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Eosinophilic Myocarditis as a Cause of Acute Cardiac Syndromes:

The Importance of Awareness*

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Keywords

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Myocarditis characterized by an eosinophil-rich infiltrate was first associated with adverse drug reactions during the 1940s (1). The diagnosis was most often confirmed after clinical presentation of acute heart failure or sudden death (2). In the subsequent decades, multiple case reports and small case series described eosinophilic myocarditis (EM) in association with other disorders, including eosinophilic granulomatous polyangiitis (formerly Churg-Strauss syndrome), Loeffler endomyocardial disease, parasite infections, and idiopathic hypereosinophilic syndrome (3). Although the spectrum of clinical presentations associated with EM became remarkably broad, the prognosis remained poor.

In this issue of the *Journal*, Brambatti et al. (4) present a reanalysis of EM cases from a systematic review of published reports. These investigators identified 179 patients admitted to hospitals with histologically proven EM. The average age was only 41 years, and most patients presented with dyspnea or chest pain.

Brambatti et al. (4) confirm and quantify the overall poor prognosis of EM and identify clinically important differences in the characteristics of EM subgroups. Hypersensitivity myocarditis (HSM) had the highest rate of ventricular tachycardia (19.6%) and cardiac arrest (44.6%). The in-hospital and overall mortality rate was also the greatest in HSM (36% compared with 22% overall), with 19.7% of patients requiring temporary mechanical circulatory support. This degree of morbidity is greater than one would expect from the severity of HSM histological lesions, which often have less necrosis and a relatively focal, perivascular distribution (5). In HSM, the inflammation often involves other organs, including eosinophilic lesions in the liver and blood vessels that may partially account for the severity of this condition.

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Several of the findings of Brambatti et al. (4) deserve comment and highlight the unique characteristics of this disease group. Thrombosis was much more common than one would expect in typical post-viral lymphocytic myocarditis, possibly because of the prothrombotic properties of major basic protein, contained within the eosinophilic granules. Acute myocardial infarction may be caused by thromboemboli, coronary vasculitis, or coronary spasm, or it may represent regional inflammation. Although 7.7% of the HSM cases in the report by Brambatti et al. (4) were associated with a vaccine, it is important to emphasize that, with the exception of some smallpox vaccines, all clinically available vaccines have an excellent safety profile.

Cardiac magnetic resonance (CMR) imaging findings are often abnormal in acute myocarditis, but the imaging features in EM may be atypical. For example, in the available CMR studies of eosinophilic granulomatous polyangiitis–related EM, the most prevalent delayed enhancement pattern was sub-endocardial, rather than the typical epicardial or midmyocardial pattern (6). Moreover, the value of CMR in identifying focal lesions of HSM remains to be established. Microscopic lesions that can cause arrhythmias may fall below the spatial resolution of CMR. In the setting of suspected acute HSM, quantitative T_1 and T_2 parametric mapping should be used because of the likely better diagnostic performance compared with the standard Lake Louise CMR criteria for myocarditis (6,7).

Endomyocardial biopsy for suspected EM has a 2a (probably helpful) recommendation in the current American Heart Association/American College of Cardiology Foundation/ European Society of Cardiology scientific statement because of the incremental prognostic and probably therapeutic information that can be gained from biopsy (8). The 2013 European Society of Cardiology position statement on management of myocarditis recommends endomyocardial biopsy and suggests obtaining left as well as right ventricular samples (9). The findings of Brambatti et al. (4) strengthen these recommendations.

The study by Brambatti et al. (4) raises several unresolved questions regarding the optimal treatment for EM and its subtypes. First, in this series, 78% of patients received corticosteroids, and a minority had an additional immunosuppressant. It is uncertain to what degree immunosuppression affected outcomes. An area of current investigation not evaluated in this paper is the use of an anti–interleukin-5 antibody that selectively targets eosinophil production (10). Second, 13% of patients had evidence of an intracardiac thrombus. Should patients routinely receive anticoagulant agents given this level of risk? In addition, what is the risk of thromboembolism after left ventricular biopsy in this prothrombotic state? Finally, bridge to recovery after mechanical circulatory support was common. What are the time course and predictors of recovery? Does immunosuppression during mechanical support affect the risk of device infection or the rate of recovery?

In summary, the report by Brambatti et al. (4) helps to raise awareness about the uncommon but life-threatening complications of EM. It is most important to note that only endomyocardial biopsy is diagnostic, and it should probably be performed when EM is suspected. The challenge is suspecting the diagnosis when the serum eosinophil count is elevated in only 76% of cases. One feasible next step would be to investigate a role for novel serum bio-markers, such as major basic protein or eosinophil derived neurotoxin, in addition

to troponins and natriuretic peptides to refine the cohort of patients who should have a biopsy.

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