MEDICAL PRACTICE

Clinicopathological Conference

A Case of Acromegalic Heart Disease

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL ARRANGED BY DR. G. F. JOPLIN AND DR. PAUL LEWIS

British Medical Journal, 1973, 1, 718–724

DR. G. F. JOPLIN (1): The grounds for selection of this particular acromegalic for discussion this morning was that he was a Hammersmith patient for 10 years, and we had the results of the necropsy done here. As acromegalics go, he was a pretty average sort of case.

Case History

This man was 62 when he died in 1970. His acromegalic story goes back to the age of 35, when he first recalled enlarging hands and feet and changes of facial appearance, but he was not seen medically until he was 48. His complaints were rather non-specific when he first went to the doctor, and he drew attention to a small nodular goitre which had been growing visibly over the previous few years. At that time he was also seen here, and the acromegaly was obvious clinically. He was complaining of mild tiredness; there were also very mild finger paraesthesiae and excessive sweating. Exercise tolerance was normal. Only on direct questioning would he admit to headache, which was slight. Blood pressure was 140/100, and the small nodular goitre was noted. At that stage his general pituitary function, as well as could be assessed in 1956, appeared to be very satisfactory. Sex function was normal, urinary FSH (bioassay) was normal, 17-oxogenic steroids were 12 mg/24 hours, and ^{131}I test of thyroid function normal. *X*-ray films showed a small pituitary tumour; a chest radiograph was reported as being normal, and so was the electrocardiogram.

In those days, the first line of treatment for an acromegalic was considered to be external pituitary irradiation, and he therefore had a conventional dose of 4,000 rads delivered by the linear accelerator given over three weeks (Dr. R. Morrison).

When reassessed a year later, his headache was a little worse, and he was now impotent; otherwise there had been no change either clinically or in any of the test results. He was therefore recommended for further treatment by needle implantation of radioactive seeds directly into the tumour. The isotope then in vogue was gold-198, which is a gamma-emitter. Two platinum-screened seeds of radioactive gold were implanted

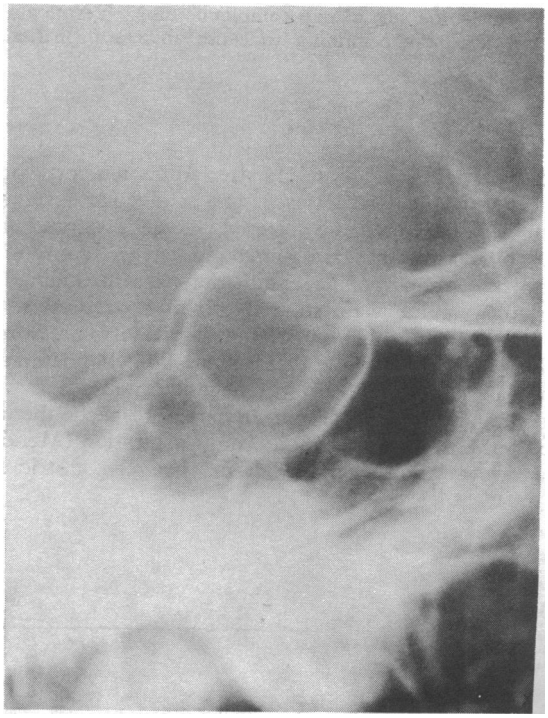

FIG. 1—Lateral radiograph showing eccentric expansion of the sella.

