CASE REPORT

Breathless after bypass

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SUMMARY

A 65-year-old normotensive, non-athletic man presented to the cardiology clinic with exertional dyspnoea and chest discomfort. Echocardiography revealed mild left ventricular hypertrophy with good systolic function but with regional wall motion abnormalities suggesting ischaemia. Coronary angiography showed significant three-vessel disease. He underwent coronary artery bypass surgery, which was complicated by recurrent pericardial and pleural effusions, requiring a pericardial window procedure. Over the following year he became increasingly oedematous and breathless. On ECG the complexes were low voltage with impaired R wave progression and atrial fibrillation. Echocardiography revealed progression of the left ventricular hypertrophy (LVH) with a bright myocardium and restrictive filling pattern. MRI scanning confirmed the diagnosis of cardiac amyloidosis. He was referred for transplant but was considered unsuitable due to extensive mediastinal scarring. This case demonstrates the importance of a high index of suspicion for amyloidosis, especially in patients with unexplained LVH. Cardiac MRI or biopsy may expedite the diagnosis.

BACKGROUND

Heart failure in the context of left ventricular hypertrophy (LVH) is most commonly due to hypertensive heart disease with predominant diastolic ventricular dysfunction. However, before ascribing LVH to hypertension, a rare but important condition must be considered and excluded—myocardial infiltration. We present a case of progressive heart failure with LVH following coronary artery bypass surgery (CABG) due to amyloidosis.

CASE PRESENTATION

A 65-year-old man presented with exertional breathlessness and chest pains at a New York Heart Association (NYHA) II and Canadian Cardiovascular Society (CCS) II level. There was no significant medical history. On examination blood pressure was 124/72 with normal heart sounds and no signs of heart failure. His ECG was normal. Echocardiography revealed mild LVH with septal and posterior wall thickness in diastole of 1.3 and 1.5 cm, respectively. Systolic function was preserved but with regional wall abnormalities suggesting coronary artery disease. Coronary angiography revealed three-vessel disease and he underwent CABG. The postoperative course was complicated by recurrent pleural and pericardial effusions requiring a pericardial window procedure.

Six months later the patient complained of breathlessness on minimal exertion (NYHA III).

Examination revealed marked peripheral oedema, the neck veins were engorged but the lungs were clear and heart sounds normal.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis at this stage included recurrent pericardial effusion, constrictive pericarditis, restrictive cardiomyopathy and extensive post-operative infarction involving the right ventricle. Diagnosis of effusions and systolic dysfunction is straightforward on echocardiography. Differentiation between constrictive pericarditis and restrictive cardiomyopathy is more difficult and depends largely on the variation of mitral valve inflow patterns seen during respiration on Doppler imaging in the former (analogous to Kussmaul's sign, in which jugular venous pressure rises during inspiration seen where the heart functions in a confined space—tamponade and constriction).

TREATMENT

The ECG showed atrial fibrillation (AF) with low-voltage complexes and poor R waves anteriorly.

Echocardiography demonstrated moderate LVH (septum 1.6 cm) with mildly impaired systolic function and a small localised effusion; however, there was severe diastolic dysfunction with a restrictive filling pattern. The myocardium appeared bright.

The patient underwent a cardiac magnetic resonance scan, which showed a circumferential pattern of late gadolinium uptake and a pericardial effusion (figure 1). This pattern is typical of cardiac amyloidosis. Subsequent plasma electrophoresis, rectal biopsy, bone marrow aspirate and nuclear scanning excluded amyloid deposition in other viscera and he was diagnosed with senile-type amyloid disease.

OUTCOME AND FOLLOW-UP

The patient was referred for cardiac transplantation but was deemed unsuitable on the basis of extensive mediastinal scarring and deranged liver function.

