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Review Article

Cardiac amyloidosis: A comprehensive review ☆

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ABSTRACT

Cardiac amyloidosis is characterized by clinically significant extracellular amyloid infiltration of the heart that is usually, but not always, associated with the involvement of other organs depending on the type of amyloid. Cardiac involvement represents the most important prognostic factor especially in AL amyloidosis and thus early diagnosis of amyloid heart disease is of utmost importance influencing further management of the patients. This review aims to broadly discuss pathogenesis, manifestation and complex diagnostics of amyloidosis with the main focus on amyloid cardiomyopathy. Also, the summary of current therapeutic options that have great potential to improve existing poor prognosis of affected individuals is given.

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1. Introduction

The amyloidoses are a group of diseases which are caused by extracellular deposition of a similarly appearing morphologically indistinguishable material called amyloid. Amyloid consists of approximately 95% of fibrils formed by an aggregation of misfolded insoluble proteins, the remaining 5% being the P component (pentameric protein, member of the pentraxins family of serum proteins) and other glycoproteins such as proteoglycans and sulfated glycosaminoglycans [1]. The protein fibrils can be made of more than 28 different unrelated proteins which misfold in parallel or as an alternative to physiologic folding. P component may contribute to amyloid deposition by stabilizing the fibrils and decreasing their clearance [2–4].

Under the light microscope the amyloid appears as an eosinophilic amorphous substance in hematoxylin–eosin stained sections. Amyloid binds Congo red dye and when stained produces apple green birefringence under polarized light, which is used as "gold" standard in diagnosis (Fig. 1) [1].

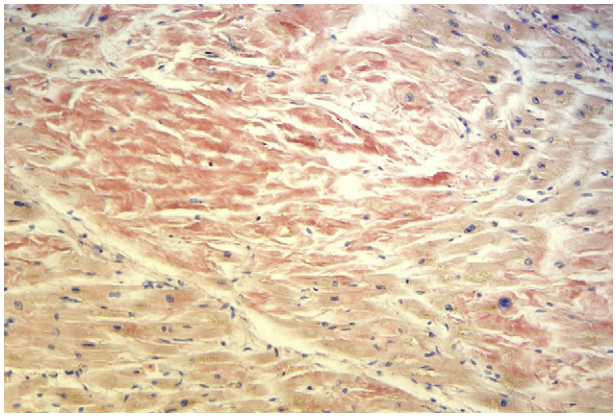

Fig. 1 – Amyloid infiltration of the myocardium (Congo red stain, original magnification × 200).

The affinity to Congo red dye is caused by special β-pleated sheet confirmation of amyloid, as could be seen by X-ray crystallography. Ultrastructurally, randomly oriented fibrils with a diameter of 7.5–10 nm can be shown by electron microscopy (Fig. 2). Thioflavin T is another molecule which binds amyloid fibrils but is less frequently used than Congo red. The Congo red staining and ultrastructural examination is used for routine histopathologic diagnosis; however, it cannot differentiate between amyloid subtypes [5].

The classification of amyloid is based on the immunohistolabeling techniques with a panel of antibodies against known amyloidogenic proteins or proteomics techniques (Fig. 3) [6–8].

2. Types of amyloidosis and heart involvement

Based on the spectrum of involved organs amyloid diseases can be divided into systemic amyloidosis, where amyloid deposits can be found in different organs and tissues, and localized forms with the deposits present in only one particular tissue or organ [9]. The nature of the diversity of organ and tissue involvement still remains unclear [10]. The heart is frequently the predominant organ affected; however, in some types of amyloidosis, isolated heart involvement can occur. Amyloid deposition in the heart may occur in all anatomical distributions, including the atria, ventricles, and perivascular space as well as valves and conduction system in some cases [11]. Regardless of the type of systemic amyloidosis, the presence and severity of amyloid cardiomyopathy is the major factor influencing prognosis of affected subjects [11–13]. According to consensus opinion from the 10th International Symposium on Amyloidosis, cardiac involvement is described as either a positive cardiac biopsy demonstrating amyloid infiltration or as an increased left ventricular (LV) wall thickness > 12 mm in the absence of