Clinical demonstrations

PROFESSOR J. F. GOODWIN

WE present the case histories and documentation on a number of patients who illustrate certain aspects of the cardiomyopathies, starting with three patients who demonstrate some of the features and problems of congestive cardiomyopathy. Case 1 is a so-called 'index' case with the clear characteristics of congestive cardiomyopathy. Case 2 confused the issue by presenting with angina and therefore simulated ischaemic heart disease, an important and difficult problem. Case 3 did the reverse; he presented with heart failure without a definite episode of cardiac infarction but was found to have severe coronary artery disease and thus his myocardial failure was due to this and not to cardiomyopathy. Then three patients (Cases 4, 5 and 6) with hypertrophic cardiomyopathy will be presented who illustrate some of the familial aspects, some of the diagnostic difficulties and the importance of histological evidence. Finally, we shall discuss some patients who demonstrate certain forms of secondary cardiomyopathies. These will be three patients with skeletal muscular dystrophy (Cases 7, 8 and 9) and a patient with acromegaly (Case 10) all of whom presented with, or came to our notice with severe myocardial disease and heart failure.

Case 1 (Presented by Dr Geoffrey Lane)

A 42-year-old male architect whose only past history was mild asthma in childhood and who remained perfectly well and fit up until December 1970. He then developed nausea and diarrhoea followed by shortness of breath, tightness in the chest and wheezing when walking. Effort dyspnoea persisted and in January 1971 he developed paroxysmal nocturnal dyspnoea. He was admitted to hospital at this time with signs of bilateral heart failure and improved on treatment with digoxin and diuretic therapy. Tachycardia persisted however, and cardiomegaly on X-ray was unchanged. Three months later he developed further nausea, diarrhoea and dyspnoea and was again admitted to hospital, and 2 weeks later was transferred to Hammersmith Hospital (April 1971). His symptoms were dyspnoea on minimal effort, orthopnoea, paroxysmal nocturnal dyspnoea; he also had intermittent colicky right iliac fossa pain, a symptom which he had had intermittently over a period of fifteen years.

On examination he was a chronically ill man with gross congestive cardiac failure. Blood pressure was 100/80 mmHg, pulse 120/mm with frequent ectopics, jugular venous pressure markedly elevated with very prominent 'a' wave. There was an accentuated pulmonary component of the second sound and a third heart sound. The apical impulse was diffuse and there was a left parasternal impulse. He had marked oedema, basal crepitations and an enlarged liver.

Investigations. His ECG showed sinus tachycardia, a poor progression of the R wave from V_1 to V_4 and repolarization changes, with an occasional ventricular ectopic beat. The chest X-ray showed gross cardiomegaly and prominent upper zone vessels. The haemoglobin was 16.3 g/100 ml, WBC 6600 cells/cm³, PBI 5.6 µg/100 ml, VMA 8 µg/mg creatinine, his serum albumin was 1.8 g/100 ml. On admission he showed quite severe hypokalaemic alkalosis; potassium 2.4 mEq/l.

Course. Congestive cardiomyopathy was considered as the most likely diagnosis and treatment was continued with digoxin and frusemide 160 mg/day with potassium supplementation. However, his course was complicated first by the development of acute tubular necrosis with oliguria and hyponatraemia (urea 129 mg/100 ml, Na 117, K 6.9 and HCO₃ 11 mEq/l) requiring therapy initially in the form of hypertonic saline and glucagon, and then frusemide in large doses. With this combination of therapy he showed transient improvement but then developed further complications; atrial fibrillation (from which time he was put on anticoagulants) and later two episodes of staphylococcal septicaemia. He steadily became more jaundiced and he died in congestive cardiac failure approximately 6 months after the first onset of symptoms attributable to cardiac disease.

Necropsy findings (Dr E. J. G. Olsen)

(1) Mural thrombus in a dilated and hypertrophied heart. Post-mortem coronary arteriography showed normal coronary arteries.

(2) Pulmonary emboli from venous thrombosis in legs.

(3) Early renal papillary necrosis.

(4) Two gastric ulcers; islet cell adenoma of pancreas.

Professor Goodwin

This is a distressingly common, though by no means invariable, course for congestive cardiomyopathy; a 6 months' downhill progression. Some factor or factors unknown had destroyed the contractile power of the myocardium. Virus studies in this patient, and in other patients, have been negative in our experience, possibly because we see these patients late in the condition. One is left, even after detailed pathology, with a huge question mark as to the causation.

Discussion

DR FORSTER (Zurich): At necropsy this patient showed an islet cell adenoma of the pancreas and gastric ulcers as well as diarrhoea. Could he be a case of Zollinger-Ellison syndrome with cardiomyopathy? Do you think that some disturbance of carbohydrate metabolism could be responsible for this cardiomyopathy and have you seen a similar case previously?

