MULTIPLE MYELOMA AND CARDIAC AMYLOIDOSIS

A 77-year-old white male, non-smoker with a two-year history of multiple myeloma (diagnosed by agarose electrophoresis with a finding of a monoclonal-free lambda light-chain in the gamma globulin region from a urine sample) presented with a six-month history of progressive dyspnea on exertion, fatigue, peripheral edema and enlarging abdominal girth. His oncologist reported clinical remission of the multiple myeloma but was referred to a nephrologist for evaluation of modest renal dysfunction (BUN 35, creatinine 2.5). Fluid retention and renal function subsequently improved with diuretic therapy. There was no prior history of cardiovascular disorder or hypertension. He had been a strenuous exerciser all of his adult life.

Physical examination revealed a right-pleural effusion, hepacomegaly, mildly positive HJ reflux and 2+ peripheral edema below the knees. No heart murmur or extra heart sound was heard. An electrocardiogram (Figure l) indicated non-specific ST-T changes, low voltage and QS VI through V3.

An echocardiogram (Figure 2) indicated concentric LVH, normal right- and left-ventricular chamber size and function, and mildly enlarged atria. PA pressure was estimated at 44 mmHg. Doppler findings were consistent with diastolic dysfunction manifested by impaired left-ventricular relaxation and marked increase in left-ventricular filling pressures(> 25 mmHg). Most striking was the speckled or granular appearance of the myocardium, consistent with a diagnosis of cardiac amyloidosis. No additional diagnostic studies were performed.

Six months after the onset of heart failure symptoms and four months after diagnosis by echocardiography, the patient remains alive. Present therapy consists of supportive measures.

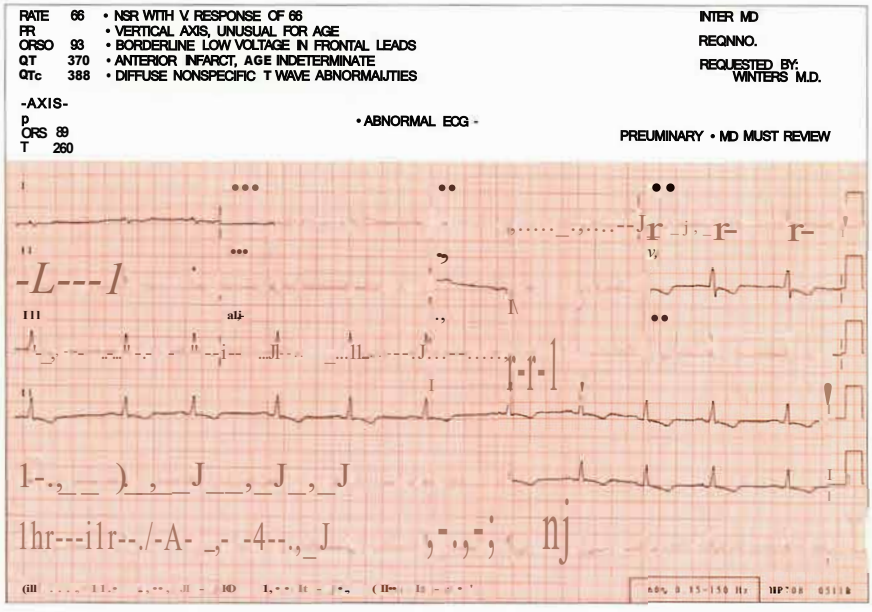
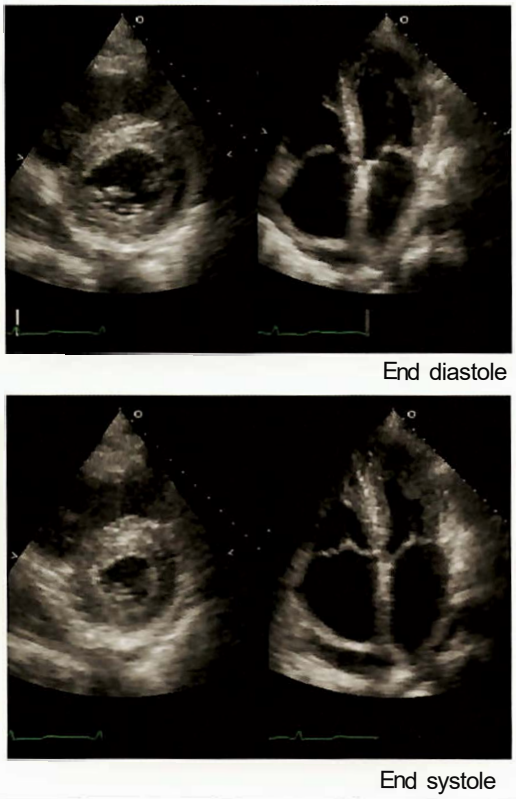


Figure 1.
ECG with low voltage; diffuse, no-specific ST-T changes. OS, VrV3.



