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【 CASE REPORT 】

Refractory Systemic Lupus Erythematosus-associated Pericarditis Treated with Anifrolumab

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Abstract:

A 30-year-old woman with cutaneous lupus erythematosus, Kikuchi disease, and anti-ribonucleoprotein (RNP)/SS-A antibodies presented with fever and anterior chest pain. Initial echocardiography showed no pericardial effusion; however, follow-up revealed pericardial effusion, thus leading to a diagnosis of systemic lupus erythematosus (SLE)-associated acute pericarditis. Anti-RNP/SS-A antibodies are associated with serositis and elevated type I interferon (IFN) activity. Despite treatment with prednisolone, her condition persisted, thus prompting the administration of anifrolumab (300 mg), a monoclonal antibody that targets the type I IFN receptor. Following treatment, both pericardial effusion and the C-reactive protein levels promptly improved. This case highlights the fact that anifrolumab is a promising therapy for steroid-resistant SLE-associated pericarditis.

Key words: systemic lupus erythematosus, acute pericarditis, anifrolumab, refractory pericarditis, echocardiography

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Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that affects multiple organs owing to immune dysregulation, which is driven by genetic and environmental factors. A key feature of SLE is the activation of the type I interferon (IFN) pathway which contributes to the disease activity by promoting autoantibody production and immune dysfunction (1). Pericarditis is a common cardiac manifestation of SLE and it is typically treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids with or without hydroxychloroquine (2). However, cases refractory to standard therapy present significant treatment challenges.

Anifrolumab, a fully human monoclonal antibody targeting the type I IFN receptor, inhibits the IFN pathway and it has demonstrated efficacy in reducing the SLE disease activity (3). In Japan, anifrolumab has been approved for the treatment of SLE since 2021 and it has shown promise in managing the systemic manifestations of the disease. Although its efficacy has been established for the treatment of refractory cutaneous lupus, its potential role in the treatment of SLE-associated serositis, particularly pericarditis, remains unclear. This report presents a case of acute SLE-associated pericarditis that was refractory to standard therapy, but was successfully managed with anifrolumab.

Case Report

A 30-year-old woman presented to the emergency department with a fever and anterior chest pain. She had a history of cutaneous lupus erythematosus for nine years and Kikuchi's disease for five years but was not on any medication and had been under regular follow-up. Four days before her visit, she developed chest tightness and dyspnea, which progressed to a fever of up to 39°C, and anterior chest pain exacerbated by exertion and inspiration.

At the initial visit, her blood pressure was 103/73 mmHg, pulse 114 bpm (regular), respiratory rate 14 /min, SpO_2 98% on room air, and temperature 38.0°C. Cardiac auscultation revealed normal heart sounds with a pericardial friction rub

