

Case Report

Does the "Evans" Bite the Heart?

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Background

Evans syndrome (ES) is a rare hematologic disorder with the coexistence of an autoimmune hemolytic anemia (AIHA), thrombocytopenia and/or neutropenia. The autoimmune destruction can be simultaneous or sequential.[1-3] While the precise pathophysiology is not known, it is assumed to be related to autoantibodies against antigens specific to RBCs, platelets and T-cell abnormalities.[4,5] The symptoms and severity of ES can vary significantly and the syndrome can cause severe life-threatening complications. Common complications are hemorrhage and infections. Cardiovascular manifestations are less common and occur in small percentage of patients. We present a case of myocarditis in a young woman with history of ES. The diagnosis of viral myocarditis with lymphocytic infiltrate was confirmed postmortem. Previously a case of fatal myocarditis following immunosuppressive therapy was reported in a child with ES;[6] myocarditis in adult with ES has not been reported to the best of our knowledge.

Case Presentation

A 32 year old woman non-smoker who was diagnosed with ES at the age of 26. She is status post multiple immunosuppressive therapies (cyclosporine, rituximab, and prednisone) as well as TPO agonist (eltrombopag) and splenectomy. The patient presented with sudden onset of epigastric pain and emesis followed by cardiac arrest requiring prolong resuscitation and mechanical intubation. She was on bactrim and valacyclovir for opportunistic infections prophylaxis. The patient's initial ECG showed ST-segment elevation in antero-inferior leads. On admission the patient's labs were significant for WBC 12.2 10 × 9/l, PLT 149 10 × 9/l, Hb 9.4 g/dl. Troponin was 1.69 ng/ml with peak at 94 over two days. CT scan of the chest showed bilateral diffuse pulmonary infiltrates. Transthoracic echocardiogram revealed that the patient's systolic function was severely reduced with diffuse hypokinesis. The hospital course was complicated by thrombocytopenia, coagulopathy and multiorgan failure. Serial ECGs showed accelerated junctional tachycardia and bidirectional ventricular tachycardia in addition to persistent anterior ST-segment elevation. Over the subsequent four days the patient remained unresponsive on mechanical ventilation. On day five of her hospitalization the patient was found pulseless and she expired after unsuccessful resuscitation efforts. The diagnosis of viral myocarditis with lymphocytic infiltrate was confirmed postmortem.

Discussion

ES first described in 1951 by Dr. RS Evans.[3] While the pathophysiology of the syndrome is not completely understood, it is assumed to be related to possible immune dysregulation with autoantibodies against antigens specific to RBC's and platelets. Frequent cytopenias related to T-cell abnormalities include decrease in helper T cells and increase in suppressor T cells. There is also decreased IgG, IgM and IgA serum immunoglobulins.[2,5,7] ES can occur as a primary (idiopathic disorder) or in association with other disorders such as SLE, chronic lymphadenopathy, hypogammaglobulinemia, autoimmune lymphoprolipherative syndrome (ALPS).[2,8,9] According to the result of national pediatric survey in 1997 the median age at diagnosis was 7.7 years (range, 0.2-26.6 years). Major manifestations of ES were thrombocytopenia, anemia, and to a lesser degree neutropenia, and pancytopenia. The clinical course is significant for periods of remission and exacerbation with frequent recurrences of thrombocytopenia (60%), anemia (31%), neutropenia/serious infections (15%). Due to the rarity of this condition long-term survival data is limited. In patients followed for a median range of 3-8 years, mortality ranged from 7-36%.[10]

Therapy consists of steroids, IVIG, immunosuppressive agents such as cyclophosphamide, azathioprine, vincristine, cyclosporine, mycophenolate mofetil or monoclonal antibodies. Rituximab, a monoclonal antibody against the protein CD20 is reported to be the most successful treatment in current literature.[2,11-13] Alemtuzumab a humanized monoclonal antibody against CD52 has shown some positive effect in refractory cases.[12] Splenectomy is reserved for refractory cases. The allogeneic or autologous stem cell transplantation have been used as a last resort with mixed results.[7]

Common complications are hemorrhage and infections. Serious infection in patients with neutropenia included pneumonia, sepsis, meningitis, and osteomyelitis.[2] Cardiovascular manifestations (ACS, stroke) occur in 21.5%.[2] A

case of fatal myocarditis following immunosuppressive therapy was reported in a child with ES;[6] myocarditis in adult with ES has not been reported to the best of our knowledge. The diagnosis of myocarditis is a clinical challenge by itself often made on the basis of history, clinical presentation, ECG changes, elevated cardiac enzymes in a patient with no evidence of coronary artery disease. The diagnosis is confirmed by MRI/histopathology. It is important to keep in mind that certain groups appear to be at increased risk for fulminant viral myocarditis, particularly those who are immunocompromised and may have a severe illness with hemodynamic compromise.

From primary care perspective, it is important to be cognizant about different presentations and complications of this rare hematologic disorder and what preventive measures should be taken. Due to high risk for fulminant infections and high mortality rate it is especially important to make sure patients with ES are current with routine immunizations according to the Advisory Committee on Immunization Practices.[14] Opportunistic infection prophylaxis in patients on immunosuppressive therapy should be instituted when necessary. Splenectomy patients should be counseled about avoiding dog bites, scratches, and contact with dog saliva to prevent *Capnocytophaga canimorsus* infection and avoiding tick bites in *Babesia* endemic regions in addition to other preventive measures.

Conclusion

Fulminant viral myocarditis in ES with hemodynamic compromise may be related to immunosuppressive state. It is important to be aware of this entity and recognize it promptly. For the primary care physicians it is important to be aware of variable manifestations of this rare disease and undertake preventive measures early. Physicians should have a high index of suspicion for myocarditis in a young patient with no cardiovascular risk factors. Additional case reports like this are needed to provide insights and enhance our understanding of this rare hematologic disorder and improve therapeutic strategies and quality of care for patients with this rare disorder.

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