

Cardiac Amyloidosis from the Pathologist's Perspective

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Abstract

Amyloidosis is a systemic, yet an uncommon and probably underdiagnosed disorder which may have cardiac manifestations drawing the cardiologist's attention to its existence.¹⁻³ Endomyocardial biopsy material is then referred to the pathology laboratory, mainly as a means to establish or confirm the clinical diagnosis.

Although the disease has four major types of clinical presentation, the histopathological findings are the same.

Microscopically, amyloid is deposited in different parts of the heart such as the interstices of the myofibers to endocardium, blood vessel walls, valve structures, and epicardial fat. The SA and AV nodes as well as the bundle branches are also shown to be involved by the deposits.

Based on the routine staining methods, amyloid is pale pink in color and looks homogeneous, distributing in the subendocardial tissue and interstitial myocardium thus producing myocyte compression and atrophy.

Conventionally, the Congo red staining method reveals the characteristic amyloid material under the polarized light, where the apple-green birefringence is noted.

Alcian blue stain, Crystal violet, and thioflavin-T fluorescence are also employed to demonstrate amyloidosis in biopsy samples.¹⁻² (*Iranian Heart Journal 2011; 12 (4):22-24*).

Key words: Cardiac amyloidosis ■ Cardiomyopathy ■ Congo red stain

Amyloidosis is a systemic infiltrative disorder which may be suspected by cardiologists on clinical and imaging grounds, and consequently the samples are referred to pathologists, mainly as material for endomyocardial biopsy. It is more common in men and more usual in later life. The different varieties have in common a wide spectrum of clinical manifestations, but evidently the most frequent presentation is that of

heart failure. Differential diagnosis from other causes of restrictive cardiomyopathy is of paramount importance.⁵

Although the major manifestation of the disease is a restrictive cardiomyopathy picture, it basically has five different types of involvement as follows:

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- 1- The primary form is due to plasma cell dyscrasias and the amyloid deposit consists of the immunoglobulin light chain (AL).
- 2- The secondary form follows long-standing infections where the amyloid material comprises serum amyloid A, an acute phase reactant (AA).
- 3- The third category includes those cases where the genetic and hereditary factors play a role. The type of material deposited is part of the prealbumin transthyretin protein. This protein normally binds thyroxin (AF).
- 4- The senile type may exclusively affect the atria or may also involve the ventricles.
- 5- Here, the symptoms are either few and thus cause no significant problems for the patient or extensive enough as to cause the heart to fail. The atrial natriuretic factor produced by atrial myocytes is the culprit in this group (IAA).
- 6- In a rarer group hemodialysis-related amyloidosis occurs, where the deposit is composed of β 2-microglobulin.^{1-6 & 7}

In all these types of amyloidosis, regardless of the type of involvement, the histomorphology is the same.

Grossly, mild atrial dilation and ventricular wall thickening are detected. The latter acquires a firm and rubbery consistency. If the septum shows an asymmetric thickening, a hypertrophic cardiomyopathy may be mimicked.

Microscopically, the deposition of amyloid occurs in different parts of the cardiovascular system, ranging from the interstices of the myofibers to endocardium, blood vessel walls, valve structures and epicardial fat. Frequently, in the familial form the SA and AV nodes as well as the bundle branches are seen to be involved by such deposits, hence the appearance of conduction disturbances in such patients.

The amyloid material is pale pink in color and looks homogeneous, distributing in the subendocardial tissue and interstitial myocardium thus producing myocyte compression and atrophy. We should remember that in early disease, amyloid deposits may be visible only with electron microscopy.⁶

The meticulous pathologist should also consider the walls of adipocytes, where deposits may accumulate. Sometimes a provident pathologist finds nodular perivascular aggregates of amyloid adjacent to the unremarkable myocardium. Last but not least, attention should be paid to the unusual thickening of the blood vessel walls.¹⁻⁶

Endomyocardial biopsy is doubtlessly a useful diagnostic tool, which brings out not only the extent, but also the severity and pattern of cardiac involvement in amyloidosis patients.^{1 & 4}

Conventionally, the Congo red staining method is used to reveal the characteristic amyloid material under the polarized light. The apple-green birefringence is expected to be seen in the areas which appear pale pink on the hematoxylin and eosin (H & E) stained slides. Alcian blue stain is another special staining method which gives the amyloid nodules a blue green hue. Crystal violet and thioflavin-T fluorescence are also employed to demonstrate amyloidosis in biopsy samples.^{1-2 & 6} Thioflavin-T is a more sensitive method than is the Congo red method; however, it requires fluorescence microscopy.

The differential diagnosis of amyloidosis under the light microscope is with hyalinized

collagen, which may appear similar to amyloid on hematoxylin and

eosin-stained sections. More puzzling is the fact that Congo red may produce false-positive birefringence in collagen if the staining method is not optimal.

Last but not least, we should bear in mind the fact that Congo red staining varies with the type of amyloid.⁶

Conclusion

Amyloidosis is a systemic infiltrative disorder and has at least five different types of involvement, but histomorphology is the same in all types of the disease.

Grossly, mild atrial dilation and ventricular wall thickening are detected.

Hematoxylin and eosin (H & E) stained slides impart a pale pink appearance to amyloid. Subendocardial and interstitial myocardium may show the deposition. Alcian blue, crystal violet, and thioflavin-T fluorescence are employed to demonstrate amyloidosis in biopsy samples.

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