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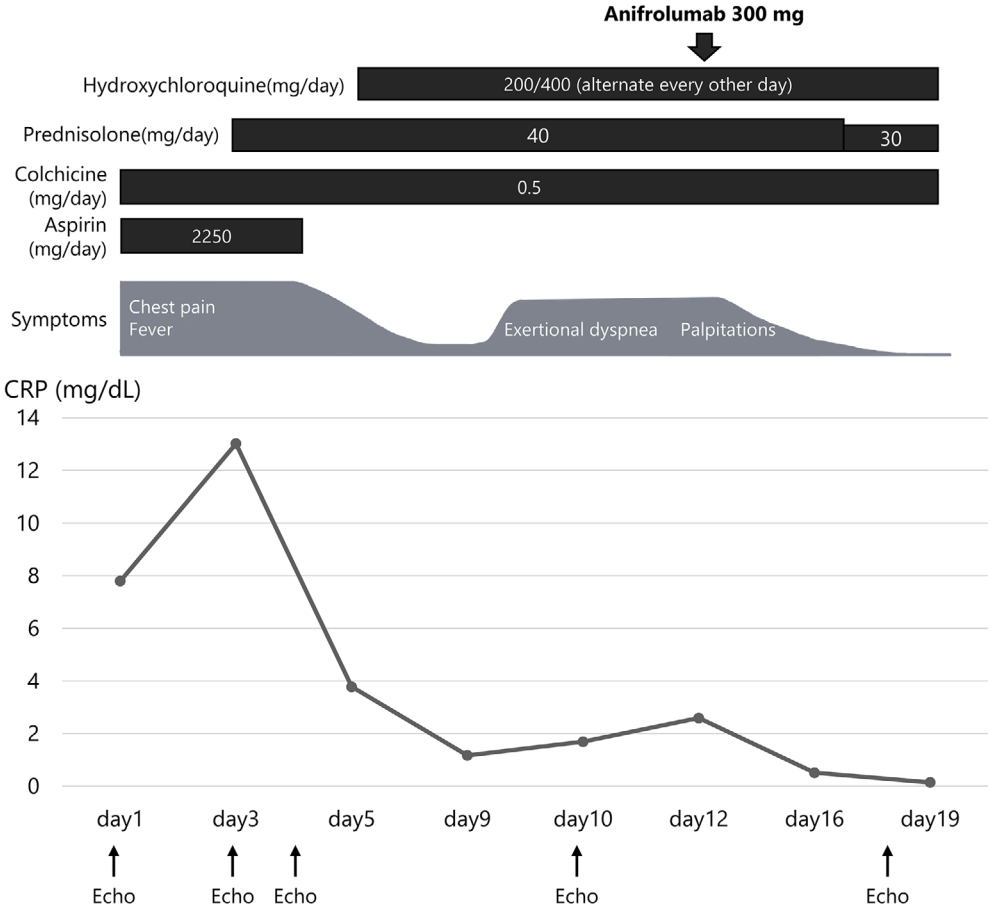

Figure 1. **Clinical course of the patient. CRP: C-reactive protein**

and vesicular breath sounds without rales. The extremities showed peripheral swelling of both fingers without pitting edema. Laboratory tests revealed an elevated C-reactive protein (CRP) level of 7.80 mg/dL (Fig. 1), and electrocardiography (ECG) revealed diffuse ST-segment elevation with reciprocal PR-segment elevation in lead aVR (Fig. 2a). Contrast-enhanced chest computed tomography (Fig. 2b) and echocardiography revealed no abnormalities, including the absence of pericardial effusion (Fig. 3a). With normal troponin levels ruling out myocarditis, the patient was diagnosed with acute pericarditis and thus was prescribed NSAIDs and colchicine. She was deemed to be stable and therefore was discharged from the hospital with a follow-up appointment scheduled two days later.

At the follow-up visit, anterior chest pain persisted, and echocardiography detected a newly developed pericardial effusion along with mild left ventricular hypokinesis (Fig. 3b). Based on these findings, the patient was admitted for further management. Chest radiography demonstrated cardiomegaly, with a cardiothoracic ratio of 55.8%. Laboratory tests revealed thrombocytopenia ($100\times10^3/mm^3$), elevated IgG level (3,063 mg/dL), and positivity for autoantibodies, including antinuclear antibody (titer: 1:1,280), anti-ribonucleoprotein (RNP) antibody (≥550 U/mL), anti-SS-A/Ro antibody (785 U/mL), and lupus anticoagulant (1.2). Considering these findings, along with fever, acute pericarditis, joint involvement, and normal troponin levels, which ruled out myocarditis, the patient met the 2019 European League Against Rheumatism/American College of Rheumatology SLE classification criteria with a score of 20 and therefore was diagnosed with SLE-associated acute pericarditis (4).