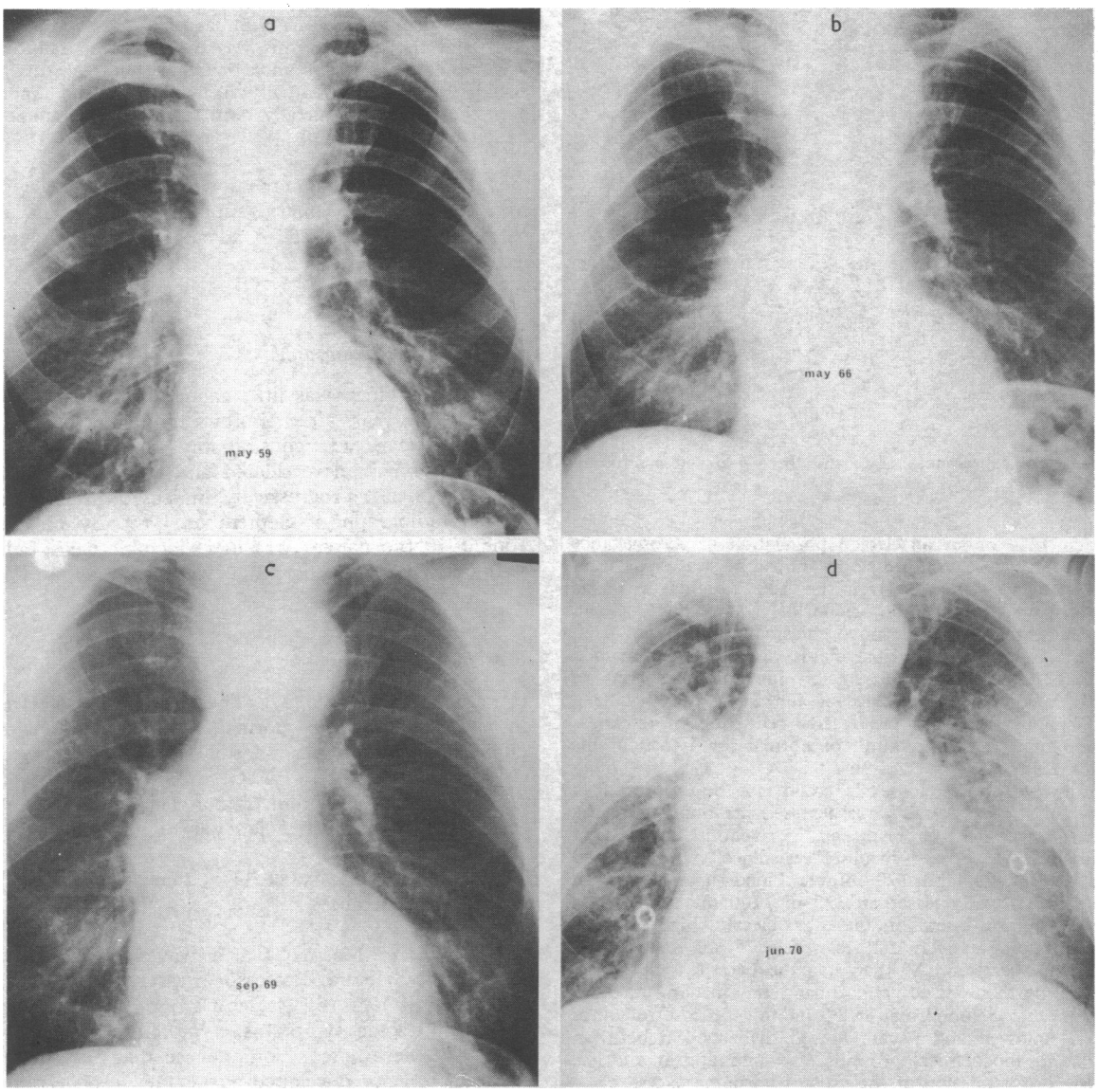

FIG. 2a-d—Sequence of chest radiographs from May 1959 to June 1970. Progressive enlargement of the heart and dilatation and elongation of the thoracic aorta are shown. The last radiograph is an antero-posterior projection using a mobile *x*-ray unit on the ward. The patient was by this time in intractable cardiac failure with pulmonary oedema.

into the centre of the tumour in 1959, the dose at the tumour surface being calculated to be about 10,000 rads. During the procedure it was noted that there was a small cyst on one side of this tumour; it was outlined with Hypaque. This was of no particular importance, as it is quite a common finding in these tumours. We will ask Dr. Doyle to go through the pre-treatment *x*-ray films.

