

# Intracellular Cardiac Amyloid - like Deposition in a Young Girl

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## Abstract

Herein we report a significant observation in 12 year old female, clinically diagnosed as a case of restrictive cardiomyopathy. During the histological study of postmortem examination of explanted heart, our attention was diverted to histochemical reaction that demonstrated the presence of a substance within cardiomyocytes of both the atria. Ultra structurally and immunohistochemically it was suggestive of amyloidosis, but in the absence of a positive Congo red stain (CR) and apple-green birefringence, the diagnosis remains unconfirmed. Although rare, atypical intracellular cardiac amyloidosis such as the familial amyloidotic polyneuropathy of the Portuguese type has been documented. Amyloidosis acquired secondary to chronic inflammatory disease like rheumatic cardiac disease is also well known. Herein we report a rare intracellular cardiac amyloid-like deposit in both atria. This is unlike normal Periodic Acid Schiff's (PAS) positive glycoprotein deposition present in cardiac conducting tissue.

## INTRODUCTION

Intracellular accumulation is one of the cellular manifestations of metabolic derangements in pathology. These can be normal cellular constituents, an abnormal substance (exogenous or endogenous) or a pigment. Excess of proteins appear as rounded, eosinophilic droplets, vacuole or masses. Ultrastructurally accumulation of filament protein is evident in ischemic heart. This is due to increased degradation of the intermediate filament protein vinculine.

Amyloid is a pathologic proteinaceous substance, deposited between cells in various tissues and organs in the body in a wide variety of clinical setting. Clinical recognition of Amyloid ultimately depends on its morphological identification. On light microscope, it appears as an amorphous, eosinophilic, hyaline, and extracellular substance. Despite the fact that all deposits have uniform appearance and tinctorial characteristics, it's quite clear that amyloid is not chemically a distinct entity.<sup>1</sup>

To differentiate amyloid from other hyaline deposits (e.g., collagen, fibrin) special stains are routinely done. Congo red imparts a pink or red color to tissue deposits. More specific is apple-green birefringence. Ultrastructurally amyloid is mainly composed of nonbranching fibrils of indefinite length and diameter of approximately 7.5 to 10nm.<sup>2</sup> The P component, a glycoprotein is closely associated with all

forms of amyloidosis. It is responsible for staining with PAS, and is diastase resistant.<sup>1</sup>

Our attention was diverted to the intracellular cardiac PAS positive, diastase resistant material in postmortem examination of the heart in 12-year old female girl. Ultra structurally they were suggestive of Amyloid and were immunohistochemically positive for both kappa and lambda light chains. The significance of this observation is inconclusive. However, certain causative factors have been discussed.

## CASE REPORT

We received postmortem explanted heart of a 12-year-old female. The specimen was distorted, as part of bilateral ventricular outlet was sent to a local pathologist. Grossly right ventricle, interventricular septum and left ventricle were hypertrophied. Both the atria were dilated. Endocardium was thickened. Chordae tendinae and papillary muscle showed mild focal fibrosis. On light microscopic examination, sections from tricuspid and mitral valve revealed focal myxomatous change. Occasional foci of lympho-plasmacytic aggregates in lamina fibrosa were noted. Endocardium showed increased fibrosis, which was extending to adjacent myocardium. No extracellular amyloid like material deposition

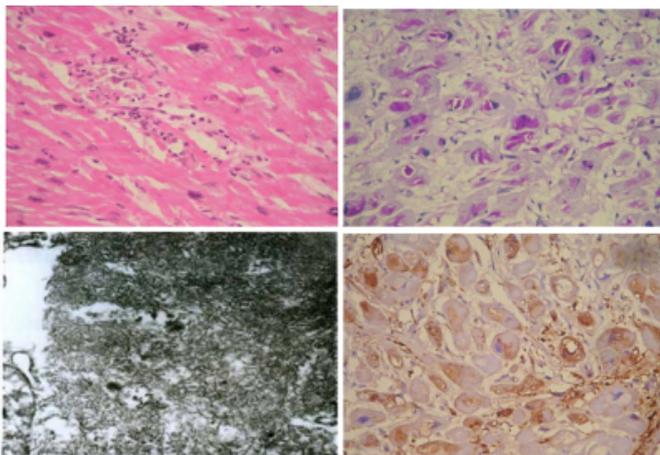
was noted. The myocardium showed mild to moderate myocardial fiber disarray in both the atrium.