PROFESSOR JOHN GOODWIN: No, we have not seen this combination before but I suppose it is feasible.

Case 2 (Presented by Dr C. M. Oakley)

The next patient, aged 55, worked as a packer. He presented earlier this year with a 4-year history of epigastric and retrosternal pain which went into the left arm on exertion. The pain sounded typical of ischaemic cardiac pain and was diagnosed as angina. In December 1970 he went into left ventricular failure for the first time and shortly afterwards was admitted to hospital (January 1971). A diagnosis of cardiac infarction leading to left ventricular failure was made and while in hospital he had a cerebral embolus whose effects were transient. In March 1971, he was re-admitted to hospital with chest pain, again in cardiac failure. On this occasion he was very ill and went into ventricular fibrillation but recovered from these episodes. In May 1971 he was referred to Hammersmith Hospital with a diagnosis of left ventricular aneurysm.

On examination he was a thin, small, quiet man with arcus senilis. Blood pressure 95/60 mmHg; sinus rhythm with slight pulsus alternans. The left ventricle was obviously enlarged with a sustained impulse and a palpable gallop; apical fourth and third sounds present. The chest X-ray showed a large dilated left ventricle. The ECG showed complete left bundle branch block and atrial parasytostole. Serum cholesterol 221 mg/100 ml, serum triglyceride (fasting) 68 mg/100 ml, haemoglobin and uric acid levels normal. Cardiac catheterization revealed a very low cardiac output, a high left ventricular end-diastolic pressure and moderate pulmonary hypertension. Selective coronary angiography and a left ventricular angiogram were carried out. The left ventricle was very large and beat with decreased vigour; there was no evidence of a

ventricular aneurysm and no thrombus was seen in the cavity. The coronary arteries were normal.

For left ventricular failure to be explained by coronary artery disease, we expect to see major occlusive disease affecting at least two vessels. Thus despite the history of angina for 4 years and the striking physical signs suggesting aneurysm, this patient has generalized left ventricular failure of undetermined (but non-coronary) cause, i.e. congestive cardiomyopathy. Some clinical clues pointing away from the diagnosis of ischaemic heart disease were the absence of major or minor coronary 'risk' factors and the complete left bundle branch block on the ECG. The latter admittedly obscures the diagnostic changes of cardiac infarction but a presentation in left ventricular failure with left bundle branch block more often means cardiomyopathy than coronary disease.

Discussion

QUESTION. Why do you think this patient has had angina or pseudo-angina?

DR CELIA OAKLEY: I don't *know* why he has angina but I can suggest some reasons why he should have angina. I think it is not pseudo-angina, but real angina and it is not uncommon in congestive cardiomyopathy. These patients must have a greatly increased myocardial metabolic demand. Firstly, they have an increased cavity size and therefore for any pressure generated, the wall tension must be greater than usual; wall tension is one of the main factors concerned with metabolic demands. Secondly, the left ventricular muscle mass is greater than normal. Thirdly, patients with congestive cardiomyopathy maintain their minute output by means of tachycardia, and metabolic demand is directly related to cardiac rate. Finally, this high rate will also reduce diastolic filling time so that myocardial blood flow may be curtailed. These are the several reasons why he might have angina!

PROFESSOR JOHN GOODWIN: Do you think that the most important factor is the increased ventricular size with increased wall tension and increased oxygen demand?

DR CELIA OAKLEY: I think it is increased oxygen demand from a number of different factors, all of importance.

DR WALLACE BRIGDEN: How do patients with cardiomyopathy and angina respond to trinitrin?

PROFESSOR JOHN GOODWIN: I am not sure I know the answer to that. I suppose they usually respond because the effect of trinitrin is to reduce cardiac work.

Case 3 (Presented by Dr Michael Dean)

This patient was a 49-year-old man (a public relations officer) who illustrates the way in which ischaemic heart disease can mimic the picture of congestive cardiomyopathy. In 1966 he was found to have mild diabetes which was adequately controlled by diet and in 1968 a chest X-ray revealed mild cardiomegaly. Over a period of 3 weeks in early 1971 he developed increasing breathlessness

on exertion and paroxysmal nocturnal dyspnoea, and was promptly admitted to hospital. He was noted to have a tachycardia, elevation of jugular venous pressure, basal crepitations and an atrial gallop. Treatment with digoxin and diuretics produced rapid improvement and he was referred to Hammersmith Hospital for further evaluation with a tentative diagnosis of congestive cardiomyopathy. It is of interest that at no time was there any chest pain to suggest angina pectoris or myocardial infarction. He smoked about thirty cigarettes per day, and there was a fairly heavy intake of alcohol.

