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Case Report

An Unusual Cause of Reversible Cardiomyopathy

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A 58-year-old male presented with a two month history of paroxysmal nocturnal dyspnoea, 2 pillow orthopnoea and bilateral ankle swelling. He was a 15 pack year smoker. His past medical history was unremarkable. Clinical examination revealed features of congestive cardiac failure, including a raised jugular venous pressure, peripheral oedema and bilateral lung crepitations. Blood pressure was 137/56 mmHg. Electrocardiography showed rate controlled atrial fibrillation (AF), QRS duration was within normal limits. Chest radiograph revealed cardiomegaly and increased pulmonary vascularity. Brain natriuretic peptide (BNP) was raised at 660 pg/ml (Normal Range: 0-100). Serum troponin I and inflammatory markers were normal. Transthoracic echocardiogram showed severe, global, dilated cardiomyopathy with a left ventricular ejection fraction (LVEF) of 25% (biplane simpson's method). There was no significant valvular heart disease. He was treated with intravenous furosemide with clinical improvement. Cardiac catheterisation demonstrated angiographically normal coronary arteries. Extensive investigations for autoimmune, infective and infiltrative causes of cardiomyopathy were negative; cardiac Magnetic Resonance Imaging (MRI) with gadolinium enhancement showed no areas of delayed contrast enhancement to suggest cardiac amyloidosis or myocardial fibrosis and there was no evidence of myocardial oedema (Fig.1). The patients reported alcohol intake was limited to 4-5 units per week. There was no known family history of cardiomyopathy.

The patient was treated with full standard heart failure medication, including ACE inhibitors, beta blockers and aldosterone antagonists. Ambulatory ECG monitoring revealed paroxysmal rate controlled atrial fibrillation. The patient was warfarinised. At routine follow up clinical features of heart failure had resolved but left ventricular systolic function remained severely impaired on follow up echocardiogram.

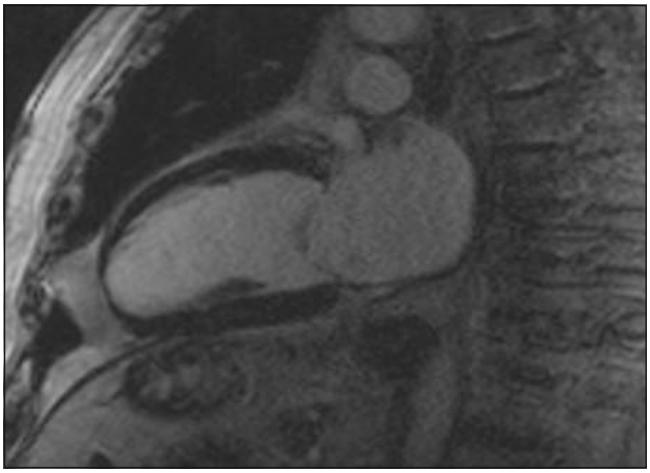

Fig 1. Cardiac Magnetic Resonance Imaging with gadolinium, demonstrating no areas of delayed contrast enhancement.

Two years after initial presentation his clinical condition had deteriorated with recurrent decompensated heart failure, severe proximal muscle wasting and debilitating lethargy complicated by newly diagnosed type 2 diabetes mellitus (fasting plasma glucose 7.7 mmol/l, HbA1c 7.8%) and bilateral femoral deep vein thrombosis. Blood pressure was 125/75 mmHg. On examination he was noted for the first time to be clinically cushingoid, with rounded facies, centripetal adiposity and supraclavicular fat pad accumulation. Subsequent investigations confirmed hypercortisolism biochemically with an elevated urine free cortisol (897 nmol/24h) and failure of suppression of 8am serum cortisol (239 nmol/l) after a 1 mg overnight dexamethasone suppression test. A diagnosis of ACTH-dependent Cushing's syndrome was confirmed with elevated plasma ACTH concentrations of 70-80 ng/l. A high dose dexamethasone suppression test (2 mg qds for 48 hrs) showed partial suppression (74%) of serum cortisol to 134 nmol/l. He was subsequently transferred to the regional centre for further investigations for tumour localisation to guide surgical treatment. No definite source of the excess ACTH was found following bilateral inferior petrosal sinus sampling (central to peripheral ACTH ratio of 1.6 : 1 after administration of corticotropin-releasing hormone). Pituitary gadolinium-enhanced MRI was normal, computerised tomography (CT) chest, abdomen and whole body PET-CT scan were unremarkable.

Because of the urgency of the deteriorating clinical situation, arising from the effects of severe hypercortisolism, a decision to proceed to bilateral adrenalectomy for definitive treatment was agreed. Initially, he was commenced on metyrapone 1 gram twice daily, which blocks cortisol synthesis through inhibition of 11β-hydroxylase, until bilateral adrenalectomy was performed three months later without complication. Four

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TABLE 1

Serial echocardiography measurements at initial presentation and 4 months after bilateral adrenalectomy

Variables	At presentation	4 month post bilateral adrenalectomy
Left Ventricular dimensions		
LVIDd (cm) (4.2-5.9)	**6.4**	**4.9**
LVIDs (cm) (2.0-3.8)	**5.9**	**3.5**
IVSd (cm) (0.7-1.2)	**1.3**	**1.3**
LVP wall thickness (cm) (0.6-1.2)	**1.2**	**1.2**
Left Ventricular function		
Ejection fraction* (%)	**25**	**63**

*using Biplane Simpson's method

LVIDd, left ventricular internal diameter end-diastole; LVIDs, left ventricular internal diameter end – systole; IVSd, interventricular septal wall thickness at end-diastole; LVP wall thickness, left ventricular posterior wall thickness at diastole.

months post operatively and thirty five months from initial presentation his symptoms have improved with no clinical evidence of heart failure, normalised serum BNP and normal left ventricular dimensions and function on echocardiography (Table 1). His ejection fraction had improved from 25% at presentation to 63%, four months post bilateral adrenalectomy. At follow up the patient had remained in normal sinus rhythm on ambulatory ECG monitoring.

Cushing's syndrome is an uncommon but potentially reversible cause of dilated cardiomyopathy, most often reported in patients with hypercortisolism arising from an adrenal adenoma[1-2]. Common causes of reversible cardiomyopathy include alcohol, tachycardia-related cardiomyopathy, myocarditis and ischaemia, all of which were effectively excluded in this case. Previous studies examining the relationship between hypercortisolism and cardiac dysfunction, suggest that cardiac remodelling occurs in Cushing's syndrome, independently of hypertension[3-4]. It is believed that cortisol may act directly on myocardial tissue as glucocorticoid receptors have been shown in animal[5] and human heart tissue[6]. The striking change in cardiac function after resolution of hypercortisolism in the present case after bilateral adrenalectomy suggests that the cardiomyopathy was attributable to hypercortisolism and responsive to a eucortisolaemic state, despite an initial delay in recognition of the underlying diagnosis.

This case highlights the importance of considering Cushing's syndrome in the differential diagnosis of cardiomyopathy. It also demonstrates the benefits of definitive treatment with bilateral adrenalectomy in patients without a definite source of ACTH secretion. This patient remains under careful long-term surveillance for emergence of the source of the ACTH secretion. However, with stabilisation of his cardiac status following bilateral adrenalectomy, longer term follow up will be achievable.

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