Cardiomyocytes showed hypertrophic changes, marked in both the atrium. There was marked interstitial fibrosis with focal atrophic fibers. Focal intracytoplasmic vacuolation was noted. Section from the bilateral ventricles showed increased perivascular fibrosis in addition to minimal hypertrophic changes. Occasional foci showed mild mononuclear infiltrate in ventricular myocardium with associated myocyte damage indicating myocarditis (Fig. 1a).

Our attention was diverted to eosinophilic, hyaline appearing material, marked in both the atrium. It was PAS positive, diastase resistance (Fig. 1b). Sulphated alcian blue stain showed non-specific positivity within these cardiomyocytes. Congo red stain was negative. Electron microscope showed intracellular cardiac deposition of rigid, straight, nonbranching, randomly oriented fibrils with measured diameter of 13 nm (Fig. 1c), suggestive of amyloids. These fibrils were different from normal cardiac myofilaments. Immunohistochemistry for kappa (Fig. 1d) and lambda were done which predominantly showed intracardiomyocyte positivity for both these light chains.

### Figure 1

Figure 1: (a) Section showing focal mononuclear infiltrate with cardiomyocyte damage in ventricles (High power view 40x, H&E). (b) PAS positive, diastase resistant amyloid-like material in atrium (High power view 40x). (c) Ultrastructure showing nonbranching, rigid filaments. (d) Intracellular positivity for kappa light chain (High power view 40x, IHC).



### DISCUSSION

All fibrils identified on ultrastructurally do not represent amyloid. The finding of fibrils on electron microscope is strongly suggestive, but in the absence of a positive CR stain and apple-green birefringence, the diagnosis remains unconfirmed.<sup>2</sup> Electron microscope of heart tissue may

reveal fibrils that resemble amyloid except that they have larger diameter. Characterization of amyloid deposits as to their type is possible by use of Immunohistochemistry. The pathogenesis of light chain deposits (LCDD) is similar to that of primary amyloidosis. Ultrastructurally these deposits are nonfibrillar.<sup>3</sup>

In our case, local pathologist had diagnosed these findings in favor of Glycogen storage disorder. Some subtypes of GSD (e.g. Cori disease, Danon disease, Amylopectinosis, etc.) accumulate glycogen having an abnormal structure.<sup>4</sup> These deposits stain with PAS and at least their central portion are diastase resistance. In amylopectinosis (Type IV glycogen storage disease), cardiomyocytes ultra structurally show glycogen particles and rosettes, as well as 6nm wide filaments separated from myofilaments by electron-lucent areas. These deposits are not membrane bound in comparison to usual membrane-bound lysosomal glycogen.<sup>5</sup> Light microscopic examination shows cardiomyocytes to contain colorless or basophilic deposits that are spherical to irregular.

Microfibrillar cardiomyopathy is characterized by interstitial, subendocardial, and perivascular deposits. These deposits do not stain with Congo red. They have ultrastructural features distinct from amyloid; consist of bundles of microfibrils up to 17nm wide.<sup>6</sup> These fibrils on immunohistochemistry are identified as fibrillin microfibrils. There are case reports fibrillary/ Immunocytoid glomerulopathy with cardiac involvement. Myocardial biopsy specimens demonstrated interstitial deposits of randomly arranged fibrils with average diameter of 13nm.<sup>7</sup> Studied have evaluated the presence of amyloid in both the atrium in patients with rheumatic heart disease.<sup>8</sup> The heart may be infiltrated in different forms including hereditary amyloidosis.

In our case we do not know yet, either this is a genetic or acquired secondary to rheumatic disease or to non specific myocarditis. Literatures do describe hereditary amyloidosis such as the familial amyloidotic polyneuropathy of the Portuguese type, with intracellular cardiomyocyte deposits.<sup>9</sup> A study has shown an additional constituent of conducting tissue, may be a glycoprotein, which is PAS positive, diastase resistant material.<sup>10</sup> We have not come across any intracellular cardiac deposits present mainly in atrium. Ultrastructurally accumulation of filamentous proteins is evident in ischemic heart.<sup>1</sup> We consider this fibrillar material as amyloid-like glycoprotein which is limited to atrium.

Ultrastructurally nonbranching pattern was noted in our case.

To conclude, "Amyloid is not a single disease entity; rather it is group of diseases having in common the deposition of similar-appearing protein". In light of these findings we feel ultrastructural findings needs to be sorted in all cases of Idiopathic restrictive cardiomyopathy. However, future studies should be able to tell us whether the intracellular amyloid-like glycoprotein deposits had any influence on the course and prognosis in our case.

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