On admission he was virtually symptom-free but there was clinical evidence of left ventricular enlargement and both third and fourth heart sounds were audible. The liver was somewhat enlarged, possibly as a result of his rather heavy alcohol intake. Investigations revealed slight impairment of glucose tolerance and there was elevation of both fasting cholesterol and triglyceride levels; cholesterol 350 mg/100 ml and triglyceride 290 mg/100 ml. Chest X-ray showed moderate cardiac enlargement with no evidence of cardiac failure. The electrocardiogram revealed sinus rhythm with Q waves in leads I, aVL, and across the left praecordial leads. The appearance was compatible with an old anterolateral infarction.

Cardiac catheterization with coronary angiography was performed to help clarify the diagnosis, which was felt to be either ischaemic heart disease, as suggested by the electrocardiogram, or congestive cardiomyopathy. The pulmonary artery pressure was elevated to 62/28 mmHg and the mean pulmonary capillary wedge pressure was 12 mmHg. Left ventricular pressure was 115/5–17 mmHg and the left ventricular end-diastolic pressure rose to 40 mmHg during a brief episode of junctional tachycardia. The left ventriculogram showed a large ventricular cavity with an akinetic area at the cardiac apex and relatively good contraction of the basal portions of the ventricle. The coronary arteriograms revealed complete obstruction of the left anterior descending coronary artery. Both the circumflex branch of the left coronary artery and the right coronary artery were patent but had several minor irregularities of the lumen suggesting the presence of atheroma. There was some collateral circulation from the right coronary artery to the left side.

Thus, the clinical presentation of cardiac failure in this patient seems to be on the basis of ischaemic heart disease. It is of interest that there were no symptoms to point to this diagnosis and the main piece of evidence in favour of this was the electrocardiogram. In addition there were present several of the known 'risk factors'—notably mild diabetes, elevated lipids, and cigarette smoking.

Discussion

DR F. HAAGEN (Utrecht): Were all your patients seriously interrogated regarding excessive alcohol intake?

PROFESSOR JOHN GOODWIN: This is an important question and I am glad that it was asked. In our experience, alcohol does not seem to be an important factor, although this might depend on what is regarded as a high alcohol intake. The patients we see have levels of alcohol intake which are difficult to evaluate. My personal belief is that alcohol in many patients is no more than one of the factors but it is seldom the major cause. I think there is a wide variation in individual tolerance, as with alcoholic cirrhosis. We do not find alcohol an important factor in our patients with congestive cardiomyopathy.

DR WALLACE BRIGDEN: I have no doubt that alcohol is in some situations, in some people and in some places, an outstandingly important cause of primary disease of the heart. The evidence for this is now overwhelming and comes from clinical, experimental and pathological studies and in the specific findings of electron microscopy.

DR E. G. J. OLSEN: Personally, I am unable to distinguish at histological or histochemical level, as to whether or not a patient has been subjected to a tremendous amount of alcohol. This comment extends to the electron microscopic level as well.

Familial hypertrophic cardiomyopathy (Presented by Dr Celia Oakley)

Case 4.

A female, 58 years old in 1971, was first seen at Hammersmith Hospital in 1958 (aet 45 years). Five months before being seen she had developed atrial fibrillation and was treated with digitalis. A month later she developed a left renal embolus and another month later, a saddle embolus. When referred to Hammersmith Hospital she had effort dyspnoea, palpitations and a transient right hemiplegia.

The cardiovascular findings included atrial fibrillation, an elevated JVP, and an enlarged tender pulsatile liver. The heart was moderately enlarged on X-ray but there were no murmurs and no added sounds. She developed a left hemiplegia while in hospital. There has been little change clinically during the past 13 years. Occasionally she returns to sinus rhythm and haemodynamic studies in 1959 and 1966 showed an increasing left atrial and pulmonary artery pressure with a small reduction in cardiac output. The left ventricular angiogram showed the features of hypertrophic cardiomyopathy. The left ventricular cavity was deformed but not dilated. The ventricular wall was grossly thickened but it contracted well. This patient had clinical features suggesting pump failure (congestive cardiomyopathy) with haemodynamic and angiographic abnormalities of compliance failure (hypertrophic cardiomyopathy).

As this patient recovered she said that she had lost a son at the age of 15 years. He had died suddenly while walking along the street and necropsy

had revealed 'heart disease'. It was not possible to obtain the report of the coroner's necropsy. She also said that her daughter had a heart murmur.

Case 5

Her daughter, was investigated at the age of 15. She was asymptomatic but a murmur had been noted at a school medical examination some years earlier. She was in sinus rhythm and there was no evidence of cardiac failure; the heart was not enlarged, although the left ventricular impulse was prominent and there was a palpable atrial beat at the apex. In addition there was an apical systolic murmur and a third sound or short mitral diastolic murmur.

The girl had all the clinical features, haemodynamic and angiographic findings of hypertrophic cardiomyopathy (HOCM) with mild obstruction to left ventricular outflow.

