III.2 CARDIAC INVOLVEMENT IN AMYLOIDOSIS

Rodney H. Falk

Department of Clinical Cardiology
Boston City Hospital
Boston University School of Medicine
Boston, MA 02118, U.S.A.

1. Introduction

Amyloid infiltration of the heart is the leading cause of death in patients with systemic amyloidosis. Symptoms of congestive heart failure are frequently the presenting feature of AL amyloidosis, but, because of the rarity of the disease the etiology may go unrecognized unless the clinician is particularly alert. Prior to the widespread use of echocardiography, cardiac amyloidosis was often initially diagnosed as constrictive pericarditis because of several shared clinical features. Attempts to differentiate these two entities by hemodynamic characteristics found at cardiac catheterization were generally unrewarding, due to an overlap in supposedly "specific" abnormalities (1-4).

In the past decade, M-mode and two-dimensional echocardiography have become routine tools for the assessment of cardiac disease. Echocardiography has been able to distinguish cardiac amyloid from constrictive pericarditis, and several features have been described which, when present, are considered to be highly suggestive of cardiac amyloid (5,6). Additional methods for the diagnosis of cardiac amyloid have also been described utilizing radionuclide techniques (technetium - 99m - pyrophosphate) (7), electrocardiographic criteria (8), computerized tomography of the heart (9) or endomyocardial biopsy (10). In this chapter the emphasis will be on the clinical manifestations of cardiac amyloidosis and its diagnosis. However, for a more complete understanding of the spectrum of cardiac amyloidosis a brief review of its prevalence in the various forms of systemic amyloidosis is in order.

2. Cardiac involvement in the various forms of amyloidosis

Microscopic deposits of amyloid in various body tissues is a normal accompaniment of aging. In the cardiovascular system three distinct types of age-related amyloid have been described. These are senile aortic amyloid (11), isolated atrial amyloid and senile cardiac amyloid (12). In an unselected group of 85 hearts, taken consecutively from autopsies on patients aged 80 years and above (13), senile aortic amyloid was present in all patients. Isolated atrial amyloid (IAA) usually involving both atria to a very mild degree was present in 78% of cases. One-quarter of the hearts studied had evidence of senile cardiac
Section III, Chapter 2

Amyloid (ASC1) which involving both the atria and ventricles. Cardiac involvement was generally in the form of discrete focal interstitial or vascular deposits and did not appear to have been clinically significant in the patient group studied.

Senile cardiac amyloid may, in rare instances, be associated with heart failure. In such cases myocardial infiltration is extreme. Unless this diagnosis is borne in mind the rarity of involvement of extracardiac tissues may make premortem diagnosis difficult.

Primary and myeloma-associated (AL) amyloidosis is the form of amyloidosis most frequently associated with cardiac involvement. Up to 90% of patients with AL amyloid have evidence of cardiac infiltration, and approximately half of all cases will die of cardiac disease (14,15). The presence of congestive heart failure in AL amyloid is the least favorable of all clinical features (including nephrotic syndrome and orthostatic hypotension). Cardiac symptoms correlate with echocardiographic abnormalities which generally indicate extensive myocardial amyloid infiltration (16-18). In patients with AL amyloid dying of congestive heart failure the heart is typically firm and rubbery, with thickened walls and a normal ventricular chamber size. The atrial septum may show considerable thickening due to infiltration (Fig. 1) and microscopic examination of myocardium may show massive replacement of cardiac tissue by sheets of amyloid. Unlike senile cardiac amyloid, cardiac AL amyloid is usually associated with extracardiac amyloid deposition although this may, on occasion be subclinical.

![Typical echocardiogram in AL cardiac amyloidosis. Left panel shows the heart viewed from the cardiac apex, and right panel from the subcostal view.](image)

The right and left ventricular cavities (RV and LV) are normal in size with an increased wall thickness. The right and left atria (RA and LA) are somewhat dilated with a marked interatrial septal thickening (IAST) of 12-15 mm (normal < 5 mm). The left ventricular walls show the granular, increased echogenicity typical of cardiac amyloid (echocardiogram courtesy of Dr. Jonathan Plehn).

Familial amyloid polyneuropathy (FAP) very frequently involves the heart although clinical heart failure is much less common than in AL amyloidosis. In autopsy studies cardiac involvement is almost always present, and echocardiographic and scintigraphic abnormalities have...