A case of cardiac amyloid: 'sparkling heart'

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A 63-year-old Caucasian male was admitted to the medical admissions unit with symptoms of dyspnoea on exertion, orthopnoea and paroxysmal nocturnal dyspnoea. Clinical examination on presentation was consistent with congestive cardiac failure (CCF), with bilateral respiratory crepitations and pedal oedema extending to the sacrum. Other notable examination findings were bilateral parotid swelling and submandibular lymphadenopathy. He had a known history of aortic stenosis, obstructive sleep apnoea and IgG paraproteinemia.

The initial plan was for a trans oesophageal echo cardiogram, however on cardiologist review of a recent transthoracic echo cardiogram, the nature of the problem was revealed. The very silvery, sparkling appearances on these images were strongly suggestive of cardiac amyloidosis. This diagnosis was confirmed with rectal biopsy by the National Amyloidosis Centre in London.

Figure 1 Cardiac amyloidosis: echo parasternal view showing silvery appearance of interventricular septum

Amyloidosis is a disease characterised by the deposition of amyloid, an insoluble abnormal fibrillar protein, in body tissues. It is a rare disease, with a reported annual incidence of 1-5 cases per 100,000 people. The ratio of affected men to women is 3:2 and the diagnosis is often made within the sixth decade of life.⁽¹⁾ The amyloid fibrils adopt specific configuration which have characteristic histological changes. Morbidity and mortality from this condition stems from the variety of tissues in which amyloid can be deposited, including heart, kidney, liver and the autonomic system.

There are two basic type of amyloid proteins: the primary form, known as AL, and what is often referred to as secondary or AA type. There is a recognised association of the AL type to plasma cell dyscrasia. AL amyloidosis is closely related to multiple myeloma, with 10-15% of patients with myeloma and Waldenstrom macroglobulinemia also found to have the disease.⁽²⁾ AA occurs as a late complication of chronic inflammatory disorders such as rheumatoid arthritis and

systemic lupus erythematosus. Cardiac involvement has been identified in 22-34% of AL patients in one study,⁽³⁾ but these figures are currently accepted to be as high as approximately 50% of cases.⁽⁴⁾ The incidence of cardiac involvement in the AA type is much lower, approximately 5%.

The clinical presentation of AL amyloid diseases is usually dominated by signs of right-heart failure. The pressure in the left heart is elevated but pulmonary oedema is rare.⁽⁵⁾ Deposition of amyloid in the coronary arteries can lead to angina. Patients with cardiac amyloidosis are said to present with jaw claudication. There are a few other idiosyncratic feature of amyloid heart disease that can lead the unwary astray. Significantly, coronary angiography is often normal as the disease afflicts small intramyocardial vessels, rather than epicardial vessels.

Syncope and pre-syncope is common. Exertional syncope is an ominous sign as it is indicative of severe restrictive cardiomyopathy and associated with high mortality. Life-threatening arrhythmias may also occur from disruption to cardiac conducting tissue with a study finding infra-His prolongation an independent risk factor for sudden cardiac death.⁽⁶⁾ Electromechanical dissociation can result in atrial mechanical failure and subsequent thrombus formation even despite maintenance of sinus rhythm. Embolic stroke due to intra-cardiac thrombi is common.

Physical examination may reveal a number of findings, including; elevated jugular venous pressure, hypotension due to low cardiac output and orthostatic hypotension, which suggests concomitant autonomic neuropathy. A right-sided heart third-heart sound is occasionally heard.

Investigation findings may demonstrate a moderately enlarged cardiac silhouette on chest radiograph or can be normal. The most common investigation finding is a low voltage electrocardiograph (ECG) trace, which is seen in almost 50% of patients. Other abnormalities include conduction abnormalities such as 2nd and 3rd degree AV block, atrial fibrillation and pseudo infarct pattern.

Echocardiography is the non-invasive test of choice to diagnose cardiac amyloidosis. Increased left ventricle wall thickness with evidence of diastolic dysfunction is the earliest abnormality seen and right sided systolic dysfunction can occur. In more advanced cases, wall thickening progresses resulting in restrictive cardiomyopathy and a non-dilated small LV cavity. Bi-atrial enlargement can occur as well as right ventricle dilatation and mitral and aortic valve leaflet thickening. Cardiac infiltration increases myocardial echogenicity, a so-called 'granular sparkling' or 'silvery' appearance. Intra-cardiac thrombi are common in cardiac amyloidosis and can be seen on echo.

Traditional nuclear imaging Tc is not diagnostic but can show unexpected isotope uptake during a nuclear imaging done for some other indication. Cardiac MR is not very useful in early

stages but can show Gadolinium enhancement in late stages. The 'gold standard' diagnostic test of choice is tissue biopsy. The diagnosis can be confirmed by demonstration of amyloid deposit on endomyocardial biopsy or in patients with appropriate cardiac findings, by demonstrating amyloid deposits on histological examination of a biopsy from other tissues such as abdominal fat pad, rectum or kidney.^(7,8)

Biochemical markers include abnormal renal and liver function tests and clotting profiles. Inflammatory markers may be raised. Bone marrow aspirates may demonstrate clonal proliferation of plasma cells, with gamma greater than kappa. Urinalysis may reveal proteinuria from renal involvement and may display light chains on electrophoresis. Serum electrophoresis should also be performed.

Treatment of symptomatic cardiac amyloidosis is ineffective and consists of supportive measures; with diuretics being the mainstay of treatment in AL associated cardiac failure.⁽⁹⁾ Beta-blockade and calcium channel blockers are also generally of little use and often worsen clinical state. However, certain cardiovascular medication should be used very cautiously in these patients. Digitalis, nifedipine and verapamil can induce severe ventricular dysfunction. Angiotensin converting enzyme inhibitors (ACEI) cause severe postural hypotension possibly by exposing a subclinical autonomic neuropathy. Amiodarone seems to be poorly tolerated for rhythm disturbance in amyloidosis. All patients with intra-cardiac thrombus should be assessed for anticoagulation.

Treatment of the underlying plasma cell dysfunction and subsequent reduction in amyloid deposition using chemotherapy offers another course of management. However, this can have a detrimental effect in terms of congestive heart failure with increased fluid retention found in the use of dexamethasone with melphalan, lenalidomide or bortezomib which are most widely used for AL. Stem cell transplantation may also be considered in certain patients, usually those with less organ involvement, younger age and minimal heart failure and renal impairment. In cases of symptomatic bradycardia, pacemakers may be indicated. Amyloidosis has been reported to cause approximately 1 in

1000 (0.1%) of deaths in the UK.⁽¹⁰⁾ The prognosis in AL amyloidosis is dictated by the number of organs affected and the severity of involvement.

Cardiac involvement in AL amyloidosis has the worst prognosis, with a median survival of approximately six months from onset of congestive cardiac failure.⁽¹¹⁾ The prognosis is especially poor in patients demonstrating left ventricular wall thickening, syncope and raised troponin levels. However, survival can increase to a median of 18 months in treated patients.⁽⁷⁾ Research is still in progress to improve clinical outcome for these patients, with animal studies reported to show promising results in terms of preventing amyloid precursor formation and degradation of existing amyloid deposits.⁽¹²⁾ Recognition of this disease as a possible differential diagnosis is important as evidently, management is very different from that of other causes of heart failure.

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FURTHER READING

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