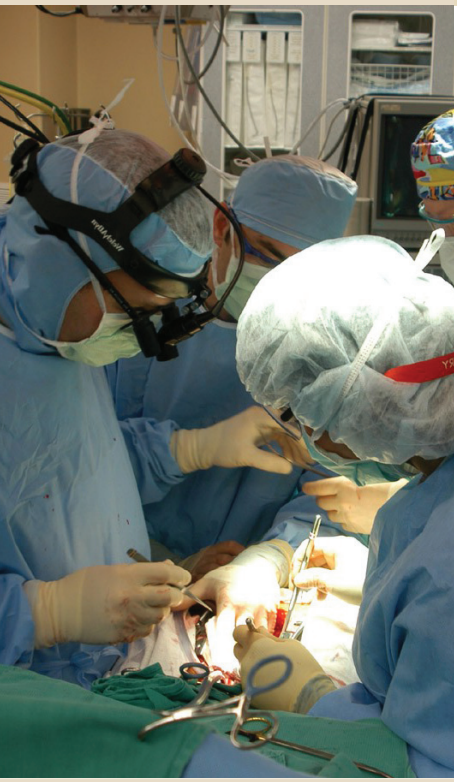
Differential Diagnoses of Eosinophilic Myocarditis in Endomyocardial Biopsies and Accompanying Challenges



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Abstract

Parasitic infections, hypersensitivity myocarditis, and hypereosinophilic syndrome are collectively regarded as eosinophilic myocarditis. Endomyocardial biopsy is the gold standard for the diagnosis in such types of myocarditis, particularly in patients with unexplained heart failure or ventricular arrhythmias.

A number of pitfalls should be remembered by the pathologist, namely a focal lesion in the left side of the heart, which is missed if the biopsy is taken from the right ventricle. Endocardial fibrosis can be a non-specific finding or it may represent a specific pathology such as hypereosinophilic syndrome. In order to overcome this problem, adequate and deep sampling from the myocardium would facilitate its identification. Finally, if superficial sampling of the myocardium is done, the pathologist may only observe pieces of thrombi rather than the myocardium proper. Therefore, one is advised to look for even minute collections of inflammatory cells, including eosinophils in the mural thrombi.

Keywords: Hypereosinophilic syndrome- Myocarditis- Hypersensitivity- Endomyocardial biopsy

Introduction

Eosinophilic myocarditis seems to be an umbrella term, encompassing a varied spectrum of diagnoses. There are three fundamental categories in this setting, namely hypersensitivity myocarditis, hypereosinophilic syndrome (HES), and parasitic infections. However, one must consider a myriad of other conditions which are often associated with eosinophilia in the peripheral blood as well as myocardial involvement. Some types of leukemias and lymphomas, lung carcinoma, or malignant melanoma of the skin are among the neoplastic causes. The Churg-Strauss syndrome and polyarteritis nodosa comprise the vasculitic forms of eosinophilic myocardial involvement (1). These are rare conditions in general, but the pathologist may sometimes be required to examine and evaluate such instances in the endomyocardial tissue specimens and, therefore, it is deemed well-advised to be familiar with the diagnostic pitfalls in such circumstances.

Hypersensitivity is caused by a number of drugs, and in many cases the myocardial inflammation vanishes once the drug is discontinued. This phenomenon is not dependent on the dose or the time of drug administration. It is not frequent in clinical practice, yet occasionally it is documented by endomyocardial biopsy.

The infiltrates in the myocardium are composed of lymphoplasma cells, histiocytes, and a predominant population of eosinophils. The location of the infiltrate is usually interstitial or perivascular. Necrosis is not a major finding, and fibrosis or granulation tissue is not often seen. In some rarer cases, the situation becomes graver with more severe infiltration, edema, and necrosis. The latter is called acute eosinophilic necrotizing myocarditis.

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HES is another entity associated with eosinophilic myocardial infiltration and is further subdivided into two groups, namely Loeffler endocarditis and endomyocardial fibrosis (1 and 5). From another point of view, recent observations have revealed that there are two distinct hematological disorders which involve the myeloid and lymphoid lineages, respectively. Both of these variants account for the hypereosinophilic state in patients who fulfill the diagnostic criteria of this syndrome (2). Some histopathological findings help differentiate hypersensitivity myocarditis from HES. HES has a larger proportion of eosinophils in the inflammatory infiltrate with eosinophilic degranulation often being evident. Microabscess or granuloma formation may be noted too. Myocyte necrosis is prominent. Eosinophils infiltrate the endocardium and also exist in the mural thrombi. A form of restrictive cardiomyopathy is the result of endocardial scar formation. Peripheral eosinophilia and multiorgan eosinophilic infiltration are common as well. The third category of myocarditis with eosinophils in the infiltration is of parasitic nature. Cardiac involvement is similar to hypersensitivity-type reaction with different infections being involved. They range from cysticercosis and hydatid disease to toxoplasmosis and trypanosomiasis (1).

Endomyocardial biopsy is believed to be the gold standard for the diagnosis of eosinophilic myocarditis, although the pathological findings are not always positive. Because the disease often has a focal distribution, biopsy sampling from the right ventricle may miss the left-sided disease. Endomyocardial biopsy is, therefore, essential and should be considered for all patients who present with unexplained heart failure or ventricular arrhythmias (3).

With this background in mind, we now turn our attention to the use of endomyocardial biopsy in the interpretation and diagnosis of eosinophilic myocarditis. HES may be missed for a number of reasons if there is no pertinent clinical information available (1 and 5). First to consider is the endocardium, which may show a fibrous thickening as a result of a combination of fibrosis and elastosis. Endocardial fibrosis can be a non-specific finding or it may represent a specific pathology (4). Adequate and deep sampling from the myocardium facilitates the identification of the lesion. Another finding in endocardium is the presence of ulceration or necrosis as a result of HES. Second, one can find interstitial fibrosis in a certain number of conditions aside from HES. Third is the infiltration of the myocardium by eosinophils, which occurs in myocarditis of the hypersensitivity type, certain infections, and also in fulminant allograft rejection.

Finally, in the case of superficial sampling, the pathologist may come across only pieces of thrombotic material obtained during the biopsy procedure rather than the myocardium proper. One is advised to look for sparse and even negligible collections of inflammatory cells in order not to miss eosinophils in the mural thrombi (5).

Conclusion

Eosinophilic myocarditis encompasses three major categories: hypersensitivity myocarditis, HES, and parasitic infections. Although rare, these conditions should be known to the pathologist, who is sometimes required to evaluate endomyocardial specimens.

Endomyocardial biopsy is the diagnostic gold standard; nevertheless, the pathological findings are not always positive. This can be because of the focal distribution of the lesion, where biopsy sampling from the right ventricle may miss the left-sided involvement.

Endomyocardial biopsy is essential for all patients with unexplained heart failure or ventricular arrhythmias.

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