Comment

At the time that we first saw these patients we were only beginning to realize that patients with HOCM need not necessarily have murmurs or outflow tract obstruction and that they might develop or present with congestive heart failure. The features of this family with hypertrophic obstructive cardiomyopathy include sudden death in one member at the age of 15 years and a murmur detected in another at 15 years who is now in her twenties, married and has had a child. Her disease has not apparently progressed and this is typical of HOCM. In the mother, the heart disease was only recognized in her late forties when she had already had her family and she presented in congestive cardiac failure.

The mother's illness drew attention to the daughter's cardiac abnormality which otherwise might have remained undetected until she in her turn presented with complications of the disease in later life. This mother and daughter also underline the usual under-diagnosis of this disorder in childhood. The signs are often unspectacular and attributed to innocent causes so that the majority of children who are referred to us have quite atypically severe forms of the disorder.

Case 6

A housewife, now aged 36 years, was unaware of any problem until the birth of her third child (1966) when her abdomen and ankles remained swollen after delivery and amenorrhoea persisted. In 1970 she had her varicose veins stripped but without improvement and a laparotomy was performed for the suspected diagnosis of ovarian carcinoma. A liver biopsy taken at that time suggested cardiac failure, and she was referred to Hammersmith Hospital.

In the past she had been treated for asthma in

1962 and for pulmonary tuberculosis in 1967. There was no family history of heart disease. She had three children aged 2, 9 and 13 years. For about 1 year she had been short of breath, with blueness of the face and hands on stooping.

On examination she was very thin with hepatomegaly and gross ascites, peripheral cyanosis, a small volume pulse in sinus rhythm with no arterial paradox; she was obviously in a low cardiac output state. Her venous pressure was high in the neck with a dominant 'y' descent. The cardiac impulse showed a marked right ventricular diastolic thrust, such as is described in constrictive pericarditis. There was no left ventricular impulse, a loud third heart sound gallop and an intermittent tricuspid systolic murmur.

The chest X-ray showed a moderately enlarged heart. Earlier films taken during her anti-tuberculous therapy showed slight cardiac enlargement in 1969. The ECG showed definite bilateral atrial enlargement. The echocardiogram suggested a small pericardial effusion and showed a rapid diastolic closure slope quite unlike HOCM. The differential diagnosis at this stage was between constrictive pericarditis and HOCM.

Cardiac catheterization. The mean right atrial pressure (16 mmHg) was identical with the indirect left atrial pressure, which is typical of constrictive pericarditis but the left ventricular end-diastolic pressure (LVEDP) (26 mmHg) was much higher than the right ventricular end-diastolic pressure due to a grossly augmented 'a' wave. There was very little pulmonary hypertension; a high LVEDP, an augmented 'a' wave and significant pulmonary hypertension always weigh heavily against constrictive pericarditis and are more suggestive of cardiomyopathy. There was no gradient between the left ventricle and aorta after amyl nitrite. Cine-angiography showed slight systolic mitral incompetence, normal left ventricular activity, no cavity dilatation and considerable thickening of the left ventricular wall whose cavity was smooth and featureless without papillary muscle indentations.

The patient thus had no evidence of left ventricular *systolic* dysfunction with a raised filling pressure and congestive failure secondary to this. A decision had to be made as to whether the left ventricular *diastolic* dysfunction arose from pericardial restriction or myocardial disease. Although there were several features against a diagnosis of constrictive pericarditis, it was considered that it should be excluded and a thoracotomy was performed. The pericardium was normal, the left ventricle was small and grossly thickened and the left atrium was tense. Biopsies were taken from all the cardiac chambers and there were some features in the left ventricular biopsy which were suggestive of HOCM with hypertrophy otherwise unexplained.

Discussion

DR OLSEN: On conventional histological examination one can immediately see that the regular arrangement of the myocardial fibres is dissociated and that most of the fibres show considerable hypertrophy. In hypertrophy resulting from stenosis or hypertension, the fibres measure 15–20 μm in diameter; in hypertrophic obstructive cardiomyopathy the fibres are larger, from 60–90 μm . The nuclei are abnormal in shape with a perinuclear halo and there are widespread dystrophic changes within the myocardial fibres. There is also an increase in fibrous tissue between the myocardial fibres. At a histological level, these findings indicate hypertrophic cardiomyopathy and the only value of histochemical examination is to demonstrate the considerable glycogen accumulation in the perinuclear area.

On electron microscopy the individual myofibre components are dissociated and there is a striking cross-over from one fibre to another. This appearance is not pathognomonic, but it is seen more frequently and to a greater degree in HOCM. On cross-section, the mitochondria are dilated and the cristal arrangement is disrupted, with large vacuoles appearing within the cristae. The nuclear membrane is prominent and crenellated.