Treatment with prednisolone (40 mg/day) was initiated. One day after initiating the prednisolone treatment, the anterior chest pain had resolved, and by day 5, the CRP level had decreased to 3.78 mg/dL. On day 6, hydroxychloroquine (200 mg and 400 mg on alternate days) was added. The CRP level decreased to 1.17 mg/dL, and her clinical course initially appeared uneventful. However, on day 9, she developed exertional dyspnea and generalized malaise, and her CRP level increased again to 2.59 mg/dL. Although ST-segment elevations on ECG had improved (Fig. 2c), repeat echocardiography showed no findings suggestive of cardiac tamponade or myocarditis, but it revealed an increase in pericardial effusion (Fig. 3c). She was diagnosed with steroid-resistant acute pericarditis and was treated with anifrolumab (300 mg). Six days after anifrolumab administration, echocardiography revealed a significant reduction in pericardial effusion (Fig. 3d), thus suggesting a rapid response to treatment. ECG after anifrolumab therapy demonstrated resolution of ST-segment elevations and normalization of PR segments with new T-wave inversions in leads II, III, and aVF (Fig. 2d). Her CRP level normalized to 0.14

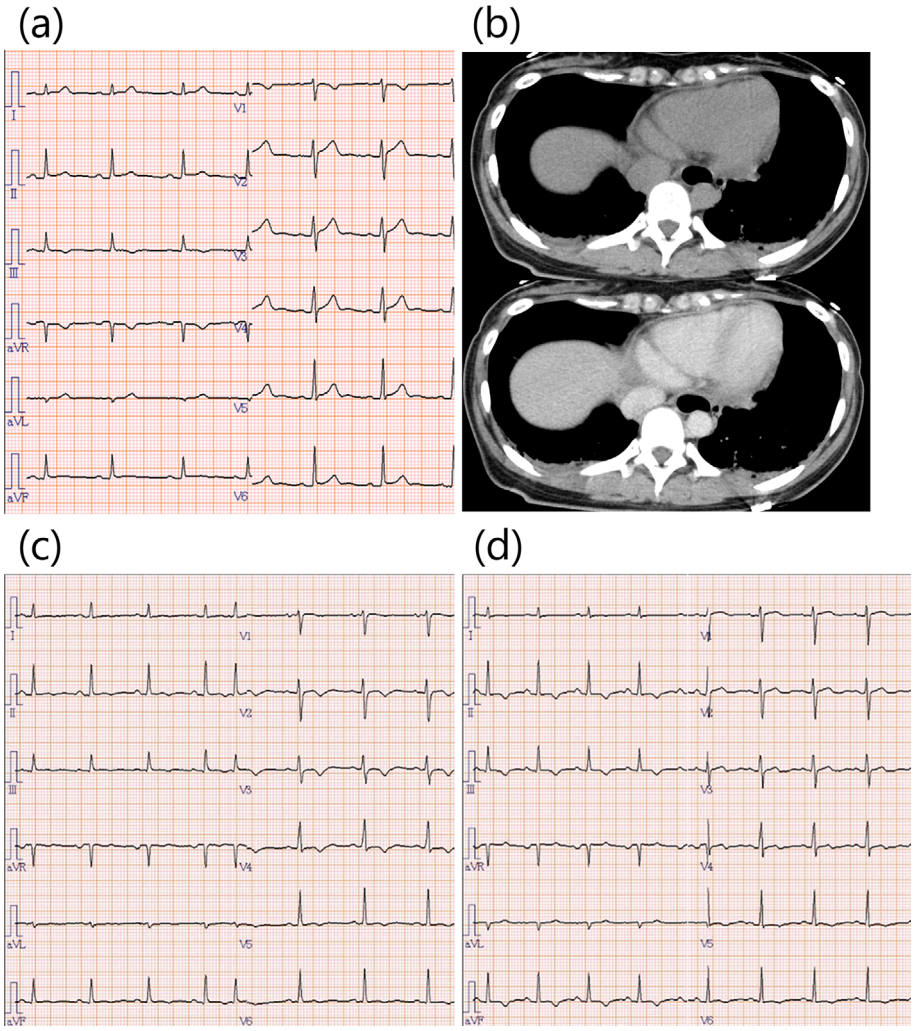

Figure 2. **Electrocardiography (ECG) and Contrast-enhanced chest computed tomography (CT) at the initial visit and before and after anifrolumab administration. (a) ECG on initial visit revealed diffuse ST-segment elevation with reciprocal PR-segment elevation in lead aVR. (b) CT at initial visit showed no abnormalities or pericardial effusion. (c) ECG performed before anifrolumab administration showed an improvement of the previously noted diffuse ST-segment elevations and reciprocal PR-segment changes. (d) ECG after anifrolumab therapy demonstrated resolution of ST-segment elevations and normalization of PR segments, with new T-wave inversions in leads II, III, and aVF.**