DR. F. H. DOYLE (2): The patient had an obvious pituitary tumour. A lateral radiograph of his skull showed two widely separated contours forming the floor and anterior wall of the sella (fig. 1). This suggested eccentric expansion of the sella, and a postero-anterior radiograph showed that this was on the left side. An air encephalogram indicated no suprasellar extension of the tumour. Radiographs of his hands and feet showed characteristic and florid changes of acromegaly. In his thoracic spine the vertebral bodies were long in relation to their height. There were quite large osteophytes at all disc levels and new bone anterior to some vertebral bodies. His lumbar spine showed no abnormality. Moderately severe degenerative changes were apparent in his left hip joint. A chest radiograph in May 1959 showed moderate dilatation and elongation of his ascending aorta and aortic arch. His heart size was within normal limits (fig. 2a).

PROGRESS AFTER OPERATION

DR. JOPLIN: We fortunately have a clinical photograph taken before operation (fig. 3a). Subsequent to operation—and this is the main point of the case—his growth hormone excess was successfully abolished, but on the other hand his cardiac problem (which was of no clinical importance at the time we first saw him) relentlessly deteriorated and finally took his life.

Endocrine Progress

His facial features regressed quite strikingly after the pituitary operation and, though this first became evident by four months, the facial features went on improving right up to the time of his death (that is, over a period of 10 years). A second photograph (fig. 3b), which was taken about three years after his operation, shows that the folds on the face are now much smoother.

His energy improved after the operation, and he felt generally fitter. The slight headaches and paraesthesiae completely disappeared, and they never recurred. The size of the pituitary fossa did not increase over the succeeding 10 years. This is quite important

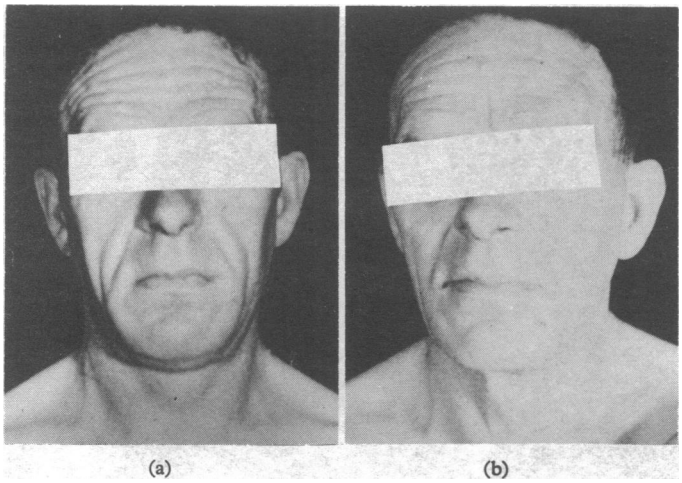

FIG. 3a and 3b—Facial appearance before and three years after pituitary implantation.

because at least 12% of an unselected population of acromegalics end up with optic nerve compression.[1] Thus, he was typical of our overall experience of well over the 100 patients we have treated by pituitary implantation, none of whom have shown subsequent sellar expansion or de novo chiasmal compression from further tumour growth. The visual fields and acuity remained perfectly normal for the remainder of his life. Measurements of the skin fold thickness of the back of the hand made with a spring-loaded caliper showed a progressive reduction in thickness from 3·3 to 2·0 mm, the upper limit of normal for a man of his age being about 2·25 mm.[2]

The serum growth hormone levels could not be measured in 1959, so growth hormone activity was assessed pre-implant by the insulintolerance test.[3] He was given an intravenous injection of soluble insulin, 0·3 U/kg, and insulin "resistance" was recorded by summing the 60, 90, and 120 minute blood-sugar levels. In normal people it is usually less than 135 mg/100 ml, and in this particular case, before operation, it was clearly high at 147 mg/100 ml; this progressively fell to reach 75 mg/100 ml by seven years after operation. At that stage it became possible to measure growth hormone itself, and during the insulin tolerance test the mean level was subnormal at 2·5 ng/ml. Glucose tolerance tests were also followed and never showed diabetes. So both on morphological and biochemical grounds it would appear that he had had a first-class remission of the growth hormone excess.

The general pituitary function for about seven years after his operation remained normal, but then he began to show signs of adrenocortical insufficiency. The 17-oxogenic steroids rose only from 6 mg/24 hours to 12 mg/24 hours on metyrapone, and the plasma 11-OHCS showed no response to lysine vasopressin. Eventually he required maintenance prednisone, 2·5 mg thrice daily, to retain normal energy; he was also started on thyroxine, although there was no objective evidence of thyroid failure at that time—nor did he report any response to this.