DR C. OAKLEY: In this patient the diagnosis before biopsy had to be reached by exclusion. She had left ventricular hypertrophy with diastolic compliance failure and therefore she had HOCM. Dr Olsen did not know the clinical problem when he made his report on the biopsies so his comments were not biased by our views. I would emphasize that one does not necessarily have to demonstrate an abnormal appearance of the left ventricular cavity on angiography, although the appearance of hypertrophied papillary muscles protruding into the cavity make the diagnosis much easier!

PROFESSOR J. GOODWIN: I never thought this patient had HOCM because of the unimpressive angiogram and this case clearly demonstrates that one cannot regard the angiographic appearance as the final arbiter in the diagnosis. This patient really did have a restrictive picture, hence the differential diagnosis from constrictive pericarditis. It is very unfortunate to miss constrictive pericarditis and I think that under these circumstances thoracotomy has to be part of the investigative programme.

DR OLSEN: I would like to emphasize that if one does attempt a biopsy, it should be an open biopsy, it should be clearly seen and it should be a reasonably large specimen. A needle biopsy is completely useless from a diagnostic point of view.

PROFESSOR J. GOODWIN: We have experience of open biopsy in four patients with congestive cardiomyopathy and the appearances were entirely non-specific. They also did not indicate any specific causal aetiology.

DR C. OAKLEY: It is important to understand that the specific features of this disease are hypertrophy and lack of compliance of the myocardium. It is only when the myocardial hypertrophy is localized to a particular site that one gets obstruction and loud murmurs. The obstructive element is only one aspect of the whole disease problem. This patient did not really have the haemodynamic features of constrictive pericarditis and if we had been a little more alert, we need not have done the thoracotomy!

DR PETER TURNER (London): I would be interested to know why this patient presented with gross tricuspid regurgitation?

DR C. OAKLEY: I don't know the answer! The right ventricle could not be grossly dilated because the heart itself is not very large. The right ventricular cavity will probably be small because she has a very large interventricular septum and an element of Bernheim's effect comes into this. If in addition, because of the septal hypertrophy the tricuspid ring and valve leaflets are displaced, opposition of the valves will not take place and we will have an incompetent valve with a small cavity, which will result in an extremely high filling-pressure. I think this is probably what she had at the time of presentation.

DR FORSTER (Zurich): I don't think you have shown that this patient did not have endocardial thickening, for the symptoms would fit very well with the syndrome with eosinophilia demonstrated by my old teacher, Professor Löffler.

DR C. OAKLEY: Certainly, mitral incompetence is not uncommon in Löffler's cardiomyopathy, but this is the only thing she had in common with Löffler's syndrome. There was no endomural thrombus, no emboli and no eosinophilia and the pathology was not that seen in Löffler's disease.

DR OLSEN: In fact there was a little bit of endocardium in this biopsy and it showed a little increase in endocardial thickening. Löffler found a considerable increase in endocardial thickening and a diffuse elastic pattern in the endocardial thickening which was not seen in this patient.

DR WALLACE BRIGDEN: Was there any fibrosis in the specimen?

DR OLSEN: Yes, there was some fine fibrosis around each individual myocardial fibre and some replacement fibrosis in the middle, but not a great deal.

DR WALLACE BRIGDEN: I asked this question because we have seen patients with a constrictive syndrome come to necropsy with endocardial fibrosis of no more than 1 mm at the thickest site. We have recently seen three patients who had mitochondrial antibodies with minimal hepatic fibrosis, probably an early stage of biliary cirrhosis. In one patient, there was a thin lattice fibrosis in the heart and that patient had a raised venous pressure, some hepatomegaly but no ascites.

DR C. OAKLEY: We have also seen two patients with biliary cirrhosis who have had cardiac involvement and tricuspid incompetence; one had paroxysmal tachycardia and one had a pericardial effusion. We have not seen localized endocardial thickening produce compliance failure of this sort on its own.

DR WALLACE BRIGDEN: Do you think that the 'x' descent in the venous pulse and the 'y' descent and the relationship between them are meaningful in this difficult differential diagnosis of pericardial constriction and myocardial disease? Did this patient have a steep or a shallow 'x' descent?

DR C. OAKLEY: I think the 'x' descent relative to the 'y' depends on factors other than the presence of tricuspid incompetence; it depends largely on the P-R interval as well, so we have not paid much attention to it.

QUESTION: Have any hearts from people suffering from the Hamman-Rich syndrome come to necropsy and, if so, is there any interstitial fibrosis in the heart?

DR OLSEN: We have seen two or three such cases but there was no increase in fibrosis in the hearts of these patients.

DR A. POMERANCE: I have only seen two hearts in this condition and they have been completely normal.

Addendum

Some months later she came in as an emergency with intestinal obstruction. Most of the small intestine was gangrenous due to volvulus around an adhesion. She died after massive intestinal resection.

