SYSTEMIC AMYLOIDOSIS WITH SEVERE AMYLOID HEART DISEASE – A CASE REPORT

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ABSTRACT

Cardiac Amyloidosis was first observed by Vichow in 1957. Since then many more cases have been documented, but there has been no case report of mortality from severe cardiac involvement in the local literature. We describe one such case seen in the Singapore General Hospital and review briefly the clinico-pathological data on this uncommon entity.

Key Words: Amyloidosis, Amyloid Heart Disease

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INTRODUCTION

Systemic Amyloidosis frequently involves the heart and results in death in approximately 50% of patients with AL (primary) amyloidosis (1). The terminal event in amyloid heart disease is intractable congestive heart failure or sudden death (2). In this paper we report a case of systemic amyloidosis presenting with predominantly cardiac complications.

CASE REPORT

A 60 year old Malay male was admitted to the Singapore General Hospital with congestive cardiac failure. He had been unwell over the preceeding 6 months; with breathlessness on exertion, weight loss and hoarseness of voice. There was no family history of a similar illness.

Examination revealed a chronically ill man. Scattered erythematous and telangiectatic patches were observed over the trunk. The arterial pulse was irregular, 90 per min, with a blood pressure of 110/70 mmHg. The jugular venous pressure was elevated 7 cm above the sternal angle. The heart sounds were dual and well heard. A right pleural effusion was present. The liver was palpable 1 cm below the right costal margin but not tender. Ascites was detected. There was sacral and ankle oedema. The voice was hoarse but the cranial nerves were intact. Laryngoscopy however revealed injected vocal cords. The tongue was not enlarged. Peripheral neuropathy was evident with thickened ulnar and common peroneal nerves. A chest radiograph (Fig 1) revealed moderate cardiomegaly, pulmonary – venous congestion and a right pleural effusion. The electrocardiogram (Fig 2) showed atrial fibrillation with low QRS voltages in the limb leads and poor progression of R waves from leads V1 to V5. The two dimensional echocardiogram revealed thickened right and left ventricular walls with a 'granular sparkling' appearance and thickened valves (Fig 3). The ventricular dimensions were normal whilst the atrial cavities were dilated. There was globally reduced left ventricular function. This was confirmed by radionuclide ventriculography which showed diffuse hypokinesia and an ejection fraction of 35%.

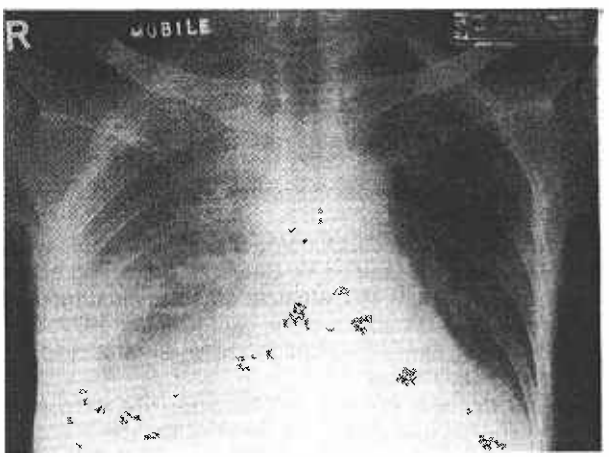

Fig. 1: CXR showing moderate cardiomegaly with pulmonary-venous congestion and a right-sided pleural effusion.

Results of the haematological investigations were normal, and the ESR was 12 mm in one hour. The total protein was 6.6 g/l and albumin 3.4 g/l; protein electrophoreisis was normal but immunoelectrophoreisis detected mild elevation of IgG (1820 mg/dl; range 760-1600 mgm/dl). Bence-Jones proteins were not detected in the urine. Liver and renal function tests were normal. Clotting profile was also unaffected. A D-xylose absorption test gave a 5 hour urinary excretion of 0.7 g of xylose suggestive of subclinical malabsorption.