Cardiac Progress

The patient first drew attention to disability arising from his heart six years after his operation was done, and at seven years after operation he was having to stop to catch his breath at the top of two flights of stairs.

His blood pressure was 175/115 at that stage, and he was treated thereafter with hypotensive drugs by his own doctor, and there were no difficulties or complications attached to that. The retinae showed slight a-v nipping only. Also at that stage his E.C.G. was beginning to show flattened T-waves, and an enlarging heart was seen on *x*-ray films.

In 1970 intractable dyspnoea at rest led to admission for his terminal illness. Initially, this was entirely a left ventricular failure. His jugular venous pressure was normal when he came in, and there was no oedema, yet there was severe dyspnoea. Eventually he developed various arrhythmias; Dr. Oakley saw him at this stage and thought that this was mainly pump failure rather than valve disease. It was found impossible to treat this heart failure effectively, and he eventually succumbed from pulmonary emboli, even though he had already been started on phenindione in anticipation of that problem.

Our final clinical comment was that, despite what appeared to be effective pituitary suppression, the initial moderate cardiomegaly continued to advance, and pump failure finally led to his death.

Serial Chest Radiographs

DR. DOYLE: There was little change in the chest radiograph in the first few years after pituitary implant. By May 1966, however, the heart was considerably increased in size, and the aorta was much more dilated and elongated (fig. 2b). Thereafter the heart progressively increased in size, as indicated in the radiograph of September 1969. By the beginning of June 1970 the patient was in intractable heart failure and his pulmonary oedema (fig 2d) never resolved.

Electrocardiographs

DR. CELIA M. OAKLEY (3): The pre-implant electrocardiogram in 1959 was perfectly normal. This coincides with a lack of clinical symptoms, near-normal blood pressure, and normal chest *x*-ray film. The E.C.G. three months post-implant was also normal apart from rather flat T-waves, which might suggest some steroid deficiency at that time.

PROF. RUSSELL FRASER (4): They could equally well be coronary ischaemia?

DR. OAKLEY: No, no. Flat T-waves are nothing to do with coronary ischaemia, Professor Fraser. The E.C.G. remained normal until 1966 (fig. 4a) and around the time he first began to develop some symptoms; hypertension and an increase in heart size were noted. You can see that he remained in sinus rhythm, has not developed any evidence of left atrial enlargement, but has now lost the Q-waves in the left precordial leads, and the QRS shows a little widening. When he was in his terminal illness, which was a cardiac one, he had atrial fibrillation and multiple ectopic beats (fig. 4b). A very nasty-looking graph.

Necropsy Findings

DR. P. D. LEWIS (5): The body was that of a well-nourished middle-aged man. He was 6 ft. (1·8 m) tall and weighed 13½ stone (86 kg). His hands and feet were broad and enlarged, and facial features were coarse, with prominent supraorbital ridges of soft tissue. There was a dorsal kyphosis.

Although visceral enlargement is common in acromegaly, many of the organs here are of normal weight (table 1). Apart from the lungs, only the heart and brain were grossly overweight. So-called

TABLE—Organ Weights in Patient (*Unfixed Specimens*)

	Weight (g)	Normal Weight (g)
Heart	1140	380
Lungs	L 1000	400
	R 750	450
Liver	1585	(normal)
Kidneys	280	(normal)
Thyroid	32	(normal)
Adrenals	9	12
Brain	1600	1300-1400