mg/dL, and her symptoms completely resolved. She was discharged in a stable condition with plans for outpatient follow-up, including monitoring of her SLE activity and scheduled tapering of the steroid dosage.

Discussion

This case highlights two important findings in the management of steroid-resistant SLE-associated pericarditis: 1) the potential efficacy of anifrolumab, a monoclonal antibody targeting the type I IFN receptor, and 2) the crucial role of echocardiography in both disease monitoring and the treatment decision-making process.

Pericarditis is a common cardiac manifestation of SLE that occurs in approximately 25% of all patients (5). Among patients with SLE, anti-RNP and anti-SS-A antibodies are associated with a higher risk of developing serositis, including pericarditis, owing to a heightened type I IFN activity (6, 7). In this patient, the presence of these autoantibodies suggested a more severe inflammatory response, which likely contributed to steroid resistance. The risk factors include a young age at diagnosis, fever, proteinuria, and the presence of specific autoantibodies, many of which were observed in this patient (8). SLE-related pericarditis is associated with an increased risk of cardiovascular complications, thus underscoring the importance of effective treatment. While traditional therapies such as NSAIDs, colchicine, corticosteroids, and antimalarial agents are often effective, steroid-resistant cases require alternative strategies (9).

SLE is characterized by dysregulation of the type I IFN pathway, which drives autoantibody production and immune complex-mediated inflammation (1). Patients with anti-RNP and anti-SS-A antibodies exhibit increased IFN activity, which contributes to persistent inflammation and reduced re-