Necropsy: the left ventricular endocardium was found to be grossly thickened. The thickening involved the inflow tract and apex but spared the outflow tract which was separated by a fibrous endocardial ridge. Involvement of the chordae and papillary muscles of the posterior mitral cusp explained the mitral regurgitation. The heart thus showed all the typical features of endomyocardial fibrosis but as she was an Irishwoman who had never lived outside Europe the appellation 'Löffler's' endomyocardial disease was given.

This case illustrates the ultimate importance of the angiographic appearance in diagnosis as well as the importance of recognizing any features which do not fit with a favoured diagnosis. In HOCM a third heart sound is uncommon when compliance failure is the problem and the echocardiogram in this patient showed a rapid diastolic closure slope which was also at variance with the physiological disturbance of HOCM. Despite the rarity of the patient's heart disease it should have been possible to arrive at the answer and it is of interest to note again that Löffler's disease is not invariably associated with eosinophilia, embolism and endocardial thrombus formation.

Clinical association of skeletal muscular dystrophy with cardiomyopathy (*Presented by Dr D. J. Coltart*)

It is well recognized by physicians, and particularly by neurologists, that patients with skeletal muscular dystrophies often terminally exhibit cardiac decompensation. It could be postulated that this sequence of events might be due to a generalized muscular dystrophy with early and serious manifestations in the skeletal muscles and latterly affecting the heart. The reverse could therefore be postulated for the cardiomyopathies with the generalized muscular dystrophic process having early and serious manifestations on the heart.

The neuro-muscular diseases, Friedreich's ataxia, progressive muscular dystrophy and myotonia atrophica can all present with secondary cardiomyopathies. 55% (thirty-three cases) of Friedreich's

ataxia exhibited some cardiac abnormality (Boyer, Chisholm & McKusick, 1962). Pathologically this was demonstrated as either cardiac hypertrophy with fatty and eosinophilic degeneration or diffuse myocardial fibrosis with eccentric hypertrophy of both ventricles (Manning, 1950). During life, paroxysmal atrial arrhythmias are fairly common in these patients and the electrocardiogram showed an abnormality in 90% of patients being either left ventricular hypertrophy, right ventricular hypertrophy or 2:1 AV block (Thorén, 1964). The combination of motor inco-ordination simulating Sydenham's chorea and of cardiac murmurs and electrocardiographic changes may lead to an erroneous diagnosis of rheumatic fever with carditis. Progressive muscular dystrophies have been reported to have an incidence of cardiac involvement ranging from 50 to 86% (Berenbaum & Horowitz, 1956) and this is demonstrated pathologically with either myocardial fibrosis, fatty vacuolations with hypertrophy or atrophy (Storstein & Austarheim, 1955). The Duchenne type of dystrophy very commonly has electrocardiographic abnormalities with tachycardia, right bundle branch block and tall R waves in the right precordial leads (Gilroy *et al.*, 1963). Q waves and non-specific repolarization changes are observed. Sudden death is also quite common (Berenbaum & Horowitz, 1956). The Erb type of limb-girdle-dystrophy frequently has right ventricular conduction disturbances (Welsh, Lynn & Haase, 1963) and also terminally progresses to congestive heart failure. In patients with facio-scapulo-humeral type of muscular dystrophy, electrocardiographic changes are infrequent (Perloff, 1961) but there has been one case report of atrial standstill (Bloomfield & Sinclair-Smith, 1965). In myotonia atrophica cardiac pathological findings are sparse and non-specific. Electrocardiographic changes were reported in 62% of these cases with intraventricular conduction defect, prolonged PR interval, left axis deviation and left bundle branch block.

Case 7

The first case illustrating the relationship of muscular dystrophy with cardiomyopathy was a 29-year-old female doctor. Two years ago her friends first noticed some abnormality in her gait. She presented for medical attention 15 months ago with difficulty in climbing stairs and on standing from the sitting position. She was found to have weakness of the pelvic girdles and quadriceps and diminished jerks in the leg. The neurologist who saw her at that time diagnosed a limb-girdle-type muscular dystrophy. Eleven months ago she noticed an inappropriate dyspnoea for the first time after climbing one flight of stairs. *On examination* at that time there was a raised jugular venous pressure,

some cardiomegaly and a gallop rhythm. The liver was enlarged and there was some sacral oedema. Chest X-ray demonstrated cardiomegaly and the investigations at that time showed a 15% neutrophil eosinophilia with an iron deficient blood picture. The serum creatinine phosphokinase and aldolase were normal but an electromyogram indicated a primary muscular dystrophy. A skeletal muscle biopsy confirmed the dystrophic process with atrophy, swelling and hyaline sarcoplasm in the myofibrils but no inflammatory cells. The patient was treated with digoxin, diuretics and steroids with good symptomatic improvement. Eight months ago the serum creatinine phosphokinase was found to be 151 $\mu\text{m}/\text{ml}$ (normal upper limit is 50 $\mu\text{m}/\text{ml}$). Five

FIG. 1. Case 7. Muscle biopsy. Left quadriceps. Trichrome stain. Histological stain shows widespread atrophy and hypertrophy of the muscle fibres with central nuclei and nuclear clumping. Some of the atrophic fibres are undergoing degenerative changes. There is a marked increase in connective and adipose tissue between the fibres. No inflammatory changes are seen.