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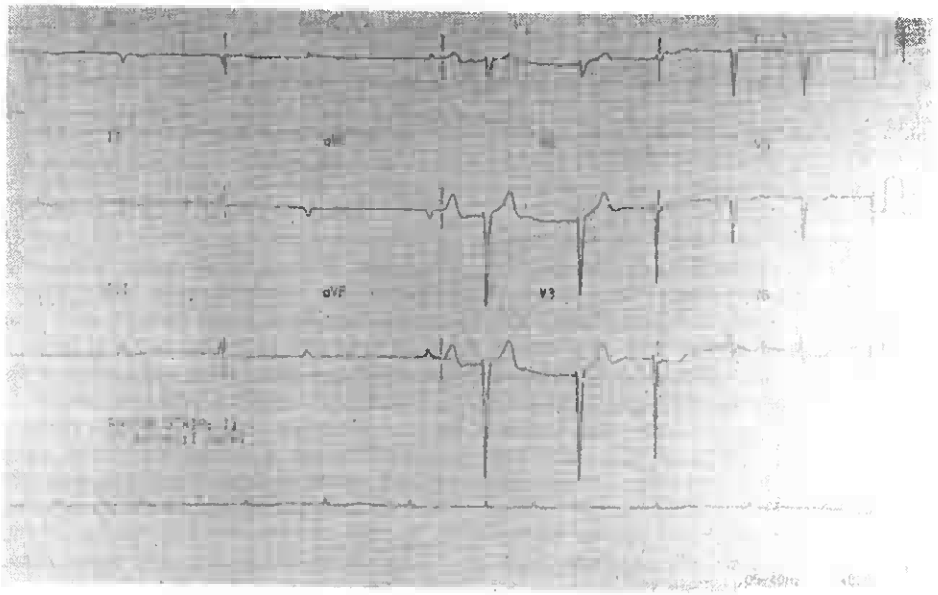
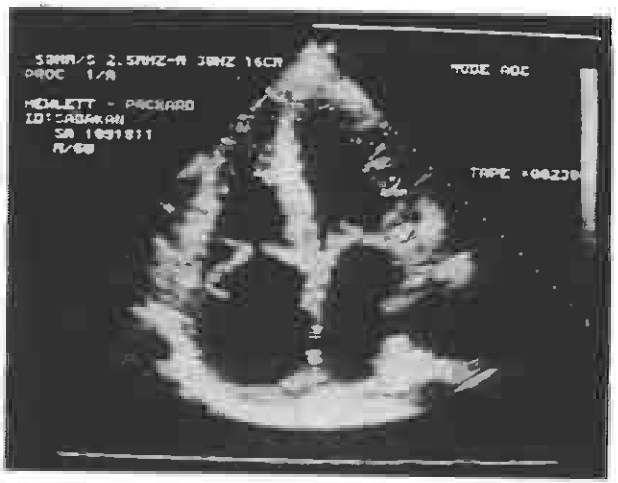


Fig. 2: ECG showing the patient in atrial fibrillation. The QRS voltages in the limb leads are low with poor R wave progression in the anterio-septal leads.



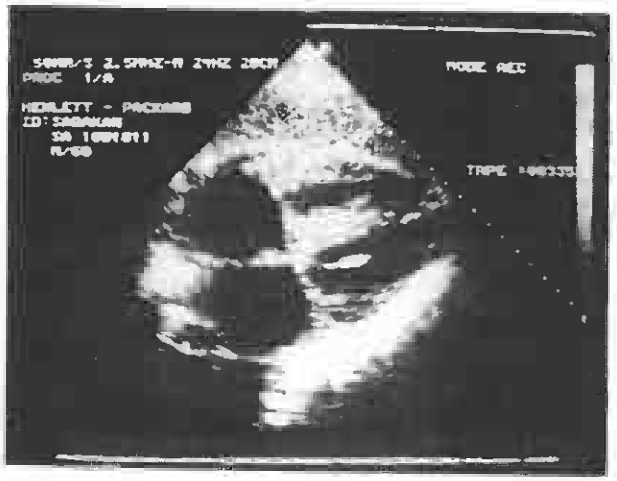


Fig. 3: Echocardiography.
(a) Apical 4-chamber view.
(b) Subcostal view.
Both views show reveal thickened right and left ventricular walls with a 'granular sparkling' appearance and thickened heart valves. The ventricular dimensions were normal while the atrial cavities were dilated. These findings are pathognomonic of cardiac amyloidosis.

Fluid aspirated from the right pleural and peritoneal cavities was transudate. Microscopic examination and bacteriological cultures were negative.

An initial rectal biopsy was negative for amyloid but biopsies from the tongue, gingivae and skin showed the characteristic apple-green birefringence when stained with alkaline congo red and viewed in polarized light (Fig 4). The tissues retained this property despite preincubation with potassium permanganate. This method excludes systemic AA amyloidosis (3).

There was no consent for cardiac catheterization to document the degree of haemodynamic impairment.

The patient had some symptomatic improvement with diuretics and fluid restriction but remained bedridden because of impaired effort tolerance. On the 26th day of hospitalization he suddenly collapsed and died. Resuscitation with ECG monitoring showed recurrent ventricular fibrillation despite DC version. Permission for autopsy was not granted by the relatives.

