Endomyocardial Biopsy - When and How?

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The utility of endomyocardial biopsy has been questioned and in many centers is not a common procedure any longer. If one asks why this is so, issues of non-specific pathological diagnoses and significant complication rates are mentioned. In skilled operator hands the complication rate is low (1). With decreasing performance of the procedure, and the resulting lower expertise, such a cycle is self perpetuating. We also risk loss of pathological expertise in the interpretation of these biopsy specimens.

In the past heart biopsies were used for diagnosis and monitoring of Adriamycin drug toxicity, with treatment decisions based upon the degree of cardiomyocyte damage. Such decisions are now made with non-invasive monitoring and imaging. Endomyocardial biopsies continue to be the gold standard for monitoring of cardiac transplant allograft rejection. Even this application is being challenged with the advent of biomarkers.

As pathologists, in this time of translational medicine and personalized health care, we should assume responsibility to provide input concerning the utility of the cardiac biopsy for specific diseases, and provide guidance for tissue triage and investigations including histology, ultrastructural examination, immunohistochemistry or fluorescence, and molecular and genetic investigations, when these are warranted or desired.

The cardiac biopsy should be regarded as complimentary to new developments in cardiac imaging and electrophysiological investigations that may increase biopsy utility. Endomyocardial biopsy for sarcoidosis or arrhythmogenic cardiomyopathy traditionally are considered low yield as sarcoid tends to involve the base of the heart, which is not the area biopsied, and biopsy of the right ventricle free wall and infundibulum is thought to be too risky. (2) Imaging and electrophysiological guided biopsy may change this reluctance.

Cardiac biopsy is useful for differentiating chronic cardiomyopathy from myocarditis in the setting of acute heart failure. Many patients actually have an acute exacerbation of a chronic cardiomyopathy. (1) Although the biopsy findings may not always be specific for a type of cardiomyopathy, such a finding has implications for reversibility, likelihood of recovery, future investigations and perhaps treatment. Giant cell myocarditis can produce a severe acute clinical picture and may be responsive to immunosuppression. Molecular biology and immunological workup of myocarditis and cardiomyopathy are of use in certain situations and if performed should always be accompanied by histology. With developing molecular biology techniques, judicious use of cardiac biopsy may be relevant to decide whether antiviral or immunosuppressive therapy is indicated. (3)

Knowledge concerning the genetics and molecular biology of primary cardiomyopathies are also evolving. Much of the genetic diagnosis will almost certainly be possible by peripheral blood analysis, but somatic mutations do occur, as illustrated by the recent discovery of somatic mutations in connexins in atrial fibrillation. (4)

Endomyocardial biopsy may be helpful for the differentiation between constrictive pericarditis versus restrictive cardiomyopathy. If the hemodynamics or imaging studies
are not clear, an endomyocardial biopsy may demonstrate a myocardial cause for restriction such as eosinophilic and non-eosinophilic primary restrictive cardiomyopathy, amyloid, or iron storage. In constrictive pericarditis such a biopsy specimen would be normal or the myocytes may show atrophy. The cardiac biopsy may spare the patient an unnecessary surgery.

Amyloid may be diagnosed and typed, with treatment implications. Amyloid may be deposited solely in the heart, so a negative extracardiac biopsy (such as a fat aspirate or rectal biopsy) does not rule out cardiac amyloid. Differentiating the amyloid type is relevant. (5,6) AL amyloid is seen in primary amyloidosis and plasma cell dyscrasia, including myeloma. Cardiac transplant in such individuals usually does not have a good outcome, unless the underlying plasma cell problem is also aggressively treated. (7) Transthyretin type amyloid is often age related and is becoming more commonly noted. It is mainly incidental, however this type of amyloid may cause heart failure and be localized solely to the heart.

Fabry disease may be diagnosed by endomyocardial biopsy. Heterozygotes may have unexplained left ventricular hypertrophy and there may be cardiac predominant Fabry’s. With enzyme replacement available, such a diagnosis may have implications for therapy and altering disease course. (8) Neoplasms and cardiac drug toxicity, such as chloroquine toxicity, may also be diagnosed. (2)

The endomyocardial biopsy procedure should not forgotten. It is important to maintain clinical interest and expertise. Pathologists should lead and actively participate in investigating the utility and cost effectiveness of the biopsy specimen and the modalities to obtain the specimen and ultimately a diagnosis for the patient. Future applications are promising and judicious use of this procedure remains an important contributor to care of our patients.

Key Words:
Amyloid
Biopsy
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Genetics
Molecular
Myocarditis
Myocardium

Selected References:


**Bullet Points:**
- Endomyocardial biopsy is a safe procedure
- It is useful in selected indications
- Always interpret the endomyocardial biopsy with clinical information
- Interpret the cardiac biopsy as a “medical” biopsy similar to a liver or kidney biopsy
- Molecular biology and genetics tests should be used with histology, not alone
- Imaging and electrophysiology advances may change how biopsy specimens are obtained and their utility
- Pathologists should lead in determining the utility of cardiac biopsy for patient diagnosis, work up and concurrent use of diagnostic modalities