FIG. 2. Case 7. Muscle biopsy. Left quadriceps. Histochemical stain shows that both Type 1 (light) and Type 2 (dark) fibres are affected but no specific enzyme changes were found.

months ago she had an attack of pulmonary oedema with no ischaemic symptoms. The patient was referred to Professor Goodwin at the Hammersmith Hospital and on examination her facies suggested steroid administration, she was in sinus rhythm with cardiomegaly and on auscultation had third and fourth heart sounds with a mid-systolic murmur. The lung fields were clear and there was no peripheral oedema. On neurological examination she had weakness of the glutei muscles, thigh adductors and quadriceps. The power was normal in the distal muscle groups. She had slight weakness of both deltoids and triceps, normal power in the forearms and hands. She had no weakness of any other muscles, no fasciculation or muscle tenderness. She had sluggish arm reflexes, the knee jerks were absent, the ankle jerks present and plantar response was flexor. There was no sensory defect. The investigations showed that she was still iron-deficient and the 15% eosinophilia persisted. The thyroid status was normal. The creatinine phosphokinase was raised to 323 $\mu\text{m}/\text{ml}$. The electrocardiogram showed sinus rhythm and left atrial hypertrophy and Q waves over the left praecordium. Chest X-ray demonstrated cardiomegaly with clear lung fields. The shoulder X-ray and pelvic X-ray were normal. At cardiac catheterization the left ventricular end-diastolic pressure was raised at 24 mmHg with a low cardiac index. The left ventricular cine-angiogram showed a poorly contracting large left ventricle and normal coronary angiograms, confirming the diagnosis of congestive cardiomyopathy. The electromyogram again gave a dystrophic record. Sections from the muscle biopsy are shown in Figs. 1 and 2. No obvious cause has been found to explain the eosinophilia which is now decreasing.

Case 8

A 36-year-old Italian restaurant-owner presented with a short history of 6 months' exercise dyspnoea and pulmonary oedema. He had weakness of his left arm and shoulder. His family history revealed sudden cardiac deaths in his mother and two brothers unsupported by any post-mortem evidence.

On examination he was mildly obese, had clinical left ventricular hypertrophy with a third heart sound and minimal weakness of abduction of the left arm and the left hip. Investigations showed a raised serum creatine phosphokinase, 75 $\mu\text{m}/\text{ml}$; electrocardiogram showed atrial fibrillation with left anterior hemiblock pattern, left ventricular hypertrophy and repolarization changes. Chest X-ray showed cardiac enlargement of left ventricular prominence and dilated upper lung vessels. The left ventricular cine-angiogram demonstrated a large ventricular chamber with poor contractility, no thickness of the walls, no dyskinesia or aneurysm

and trivial mitral incompetence with an end-diastolic pressure of 18 mmHg. Coronary angiography was normal. Electromyography showed a diffuse patchy myopathy with brief duration polyphasic action potentials.

Case 9

A 37-year-old male presented 1 year ago with an ischaemic episode and paroxysmal supraventricular tachycardia. It was noticed that he had a wobbling gait with weak and wasted sternomastoids, spinati, biceps and triceps but normal distal muscles. The creatinine phosphokinase was grossly elevated at 323 m μ m/ml and his electromyograph showed high voltage, short duration action potentials diagnostic of a primary myopathic process. He was referred to Dr Oakley for cardiac evaluation. The jugular venous pressure was markedly elevated with palpable left ventricular hypertrophy and a systolic murmur. Electrocardiogram was non-specific and chest X-ray showed cardiac enlargement with early pulmonary oedema. Whilst on the waiting list to be brought in to be investigated the patient suddenly died at home.

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Discussion

DR COLTART: Meerscham & Hootsmans (1971) in Amsterdam were stimulated to look at the electromyographs (EMG) of people with well-proven hypertrophic obstructive cardiomyopathy by the presence of proved cases of progressive muscular dystrophy among the relatives of two of their patients. In forty patients with well-proven HOCM they have found an abnormal EMG in twenty-six of these patients, sixteen had polyphasic action potentials and the others had short mean motor unit action potentials. These abnormalities were positively correlated with increase in age. None of these patients had symptomatic weakness. Of thirty-one patients, five had raised CPK and of twenty-four patients studied, six had raised aldolase. These results suggest that in an appreciable number of patients presenting the clinical picture of HOCM, a generalized myopathy with early and serious cardiac manifestation should be considered as a possible aetiological factor.

