

Case Report

Etanercept Induced Myopericarditis and Subacute Cutaneous Lupus Erythematosus

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Abstract

Introduction: Etanercept is a tumor necrosis factor inhibitor currently used for the treatment of autoimmune diseases such as rheumatoid arthritis and most spondyloarthropathies. The increased use of this medication has continued to reveal more of its adverse effects. These adverse effects include reactivation of infections such as mycobacterium tuberculosis, cutaneous disorders, systemic lupus erythematosus-like syndromes and cardiovascular-related conditions.

Case Report: 61 year old man with known history of psoriatic arthritis on long term use of etanercept, presented with new onset chest pain and emergence of sun sensitive erythematous rashes. Found to have myopericarditis and subacute cutaneous lupus erythematosus with resolution of symptoms within six weeks of discontinuation of etanercept.

Discussion/Conclusion: Having two adverse effects of this medication makes this a rather compelling presentation. Etanercept induced myopericarditis and subacute lupus erythematosus should be suspected in any patient on this medication presenting with new onset chest pain and sun-sensitive rash.

Keywords: Drug adverse effects; Etanercept; Erythematous rash; Lupus; Pericarditis; Tumor necrosis factor inhibitors

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Background

Etanercept is a widely used tumor necrosis factor -alpha blocking agent which is a crucial treatment option for patients with rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis and vasculitis [1]. An array of side effects has been reported in patients treated with etanercept. It is well known that this medication predisposes patients to infection such as reactivation of mycobacterium tuberculosis and salmonella [2]. Other notable adverse effects of this medication includes: skin disorders, malignancy and cardiovascular-related side effect such as pericarditis, myopericarditis and perimyocarditis [3].

Drug induced cutaneous manifestations may present as cutaneous lupus with its two variant Discoid Lupus Erythematosus (DLE) and Subacute Cutaneous Lupus Erythematosus (SCLE).

SCLE mostly present with erythematosus, scaly papules or annular plaques on the neck, trunk and extremities while DLE most commonly are well-defined inflammatory plaques that evolve into atrophic, disfiguring scars on the head. Common drugs notorious for inducing cutaneous lupus are anti-tumor necrosis factor agents (such as etanercept, infliximab), procainamide, hydralazine, minocycline, diltiazem, penicillamine, Isoniazide, quinidine, interferone alfa, methyldopa, chlorpromazine and practolol [4].

This case report illustrates the presentation of multiple adverse reactions to etanercept in a single subject and that prompt discontinuation of etanercept in patient with these adverse reaction to this medication often leads to good outcome.

Case Presentation

Patient is a 61 year old man with a history of roux-en-Y surgery, recent diagnosis of atrial fibrillation rate controlled with per oral metoprolol 25 mg daily, longstanding medical history of psoriatic arthritis with both axial and peripheral manifestation. His psoriatic arthritis was well controlled with long-term use of etanercept at 50 mg once weekly dosing.

He presented with chest pain, shortness of breath, fever and new onset sun sensitive erythematous rashes on his face of three days duration. Chest pain was sudden in onset, sharp and pleuritic in nature. The severity of the chest pain was 8 out of 10 on a 10 point scale and radiated across the anterior chest wall. Pain was aggravated on deep inspiration, with movement and relieved by leaning forward. He also reported fatigue; however there was no cough, orthopnea, paroxysmal nocturnal dyspnea, extremity swelling, headache, recent viral illness or sick contact.

Physical examination revealed fever of 101.8 F and pericardial friction rub. There was no hypoxia, pulmonary congestion, elevated jugular venous pulsation, peripheral edema, oral ulcers, neurological deficit or hematological abnormalities. Skin examination revealed facial eruptions, an erythema in a malar distribution in the cheeks and bridge of nose, sparing the nasolabial fold. These cutaneous findings were first noted three days prior to presentation. He also had

erythematous maculopapular eruptions involving primarily sun-exposed skin mostly at the extensor surfaces of the arms and hands (Figure 1).



Figure 1: Image showing erythematous maculopapular eruptions involving primarily sun-exposed skin mostly at the extensor surfaces of the arms.