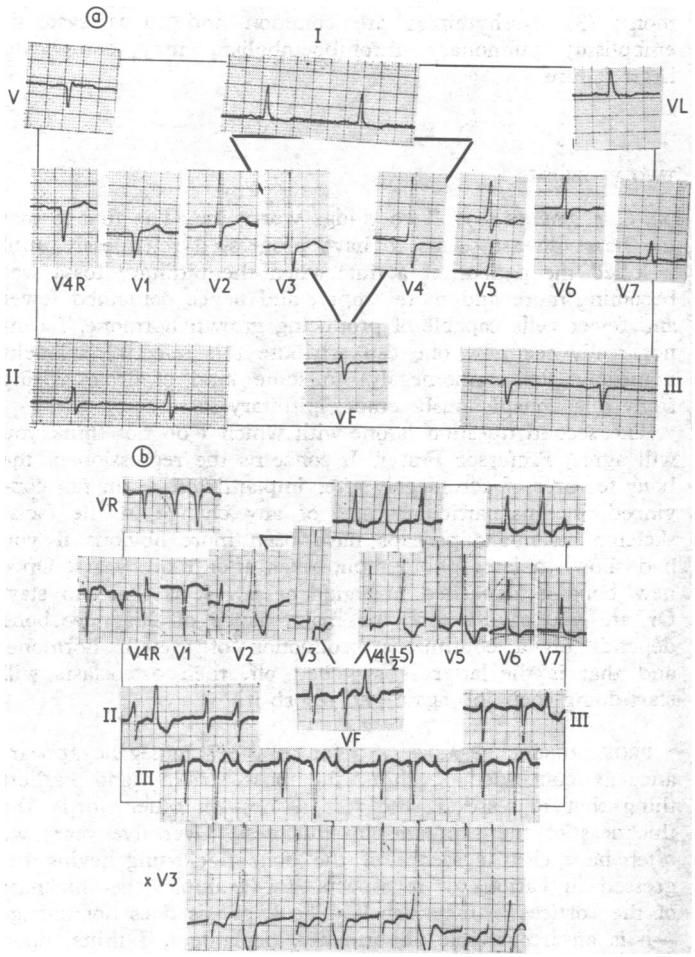

FIG. 4a and 4b—E.C.G.s of 1966 and 1970. The E.C.G. recorded in 1966 shows some prolongation of the QRS with loss of the normal Q waves in left ventricular leads, and sinus rhythm. The record suggests left ventricular disorder and probable left ventricular hypertrophy. The T waves are generally rather flat but there is no evidence of ischaemia. The E.C.G. recorded in 1970 shows progression of the previous QRS changes with higher voltage and further shift of the mean frontal QRS to the left. Q waves remain absent from left ventricular leads and it is not possible to say whether this represents a left anterior hemiblock. There is now atrial fibrillation with multiple bizarre QRS complexes due to both aberrant conduction and to ventricular ectopic beats.

megalencephaly does not seem to occur in acromegaly, and it is difficult to imagine a pathological process starting in adult life which causes a silent 25% increase in brain size. So I think his brain was always big. Apart from its size, there was no abnormality on dissection, and microscopy was normal.

The heart was three times normal weight, the increase being due to gross thickening of the myocardium. The left ventricle was 22 mm and the right ventricle 6 mm thick, twice the normal (fig. 5a). Thrombus was adherent to the left ventricular wall anteriorly, and at the apex of the left ventricle. A ball thrombus was also present in the left atrium.

The aortic valve was calcified and irregularly thickened from base to contact margin, and parts of the inter-coronary cusps were fused (fig. 5b). The valve circumference was 70 mm, so it was not stenotic and cannot account for any part of the left ventricular hypertrophy. There was no evidence of rheumatic heart disease, and the other valves were all normal. The coronary arteries were all patent and showed only moderate and non-occlusive atheromatous change. There was no myocardial infarction to account for the adherent thrombus.

The myocardium was not fibrotic and at low power appeared normal. Hypertrophy, even when as gross as this, may be difficult to recognize microscopically. At higher power, variation in muscle fibre size was visible, though it was patchy; but, more important, large nuclei, which may be octoploid or 16-oploid, were seen.

In summary, the heart showed gross myocardial hypertrophy which, in the absence of other significant disease, can be attributed to acromegaly. There was also mural thrombus formation and calcific aortic valve disease.

The abdominal aorta showed severe atheroma, with large calcified and ulcerated plaques. Calcific atheroma was also present in carotid and iliac arteries.