DR M.J. DAVIES (London): We have examined muscle histology at necropsy in a large series of subjects with congestive cardiomyopathy, diagnosed in life as being primary and with no known skeletal muscle abnormality. In ten out of ninety cases there was definite histological evidence of a skeletal myopathy.

DR COLTART: Have you examined a control group with an equal degree of cardiac failure but not due to cardiomyopathy?

DR DAVIES: Yes, we routinely examine muscle from cor pulmonale cases and in these we do not find similar changes.

PROFESSOR J. GOODWIN: Perhaps one ought to emphasize that Meerscham's work concerns hypertrophic cardiomyopathy and not congestive cardiomyopathy and thus his findings do not relate to the material Dr Davies is describing.

Myocardial disease and acromegaly (*Presented by Professor John Goodwin*)

Case 10.

The patient was a 51-year-old woman who complained of dyspnoea on effort for 7 years. On examination she had acromegalic facies, considerable cardiac enlargement (of the left ventricle) and a regular pulse at 110/min. Jugular venous pressure 8 cm above the sternal angle and third and fourth heart sounds; blood pressure 120/90 mmHg. The electrocardiogram showed grade 3 left ventricular hypertrophy and left anterior hemiblock.

Radiography of the pituitary fossa showed an expanded sella turcica (Fig. 1) and biopsy revealed an eosinophil adenoma.

Cardiac catheterization revealed grossly impaired cardiac function; left ventricular pressure $\frac{137-174}{6-33}$ mmHg; increased left atrial pressure (mean) 38 mmHg; right atrial pressure (mean) 8 mmHg ('v' wave 23,) cardiac index 2.71/min/m². Left ventricular angiography showed mitral regurgitation, a large ventricular cavity and poor contraction. Selective coronary arteriography was normal. The patient was treated for cardiac failure in the usual way, and an yttrium implant was placed in the pituitary fossa by Professor Russell Fraser.

FIG. 1. Radiograph of pituitary fossa. (Case 10)

FIG. 2. Frontal radiographs of the chest (6 ft). (a) November 1968. Nine months before pituitary implant, showing gross cardiomegaly, but no definite pulmonary congestion. (b) August 1969. Shortly before implant, showing increased left atrial pressure, some interstitial pulmonary oedema, and marked increase in the size of the pulmonary arteries. (c) October 1969. After implant, showing slight increase in heart size, but some reduction in interstitial oedema.

Most patients with acromegaly have large heavy hearts, which can generally be ascribed to persistent hypertension or coronary artery disease. But in our experience there are patients in whom cardiomegaly and heart failure occurred before hypertension, and who died of heart disease despite treatment for acromegaly. Presumably therefore, excessive growth hormone may in some way cause irreversible cardiac damage.

Discussion

DR WALLACE BRIGDEN: You may be interested in a minor historical comment. Professor Dorothy Russell of the London Hospital was interested in the cardiovascular manifestations of the neuropathies and made a practice of carefully examining the pituitary in every subject with cardiomegaly. I plotted out the heart weights of a consecutive series of subjects with primary muscle disease and the two heaviest hearts, well over 1200 g, were both acromegalic, one with hypertension and one without hypertension.

DR OLSEN: The increase in heart weight is not so much due to myocardial fibre hypertrophy but to fibrous tissue. In fact, much of the myocardial tissue shows atrophy.

DR A. POMERANCE: I have only seen one similar case, with a heart weight about 800 g. Pathological changes were minimal with a small increase in interstitial fibrous tissue and rather large muscle fibres. My general impression was that there was nothing particularly abnormal present!

DR C. OAKLEY: Is Dr Olsen really suggesting that these hearts have 700 g of fibrous tissue and 300 g of muscle?

DR OLSEN: There is some hypertrophy away from the fibrous area, but the bulk of the additional tissue is fibrous. Analysis of the constituents of these thickened myocardial fibres shows a large increase in collagen components.

PROFESSOR MICHAEL HUTT: Surely the weights of these large hearts in acromegalic subjects should be expressed

in relation to body weight? We think of idiopathic cardiomegaly as a heart which is abnormally heavy in relationship to body weight. Most of the acromegalic subjects are big heavy individuals and one wonders whether a 1200 g or 800 g heart is really that big in relation to their size.

DR B. MCKINNEY: I have recently looked at sections of acromegalic heart and merely saw a slight increase in fibrous tissue, as described by Dr Pomerance. Does Dr Olsen know of any work measuring muscle fibre size?

DR OLSEN: There are several ways in which this could be done and which we have tried, both at light microscopy and electron microscopy level. It is painstaking and I do not know of any short way around it.

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