Investigation

Laboratory work-up revealed an elevated erythrocyte sedimentation rate of 55 mm/hour and C-reactive protein of 79.1 mg/l and elevated troponin which peaked at 0.117 ng/ml. Kidney function test however remained within normal limits. Blood cultures did not yield any growth.

Chest x-ray was unremarkable. Electrocardiogram (ECG) revealed subtle diffuse concave upward ST-segment elevations and PR depression in all other limbs except a VR, these findings are suggestive of pericarditis.

Chest computed tomography with pulmonary embolism protocol were unremarkable. Echocardiogram had no wall motion abnormality and no other abnormality was noted. Exercise stress test was negative for any ischemic phenomenon. Cardiac magnetic resonance Imaging showed patchy mid myocardial and trivial pericardial effusion with late gadolinium enhancement suggestive of myopericarditis (Figure 2).

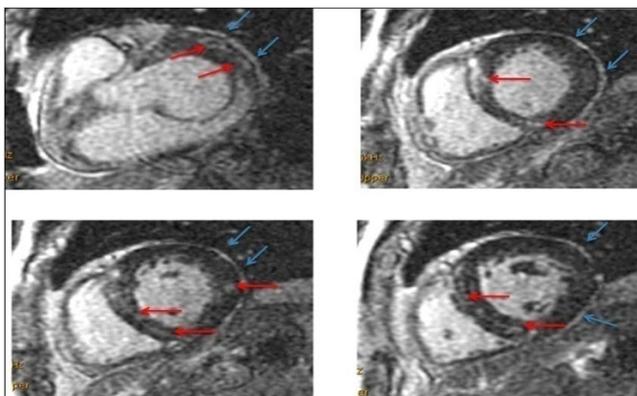


Figure 2: Late gadolinium images in the basal and mid LV myocardium show patchy mid myocardial and subepicardial late gadolinium enhancement (Red arrows). Mild pericardial late gadolinium enhancement seen along the lateral LV wall (Blue arrows).

Serologic test was performed and demonstrated Anti-nuclear Antibody (ANA) of 1:2560 (reference range <160), positive anti-histone of 5 U (reference range < 1) and positive anti-Ro/SSA antibodies of 2.1 (reference range <1.0). Biopsy of cutaneous lesions demonstrated suprabasilar lymphocytosis accompanied by suprabasilar dyskeratosis on light microscopy.

Differential Diagnosis

Drug induced pericarditis, drug induced subacute cutaneous lupus, costochondritis, musculoskeletal chest pain, myocardial infarction, angina and idiopathic subacute cutaneous lupus erythematosus were all in the differential.

The more worrisome and ominous etiologies of chest pain were appropriately ruled out. With the compilation of symptoms, signs, serological abnormalities and cardiac MRI findings, the diagnosis of etanercept induced myopericarditis and subacute cutaneous lupus erythematosus was made.

Treatment

Etanercept was discontinued; patient was started on colchicine 0.6 mg twice daily. First line of therapy is usually NSAIS which the patient could not tolerate and would put him at risk for developing marginal ulcers at the site of roux-en-Y surgery.

The patient continued to experience worsening chest pain despite colchicine therapy, decision to start patient on steroid treatment was made on day 3 of hospitalization and prednisone 40 mg daily was started.

Outcome and Follow-Up

On day 5 of hospitalization, patient started to show clinical improvement. Chest pain had decreased to 2 over 10 in severity on a 10 point scale and he was discharged home on day 7. At the time of discharge, his chest pain had drastically improved. He was discharged on only prednisone 40 mg daily with a taper, to take 40 mg of prednisone for four days, then 30 mg for four days, 20 mg for four days, 10 mg for another four days and then discontinue use.

He was seen in the cardiology outpatient clinic three weeks later. At that visit, his chest pain had completely resolved and he had tapered off the steroid. His rashes were almost resolved and he was given another three week follow up appointment.