DISCUSSION

The systemic amyloidoses are a heterogeneous group of diseases characterised by extracellular deposition of insoluble amyloid protein, which may affect any organ. This protein may be composed of immunoglobulin produced by monoclonal plasma-cells and B-cells as part of a dyscrasia, such as myeloma (amyloid light-chain (AL) amyloidosis). Amyloidosis may also be hereditary in association with specific mutations, most commonly in the transthyretin (ATTR) gene. Wild-type mutations in ATTR cause senile amyloidosis. A further category of amyloidosis (AA) is seen in association with

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Figure 1 Cardiac MRI—short-axis late enhancement view following administration of gadolinium contrast agent. Notably there is a circumferential pattern of enhancement (A) with difficulty nulling the myocardium. These findings are typical of cardiac amyloidosis.

chronic inflammatory conditions such as rheumatoid arthritis. Amyloidosis may also occur in those on long-standing haemodialysis.

Amyloidosis is a rare diagnosis, although post-mortem studies show some amyloid protein in the hearts of up to 25% of those over 80.¹ The clinical course depends on the organs involved and diagnosis is often delayed. Prognosis is largely determined by the degree of cardiac involvement, and varies between the types—those with AL amyloidosis and a markedly elevated B-type natriuretic peptide have a mean life expectancy of 8 months, whereas survival in senile amyloidosis may be several years.²

Cardiac infiltration leads to a restrictive cardiomyopathy with right-sided failure predominating in the early stages. Amyloid deposition elsewhere may cause renal failure, carpal tunnel syndrome, peripheral neuropathy and macroglossia. There is often markedly elevated venous pressure and dilatation of the atria predisposing to atrial fibrillation.

The classical ECG findings are of low-voltage complexes in the limb leads and poor anterior R wave progression, mimicking previous infarction. Echocardiography shows biventricular hypertrophy without dilatation and the myocardium may appear bright or speckled. The atria are enlarged and a pericardial effusion is common. Differentiation of these appearances from hypertensive heart disease is aided by Doppler imaging which demonstrates a severely restricted transmitral filling pattern.³ Tissue Doppler and strain analysis show predominant impairment of longitudinal contraction and relaxation. Right ventricular hypertrophy is unusual in hypertensive disease. Diastolic abnormalities occur early in the disease whereas systolic function is relatively preserved until the late stages.

Cardiac MRI is invaluable in diagnosis. Characteristic findings are of biventricular thickening with diffuse subendocardial late gadolinium uptake and difficulty nulling the myocardium from the blood pool. Endocardial biopsy is diagnostic, but may not be necessary if amyloid protein can be demonstrated in rectal or kidney tissue.

Further investigation of cardiac amyloidosis includes documentation of the extent of visceral involvement aided by serum amyloid protein (SAP) scanning. This involves injection of a radiolabelled protein common to all types of amyloidosis, which localises to affected organs. The type of amyloidosis should

then be determined. Myeloma and other dyscrasias must be sought, as well as chronic inflammatory conditions. Genetic testing for the more common ATTR mutations is available in specialist centres and genetic counselling of family members is indicated.

Therapy for amyloidosis seeks to treat any underlying cause and to manage the heart failure. Myeloma in particular may be treated with chemotherapy and bone marrow transplantation, although careful assessment is required to ensure that the patient is fit for this treatment.

Treatment of restrictive cardiomyopathy is challenging as some conventional heart failure therapies can be detrimental due to autonomic neuropathy, poor vascular tone and hypotension. The mainstays of treatment are diuretics with fluid and salt restriction. ACE inhibitors and angiotensin receptor blockers may cause severe hypotension in AL disease, but are better tolerated in hereditary and senile disease. β -Blockers are used to control AF. Long-acting nitrates are used in ATTR-related disease. Owing to the chronic progressive nature of the disease, inotropic support would usually only be considered as a bridge to heart transplantation or if an additional reversible pathology was identified.

Data on heart transplantation from the USA between 1987 and 2001 suggest that these patients fare worse than other groups, with 5-year survival of 54% as compared with 63.3% in all transplants.⁴ As the mutant ATTR protein is made in the liver, patients with hereditary amyloid have been treated with combined liver and heart transplantation.⁵

Learning points

- ▶ Cardiac amyloidosis is a rare and severe diagnosis that is frequently missed until its later stages.
- ▶ A high index of suspicion is required for symptomatic patients with unexplained left ventricular hypertrophy or restrictive cardiac physiology.
- ▶ Cardiac MRI is a powerful diagnostic aid for amyloidosis.
- ▶ Blood dyscrasias should be excluded.
- ▶ Early referral for transplantation should be considered.

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