequent improvement of myocarditis in EAM mice suggested a role for direct inhibition of IL-17 in human patients with myocarditis. In multiple studies, Th17 cells were elevated in patients with myocarditis and DCM.[7-11] Elevated Th17 cells correlated with heart failure were evidenced by the fact that biopsies with detectable IL-17A+ cells trended toward heavier fibrosis, while biopsies with no detectable IL-17A+ cells showed weaker fibrosis.

In our patient, an endomyocardial biopsy was spared given that biopsies are high risk and usually reserved for patients presenting with major clinical syndromes, such as severe heart failure and/or life-threatening arrhythmias that are refractory to conventional therapies, which was not the case in our patient. The radiographic evidence and underlying autoimmune disease, which was the likely related cause of the autoimmune myocarditis, further negated the need for a biopsy.

CONCLUSIONS

While the pathogenesis of autoimmune myocarditis and DCM and their association with the Th17 and IL-17 mediated processes were well documented in the literature, the use of direct inhibition of IL-17 within humans with myocarditis had not been reported. This case highlighted the success of IL-17 inhibition in treating autoimmune myocarditis, a disease with no truly effective treatment and with potentially devastating consequences. Thus, it provided an exciting avenue for future research in larger patient populations to assess the efficacy of this treatment modality.

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