End diastole

End systole

Figure 2.
Echocardiogram. x section left: 4 chamber right. End-diastole. Speckled, granular appearance of the myocardium. Thickening of the ventricular walls, VS, atrial septum and valve leaflets.

Pathology: Deposition of protein myofibrils diffusely in the myocardium. The fibrils are immune globulin light chains often associated with multiple myeloma. Most cases involving the myocardium occur in primary amyloidosis. Cardiac involovement is often the main determinant of prognosis.

Demographics: M/F (60/40), median age 60 - 90 {M & F); age range 30-90 years; 97% over the age of 40. Caucasian 94%.

Tell-tale Signs: Macroglossia, periorbital ecchymoses, carpal tunnel syndrome.

Multisystem Features: Isolated heart involvement {uncommon). Renal: proteinuria, nephrotic syndrome. Neurology: autonomic neuropathy (anhydrosis, orthostatic hypotension, syncope). Gastrointestinal: hepatomegaly, diarrhea, weight loss. Hematology: multiple myeloma (uncommon).

Cardiovascular Symptoms: Fatigue, dyspnea, orthopnea, chest pain atypical fur coronary ischemia. Coexisting CAD is uncommon. Sudden death (30%) not predictable by QTc interval or V T on Holter monitor.

Cardiovascular Findings: Findings of right heart failure predominant; most common findings (hepatomegaly, pleural effusion, peripheral edema, ascites, elevatedJVP); S3, S4, systolic murmurs, pulmonary congestion, supine hypotension (14%); postural hypotension (40%).

Chest X-ray: Cardiomegaly, pleural effusions.

Elecuocardiogram: Abnormal in 96%, lowvolrage (71%), pseudoinfarcrion pattern (75%). Inrramyocardial vessel infiltration by amyloid may cause small vessel disease, R or LBBB (6%), 1st, 2nd, or 3rd AV block (25%).

Holter Monitor: Ventricular tachycardia (26%) documented in sudden or non-sudden death.

Echocardiography:

- Frequently diagnostic.
- Increased myocardial echogenicity with a granular, speckled, sparkling or ground-glass appearance (65%) (diagnostic), thickened ventricular septum (86%), ventricular walls, atrial septum, valve leaflets.
- Normal ventricular chamber size (97%).
- Normal systolic function (LVEF over 85% in 55%).
- Increased LV mass. Dilated atria.
- RV enlargement: lace sign, severe disease, decreased survival

Doppler Flow: Restrictive filling pattern and impaired relaxation consistent with diastolic dysfunction. Mild to moderate incompetence common for all valves.

Survival: Median duration survival (M/F) following diagnosis of primary amyloidosis: 1.08 (0.83-1.25) years (95% C.l.). Sudden death: 34%. Survival in absence of heart failure: 2.34/1.56-2.92 years. When heart failure appears (33%) survival: 0.75 (0.59-1.00) years.

Predictors of Survival: Multivariate analysis: LV wall thickness, derived LV mass, EF. Doppler: Shortened mitral E-wave deceleration, increased E/A ratio.

For additional information or pathology and therapy, refer to these resources.

RESOURCES

1. *Otto CM The practice of clinical echocardiography. 2nd edition. W.B. Saunders Co., Phi/,adelphia, PA 2002; chapter 28:625-628.*
2. *Dubrey SW, Cha K, Anderson], Chamarthi B, Reisinger], Skinner M, Falk RH The clinical features of immunoglobulin light-chain (AL) amyloidosis with heart involvement. QJ Med 1998; 91:141-157.*
3. *Palladini G, Campana C, et al. Serum n-terminalpro-brain natriuretic peptide is a sensitive marker of myocardial dysfunction in AL amyloidosis. Circulation 2003; 107(19):2440-2445.*
4. *Kayaina], Ray-Sequin PA, Falk RH Longitudinal myocardial fanction assessed by tissue velocity, strain, and strain rate tissue Doppler echocardiography in patients with AL (primary) cardiac amyloidosis. Circulation 2003; 107(19):2446-2452.*