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Review Article

When Viral Seropositivity Obscures Autoimmunity: Multisystem SLE with Concurrent CMV Positivity in an Immunocompetent Patient

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Abstract

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease whose inflammatory manifestations can closely mimic infection, complicating diagnosis and delaying appropriate treatment. Viral seropositivity, including cytomegalovirus (CMV), may further obscure the clinical picture and may represent active or reactivated infection in the setting of immune dysregulation. We report a 28-year-old woman who presented with progressive dyspnea, orthopnea, and near-syncope following a viral-like prodrome and a recent cruise trip to the Bahamas. Initial evaluation revealed cardiomegaly, bilateral pleural effusions, a moderate pericardial effusion, and myopericarditis with preserved ejection fraction, accompanied by persistent sinus tachycardia, lymphadenopathy, elevated inflammatory markers, and recurrent hypoglycemia. Markedly elevated CMV IgM and IgG prompted treatment for possible active or reactivated CMV infection with valganciclovir, resulting in transient clinical improvement. She returned shortly thereafter with recurrent syncope and severe transaminitis, with liver enzymes exceeding 900 U/L, felt to be secondary to valganciclovir-associated hepatotoxicity. Subsequent evaluation established active SLE as the primary etiology of her cardiac and systemic manifestations, with CMV representing a concurrent but non-causal finding. This case highlights the importance of prioritizing lupus flare in the differential diagnosis of unexplained multisystem disease, even in the presence of viral seropositivity. This case emphasizes the importance of maintaining suspicion for autoimmune disease despite misleading viral serologies to avoid delays in appropriate immunosuppressive therapy.

Keywords: Systemic lupus erythematosus, cytomegalovirus infection, myopericarditis, viral seropositivity and autoimmune disease

Introduction and Patient Information

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease characterized by immune complex deposition and widespread inflammatory involvement of multiple organ systems [1,2]. Its clinical manifestations are heterogeneous and may include serositis, myocarditis, pericardial effusion, cytopenias, lymphadenopathy, and constitutional symptoms. Because many of these features overlap with infectious processes, distinguishing lupus flare from infection is often challenging, especially in patients presenting with acute systemic illness [7]. Viral infections have long been implicated both as triggers of autoimmune activation and as concurrent findings in patients with immune dysregulation [5,6]. Cytomegalovirus (CMV) infection is common in the general population and is typically asymptomatic in immunocompetent individuals. However, CMV seropositivity, including elevated IgM titers, may occur in the setting of immune activation or reactivation, complicating interpretation in patients undergoing evaluation for autoimmune disease [6].

In such cases, viral serologies may shift diagnostic focus toward infectious etiologies and delay recognition of underlying inflammatory disease [7]. Cardiac involvement in SLE, particularly myopericarditis and pericardial effusion, represents a potentially life-threatening and frequently overlooked manifestation of active disease [3,4]. When these findings occur alongside systemic symptoms and positive viral markers, distinguishing primary viral myocarditis from autoimmune-mediated inflammation becomes especially complex. This diagnostic overlap underscores the importance of maintaining a broad differential diagnosis in patients with unexplained multisystem disease.

We present a case of newly diagnosed SLE initially attributed to active or reactivated CMV infection, highlighting the diagnostic complexity introduced by viral seropositivity and the risks of prematurely narrowing the differential diagnosis. A 28-year-old African American woman with no known chronic medical conditions presented with progressively worsening dyspnea, orthopnea, and near-syncope following a viral-like prodrome. One week prior to presentation, she developed generalized fatigue, malaise, and diffuse myalgia. Over subsequent days, she experienced worsening exertional dyspnea, progressing to marked breathlessness with minimal activity and an episode of near-syncope while climbing stairs, leading to emergency evaluation. She had recently returned from a cruise o the Bahamas.