The pleural cavities each contained about a litre of clear fluid. The lungs were bulky and overweight, much of the weight increase being attributable to oedema. There were depressed fibrotic scars on the surface of each upper lobe apex. On cutting the right lung, frothy fluid poured from the cut surface. The left lung was fixed in formalin vapour before dissection and showed centrilobular emphysema and a small infarct in the lower lobe. Microscopically, the infarcted area was filled with extravasated blood, contained iron-laden macrophages, and was beginning to lose its structure. No pulmonary embolism was identified; the pulmonary arteries were free of thrombi and were not atheromatous.

The sella turcica was removed in one piece, decalcified, and sectioned horizontally. Only a rim of necrotic amorphous material remained, and there was no identifiable pituitary tissue. So the ablation was very successful, leaving no residue of his (presumed acidophil) adenoma. Did the radioactive implant damage adjacent structures? Because of an interest in this technique of treating pituitary lesions, we looked carefully at this possibility by serially sectioning the hypothalamic region. No abnormality was found using routine staining methods. The optic chiasma and tracts were also histologically normal.

The thyroid was at the upper limit of normal weight, and contained two well-encapsulated, partly necrotic nodules, up to 2 cm in diameter, in the right upper pole and right side of isthmus. They were adenomas, the larger having a follicular pattern and the smaller being an oxyphil or Hürthle cell adenoma. Such adenomatous enlargement of the thyroid is found in half of all

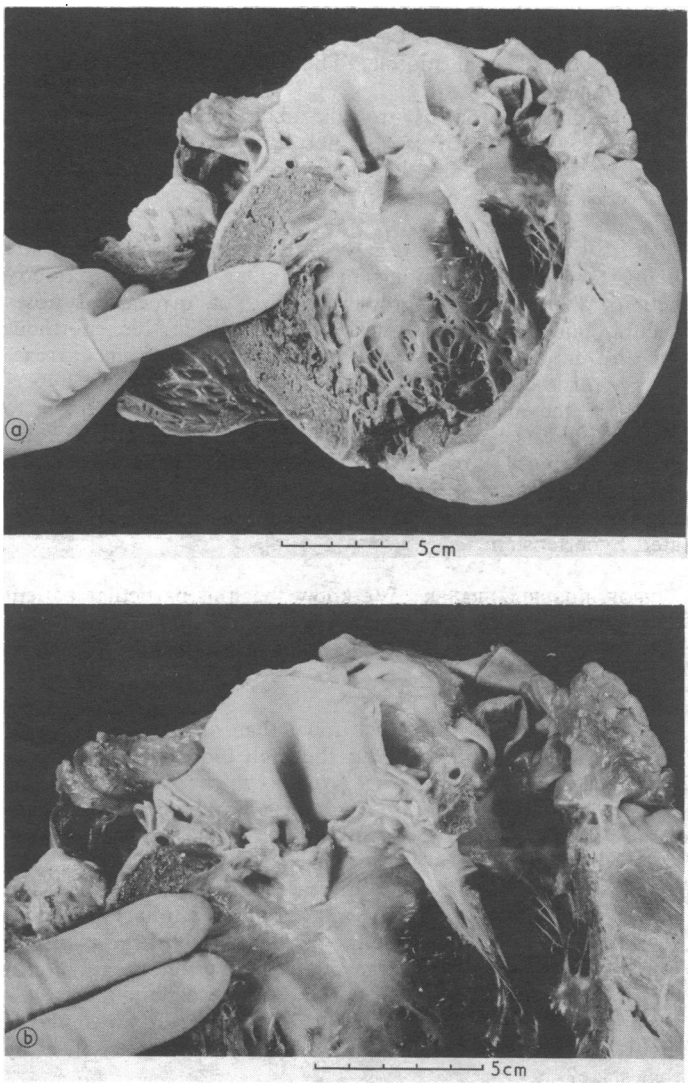

FIG. 5a and 5b—Heart opened to show increased thickness of left ventricular wall and calcific aortic valve disease.

acromegalics. The parathyroids were normal in number, position, and size, and on microscopy. The adrenals were small and had a thin brown cortex.

The left kidney (180 g) was larger than the right and contained a urine-filled cyst, 1 cm in diameter, in its upper pole. There were two small infarcts in the cortex of the right kidney, presumably related to the mural thrombus in the left ventricle.