At the sixth week appointment, his rashes were completely resolved, follow up serological titers were drawn and with the following results: ANA of 1:1250, (reference range <160), anti-histone of 2.7 U (reference range < 1) and anti-Ro/SSA antibodies of 1.1 (reference range <1.0), a notable decline from his prior values. Worthy to note that serological titers may remain detected even with resolution of symptoms up to a year.

Upon his rheumatology evaluation, he was started on adalimumab as patient who developed adverse drug reaction to a certain class of tumor necrosis factor inhibitor may tolerate a different class of anti-TNF medication. We will continue to monitor the patient closely for any adverse reaction to this new agent.

Discussion

Some of the most commonly reported adverse events (occurring in >10% of patients) associated with subcutaneously administered

anti-TNF agents are injection-site reactions such as burning and stinging [2]. An erythematous rash which typically resolves over time may also develop at the injection site [1]. Long-term follow-up and post marketing studies have highlighted several safety concerns associated with TNF-blockade including increased risks for serious infections, including tuberculosis and malignancy [5]. TNF- alpha blockers such as etanercept have been reported to cause lupus-like syndrome however etanercept induced cardiovascular complications such as hypertension, heart failure, atrial fibrillation, pericardial effusion, cardiac tamponade and pericarditis/myopericarditis are rare [6].

Subacute Cutaneous Lupus Erythematosus (SCLE) may be drug-induced in a substantial proportion of patients who presents with what is initially thought to be idiopathic SCLE and this is distinct from the typical drug-induced lupus syndrome. In a population based study of 234 patients with SCLE, the condition was found to be drug-induced in greater than one third of the patients [7]. The majority of patients with drug-induced SCLE are anti-RO/SSA positive [8]. Drug-induced SCLE typically presents as an annular or psoriasiform, photo-distributed cutaneous eruption as seen in this case [7].

The diagnostic evaluation of patients with suspected drug-induced lupus is similar to suspected idiopathic systemic lupus erythematosus because of the clinical overlap between these two disease entities; however the gold standard is spontaneous resolution of the clinical manifestation of the disease within several weeks to months after offending drug has been discontinued [8,9]. Our patient was initially started on colchicine given his chest pain and then prednisone was added as colchicine alone was unable to control his chest pain and he had good clinical improvement on these medications with complete resolution of his chest pain by the second week on steroid therapy and his rashes by the sixth week. He was however remained symptom free since discontinuation of etanercept. Steroids were used to treat his acute chest pain due to myopericarditis.

Although his symptoms resolved, his serological titers were noted to have a significant decline in the immediate six weeks follow up period, which in part may be due to the short course steroid therapy. Despite discontinuation of the steroid therapy, he has continued to be symptom free. His serological titer has however persisted. The serological titers may remain detected in drug induced cutaneous lupus even with resolution of symptoms up to a year [7].

This case exhibited the combined side effects of this medication such as lupus-like skin disorder and pericarditis/myopericarditis. More commonly, systemic lupus-like syndrome would have been considered, however patient exhibited no other classical features of systemic lupus, his only presentation related to lupus was the cutaneous manifestation, his kidney function remained normal.

It still remains unclear why patients exhibit adverse reactions to a certain class of TNF-alpha inhibitors and do well on another. There are reported cases of patients who tolerated a different class of TNF medication after developing an adverse reaction to a particular class in the literature. It is however too soon to judge if this index patient will develop any adverse reactions to his new agent adalimumab as he was on etanercept for two years before developing an adverse reaction to the medication.

Learning Points/Take Home Message

- Etanercept induced myopericarditis and SCLE should be suspected in any patient on this medication presenting with new onset chest pain and sun-sensitive rash
- More than one adverse reaction to one medication can co-exist in one patient and presentation of one, should warrant further evaluation for others
- Prompt discontinuation of Etanercept in patient with adverse reaction to the medication often leads to good outcomes

Patients Perspective

Etanercept helped curtail my psoriatic arthritis symptoms for years but unfortunately was discontinued because of adverse reaction. I will advise any patient on this medication to always look out for any of the symptoms I experienced while on this medication and report to your doctors promptly.

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