Clinical Findings and Diagnostic Assessment

On arrival, she was alert and mildly ill-appearing. Vital signs were notable for persistent sinus tachycardia, while blood pressure and oxygen saturation were within normal limits. Cardiopulmonary examination revealed tachycardia without murmurs, rubs, or gallops and clear breath sounds bilaterally. There was no jugular venous distention or peripheral edema. Initial laboratory studies revealed an elevated D-dimer. Computed tomography angiography of the chest demonstrated no pulmonary embolism but revealed cardiomegaly, bilateral pleural effusions, and a moderate circumferential pericardial effusion. Mediastinal and bilateral axillary lymphadenopathy were also present. Transthoracic echocardiography showed preserved left ventricular systolic function with an ejection fraction of

60–70%, moderate concentric hypertrophy, diastolic dysfunction, and a moderate pericardial effusion without evidence of tamponade. High-sensitivity troponin was mildly elevated with a disproportionately low B-type natriuretic peptide. Inflammatory markers were elevated, and laboratory evaluation demonstrated mild normocytic anemia and hypoalbuminemia. During hospitalization, she developed recurrent episodes of severe hypoglycemia, with blood glucose levels measuring below 20 mg/dL in the absence of glucose-lowering medications. Serologic testing demonstrated elevated cytomegalovirus (CMV) IgM and IgG titers, raising concern for acute or reactivated CMV infection. CMV polymerase chain reaction testing was obtained. Additional testing, including HIV, hepatitis panel, tuberculosis screening, and malignancy evaluation, was negative.

Given recurrence of symptoms and persistent systemic inflammation, a comprehensive autoimmune evaluation was pursued. Serologic testing revealed a positive antinuclear antibody, low-positive anti–double-stranded DNA antibodies, and hypocomplementemia. During this period, she developed a new erythematous malar rash sparing the nasolabial folds. In the context of her prior myopericarditis, pleural and pericardial effusions, anemia, lymphadenopathy, and inflammatory markers, these findings fulfilled classification criteria for systemic lupus erythematosus.

Therapeutic Intervention

Given the combination of myopericarditis, pericardial and pleural effusions, lymphadenopathy, and recurrent hypoglycemia in the setting of positive CMV serologies, the patient was treated empirically with valganciclovir for presumed disseminated CMV infection. She experienced transient symptomatic improvement and was discharged with outpatient follow-up. She returned shortly thereafter with recurrent syncope and severe transaminitis, with aspartate aminotransferase and alanine aminotransferase levels exceeding 900 U/L.

Valganciclovir-associated hepatotoxicity was suspected, and antiviral therapy was discontinued. Following confirmation of systemic lupus erythematosus, corticosteroid therapy was initiated resulting in clinical stabilization and improvement.

Follow-up and Outcomes

Following initiation of valganciclovir therapy, the patient initially experienced mild symptomatic improvement; however, this was transient. She returned with recurrent syncope and was found to have severe transaminitis, prompting discontinuation of antiviral therapy. After initiation of corticosteroid therapy, the patient demonstrated clinical stabilization with improvement in cardiovascular symptoms and no further syncopal episodes during hospitalization. Liver enzyme abnormalities improved following cessation of valganciclovir.

Discussion and Conclusion

This case illustrates the diagnostic challenge posed by overlapping infectious and autoimmune processes, particularly in the presence of viral seropositivity. CMV IgM positivity may reflect immune activation rather than true active infection, which can mislead clinical decision-making. This case highlights the diagnostic challenge posed by multisystem SLE presenting alongside viral seropositivity. Clinicians should maintain a high index of suspicion for SLE in patients with unexplained multisystem involvement. Early recognition with initiation of treatment are essential to prevent disease progression and improve outcomes.

Patient Perspective

The patient reported distress related to the uncertainty of her diagnosis and the recurrence of symptoms requiring multiple hospital visits. She expressed relief after a definitive diagnosis of systemic lupus erythematosus was established and noted improvement following initiation of corticosteroid therapy.

Informed Consent

Verbal informed consent was obtained from the patient for publication of this case report.

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