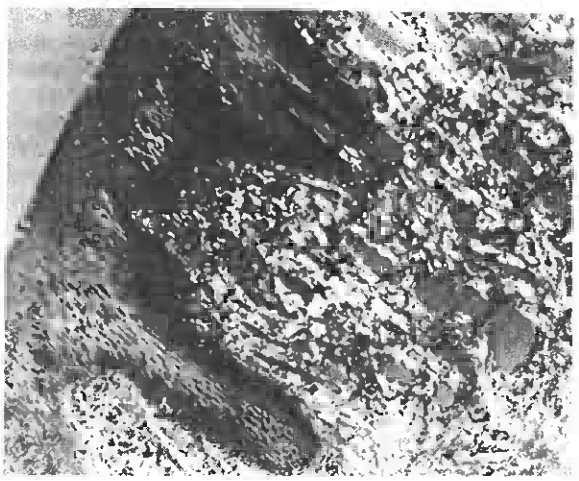


Fig. 4: Skin biopsy.
The specimen was stained with Congo Red. Polarised light gave areas of birefringence in the dermal connective tissue indicating deposits of amyloid between blood vessels (arrows).

DISCUSSION

Amyloidosis is a disorder characterized by the extracellular deposition of an abnormal protein material. Involvement of vital organs by such deposits can cause serious morbidity and mortality. Current classification of amyloidosis is based on chemical composition of the amyloid fibrils using immunohistochemical techniques (4).

Pathologically, the heart is involved in the majority of patients with systemic amyloidosis; 90% of cases of AL amyloidosis and 54% of AA amyloidosis (1).

Significant cardiac amyloidosis however, is present in 50% of cases of AL amyloidosis. It commonly presents as a restrictive cardiomyopathy with signs and symptoms of right ventricular failure, often resembling constrictive pericarditis. Previously these two conditions could only be differentiated by cardiac catheterization (5). With the advent of echocardiography, it is possible to make this distinction non-invasively (6, 7).

The degree of cardiac involvement can be further gauged in a non-invasive manner by radionuclide scintigraphy as severe cases tend to exhibit a diffuse myocardial technetium-99m-pyrophosphate uptake of equal or greater intensity than that of the ribs (8, 9).

Despite the lack of haemodynamic data from cardiac catheterization and an endomyocardial biopsy in our patient we felt that we had enough evidence for a diagnosis of significant cardiac amyloidosis viz: clinical signs of chronic congestive heart failure, distinctive echocardiographic findings and the positive tissue biopsies in the non cardiac tissues.

It has also been suggested that the presence of low voltage in the ECG and congestive cardiac failure (both of which are present in our patient) are prerequisites for the diagnosis for significant cardiac amyloidosis (10). The low voltages in the precordial leads can also mimic the pattern of healed myocardial infarction as seen in our patient.

Cardiac amyloidosis may also infrequently express itself in other ways. Nodules of amyloid can sometimes deform the heart valves, causing murmurs and valvular insufficiency. Infiltrates also can affect the sinoatrial and atrioventricular nodes causing conduction defects (11). The atrial fibrillation in our patient was probably secondary to atrial dilatation.

Systemic amyloidosis is invariably fatal, with cardiac and renal involvement as the most frequent causes of death. With AL amyloidosis, survival varies from 4 to 15 months. The prognosis with reactive systemic (AA) amyloidosis is better being 1 to 5 years. The poor prognosis is due to the absence of any therapeutic modality which can reduce the production of fibril precursors and accelerate fibril resorption.

Management is essentially supportive. With cardiac amyloidosis, it is important to be aware that congestive cardiac failure does not respond to digoxin. Increase sensitivity to digoxin is a recognized feature and can lead to fatal arrhythmias (12). Diuretics should be used with caution to avoid salt and water loss with consequent cardiovascular collapse.

In an analysis of 54 necropsy patients with significant cardiac amyloidosis, Roberts (2) reported the terminal event as intractable congestive heart failure in 85% of the cases and sudden death in 15%. Falk suggested in his study that complex ventricular arrhythmias on Holter monitoring is common in cases with sudden death and may perhaps identify this subset (13). However in our patient we did not detect such warning arrhythmias despite two days of continous monitoring in the coronary care unit.

In the past 25 years, major progress has been made in the knowledge of the biochemistry and pathogenesis of amyloidosis. However, there is still no effective therapy so that involvement of vital organs such as the heart is usually fatal.

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