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# Myocarditis. How do we make a biopsy diagnosis?


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In a Swedish autopsy study the incidence of myocarditis was observed to be 1.06%, while in autopsies of children and young adults the incidence has been reported to be 17-21%. In fact, nobody knows the (true) incidence of myocarditis.

Presenting symptoms and physical examination are often non-specific. Nearly 90% of patients give a history of a flu-like syndrome, but in less than 50% is a Viral disease recognized within the preceding month. The initial presentation may be one of acute or chronic heart (allure or cardiogenic shock or symptoms mimicking acute myocardial infarction. Patients may have life-threatening arrythmias or remain asymptomatic.

Myocarditis is best defined morphologically as an inflammatory involvement of the heart muscle characterized by a leukocytic infiltrate and resultant nonischemic necrosis/degeneration at myocytes.

With the recent onset of unexplained cardiac heart failure, chest pain, or life-threatening arrythmias, of all patients who have endomyocardial biopsy, 5-10% have morphological myocarditis. In the 1995 Task Force of WHO/ISEC on the definition and classification of cardiomyopathies it is said that "inflammatory cardiomyopathy is defined by myocarditis in association with cardiac dysfunction. Myocarditis is an inflammatory disease of the myocardium and is diagnosed by established histological, immunological, and immunohistochemical criteria. Idiopathic, autoimmune and infectious forms of inflammatory cardiomyopathy are recognized". In my view, this means that myocarditis and inflammatory cardiomyopathy are synonyms.

It is evident that the gap between clinical symptoms/clinical suspicion and morphological changes of myocarditis is wide – and in fact so wide, that we should look for the missing link or reconsider our entire concept. The causes of myocarditis are summarized in Table 1.

**Table 1. Summary of causes of myocarditis.**

| | |
|---|---|
| Infectious | All types of microorganism |
| Immune-mediated | Postinfectious<br>Systemic disorders<br>Drug hypersensitivity<br>Transplant reiection |
| Toxic | Drug induced/toxins |
| Other/unknown | Sarcoidosis<br>Giant cell myocerditis<br>Idiopathic |

Unknown causes include special types such as sarcoid heart disease or giant cell myocarditis. However, more often one is not able to explain the process and the case is then dropped in the basket of unknown/idiopathic myocarditis. This is either rational or sufficient investigations have not been carried out (or the methodology is inadequate).

What I think fit for attacking the problem when dealing with endomyocardial biopsies is the following (and of course it is my personal choice):

i) Most of the time the material is formalin fixed. The biopsies must be serially cut.

ii) Routine staining procedures include hematoxylin and eosin, elastic van Gieson's, and trichrome reactions.

ii) Having viewed these sections, special reactions for iron, amyloid, microorganisms etc. may be undertaken.

iv) Immunohistochemical reactions presently performed on fixed tissue nearly as well as on frozen material should include char-

acterization of the mononuclear cells and some basic reactions concerning autoimmunity. There are kits for immunohistological detection of microorganisms (cytomegalovirus, etc.) but *in* situ hybridization and PCR techniques on sections are also available methods in many routine labs.

v) A proper quantification of the biopsy material is important. Qualitative and semiquantitative measures are not always adequate, and correctly used morphometry is essential in this field.

vi) Most important is a meticulous correlation between clinical aspects and morphological results. This dragging exercise must never be forgotten if we want to be wiser.

Unfortunately, I know for certain that these measures are not going to solve the problem of making us understand everything about myocarditis or diagnosing it correctly – but I am convinced that we can improve the situation by using these ordinary tools and consequently reduce the gap of diagnostic frustration.