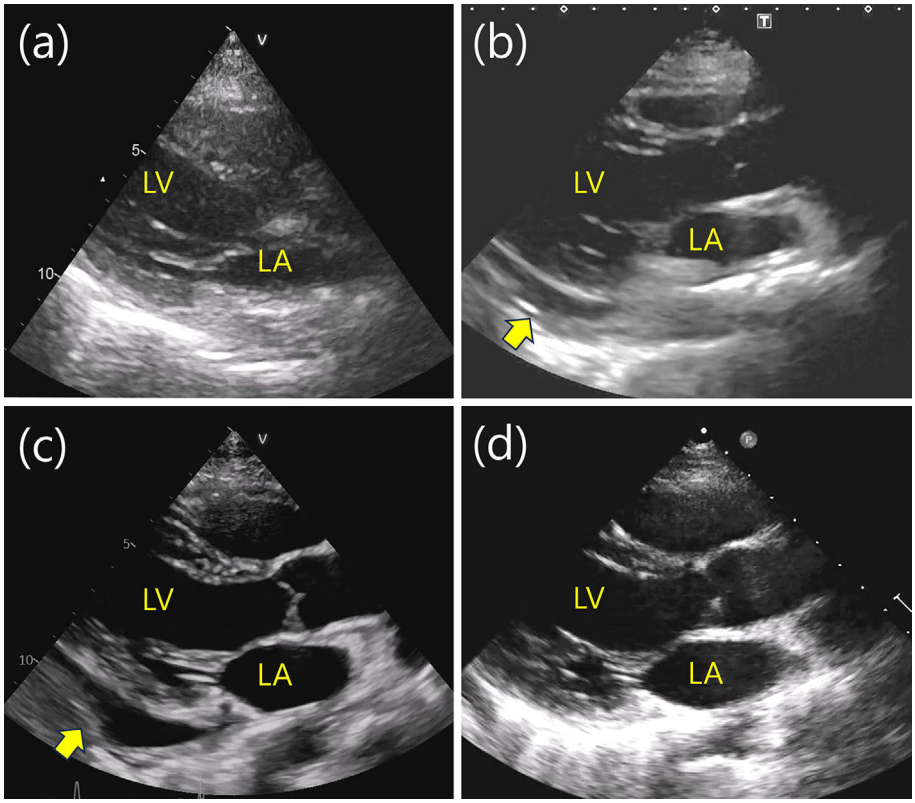

Figure 3. **Echocardiography at end-diastole on (a) day 1, (b) day 3, (c) day 10, and (d) day 18. (a) No pericardial effusion or left ventricular wall motion abnormalities were observed on day 1. (b) On day 3, a newly developed pericardial effusion (arrow) and mild hypokinesis of the left ventricular wall were observed. (c) On day 10, despite treatment with prednisolone and hydroxychloroquine, the pericardial effusion (arrow) had increased. (d) On day 18, following anifrolumab administration, a marked reduction in pericardial effusion was observed.**

sponsiveness to standard therapies (7). The rapid resolution of pericardial effusion following anifrolumab administration suggests that the targeting of the IFN pathway may be a promising therapeutic strategy in such cases. The increased expression of IFN-induced genes, such as signal transducer and activator of transcription (STAT) 1 and STAT2, in B cells and monocytes contributes to this dysregulation (10). In this patient, elevated IgG levels indicated abnormal B-cell activation, consistent with overactivation of the type I IFN pathway and its role in SLE pathophysiology. Anifrolumab is a human monoclonal antibody that targets the type I IFN receptor, thereby suppressing this pathway and reducing disease activity (3). In the TULIP-2 trial, a randomized, placebo-controlled study of patients with moderate-to-high disease activity SLE, anifrolumab reduced glucocorticoid requirements and improved skin disease severity compared to placebo (3). Although its efficacy has been reported in refractory cutaneous lupus erythematosus (11), there have also been reports of treatment discontinuation in SLE-associated serositis with pericarditis and pleuritis, and the autoantibody profile in this case was not specified. In our patient, who was positive for anti-RNP and anti-SS-A antibodies, which are markers often linked to IFN hyperactivation, anifrolumab administration was associated with the rapid resolution of pericardial effusion. Although this single observation cannot establish causality, it raises the hypothesis that serologically defined subgroups with heightened type I IFN activity may derive particular benefits from IFN-receptor blockade. Prospective studies are therefore needed to test whether anti-RNP/SS-A positivity truly predicts the response. A previous study reported that the serum IFN activity was significantly lower in patients with SLE-related pericarditis than in those without pericarditis (12). However, anifrolumab effectively resolved acute pericarditis in this patient, thus suggesting that excessive activation of the type I IFN pathway may contribute to SLE-related pericarditis in some cases. Therefore, anifrolumab could serve as an effective treatment option for steroid-resistant SLE-associated pericarditis, particularly in cases of IFN hyperactivation, thereby warranting further clinical investigation.

Echocardiography is indispensable in the management of pericarditis, allowing for the real-time assessment of pericardial effusion, the monitoring of disease progression, and early identification of complications, such as tamponade or myocardial involvement (13). In this case, echocardiography was essential for guiding treatment decisions and tracking pericardial effusion resolution, which could not be reliably assessed using ECG. Incorporating echocardiography into routine management can enhance the treatment outcomes and prevent complications in patients with SLE-associated

pericarditis.

Conclusion

In conclusion, anifrolumab is a promising therapeutic option for acute pericarditis associated with SLE, particularly in patients refractory to conventional therapies. Given the association between anti-RNP/SS-A antibodies and IFN-driven inflammation, anifrolumab may be particularly beneficial in the treatment of serositis-predominant SLE. Further studies are needed to evaluate the broader efficacy of anifrolumab in the IFN-mediated manifestations of SLE, including refractory pericarditis.

The authors confirm that written consent for submission and publication of this case report, including image(s) and associated text, has been obtained from the patient in line with the COPE guidance.

The authors state that they have no Conflict of Interest (COI).

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