The liver was normal in size and showed a nutmeg picture on slicing. Microscopically there was loss of liver cells around central veins, as is often seen in congestive cardiac failure.

Finally, his bones and joints; there was no evidence of acromegalic involvement of the vertebrae in his kyphotic spine.

Summary of Pathological Findings

(1) Acromegaly (pituitary ablation).
(2) Massive cardiac enlargement.
(3) Atrial and ventricular thrombi.
(4) Calcific aortic valve disease.
(5) Congestive cardiac failure.
(6) Pulmonary infarction and oedema.
(7) Renal infarction.
(8) Thyroid adenomata.

Discussion

PROF. RUSSELL FRASER: Thank you. Here we have a patient who clearly had a pituitary lesion and acromegaly, but the cause of his cardiac failure is not so obvious. A group in Newcastle have been studying myopathy in acromegaly. Five of their 11 patients showed raised levels of creatinine phosphokinase in the serum and they showed changes in the histology of sketetal muscle. Their studies did not include the myocardium.

It is difficult for us to talk about this as acromegalic cardiomyopathy, since we do not have evidence of pituitary over-production in the histology nor in tests over the last ten years. What do you think, Dr. Oakley?

DR. OAKLEY: In acromegaly with heart disease there are many possible contributing factors. One is direct pituitary action. We know that growth in size of myocardial fibres occurs, but it would be hard to believe that this enormous increase in myocardial weight was due only to an increase in size of the individual cells; there must be also a hyperplasia of the myocardium. This in itself would be liable to give rise to ischaemia because of a lack of comparable increase in the size of the capillary network. In addition, the work of the heart is increased, both from the increased size of all the body organs and from the very commonly associated hypertension.

PROF. RUSSELL FRASER: We know that this particular patient had well-marked hypertension over 12 years or so. Could the size of the heart reached terminally possibly be explained by that?

DR. OAKLEY: No. It is much more than one sees in ordinary hypertensive heart disease, but the high blood pressure might have provided a stimulus to growth which was met in this wild fashion because of the acromegaly. The increased incidence of high blood pressure in acromegaly is not understood, but we have at least three contributory factors here; increased myocardial work, increased myocardial bulk, and the hypopituitary state that may follow pituitary ablation. In patients with burnt-out acromegaly—either naturally burnt-out or who have been treated by pituitary ablation—we find that cardiac failure becomes more common, not less common.[5] Is it possible that the acromegalic with heart disease is better off with his acromegaly than without it by that stage?

Acromegalic heart disease may present with (1) heart failure (the acromegaly may be missed); (2) syncope that may be related to conduction defects (which are quite common); (3) dysrhythmias are common and so is systemic embolism; pulmonary thromboembolism may complicate heart failure.

TWO PROBLEMS

DR. C. A. PALLIS (6): Two things worry me. The first is that the heart disease seems to have progressed relentlessly until it killed the patient, at a time when the pituitary fossa was becoming more and more empty, and hence contained fewer and fewer cells capable of producing growth hormone. I cannot really see how one can attribute this selective splanchnomegaly (the cardiomegaly) to some kind of drive arising from this conspicuously empty pituitary fossa.

The second question is one with which I do not think you will agree, Professor Fraser. It concerns the regression of the bony features of acromegaly after implantation. I am not convinced, in this particular case, of any change in the facial skeleton. It might perhaps have been more obvious if you had shown a later photograph, taken after more years. Once new bone is deposited in hands or jaw it is there to stay. Or are you saying that the maintenance of this new bone depends on a continuous production of growth hormone, and that if the latter is switched off, then osteoclasts will start doing their job again and resorb it?

PROF. RUSSELL FRASER: So far as the acromegalic appearance is concerned, I think the most striking and earliest thing that regresses is the soft tissues—in other words, the thickness of the skin and lip thickness. Over five years we often have clear evidence of the bone thickening having regressed in various of is aspects—for example, the thickness of the cortices in metacarpals. The kyphosis does not change—it is an irreversible abnormality, dependent, I think, upon lengthening of the ligaments.

DR. PALLIS: What about the phalangeal tufting?

PROF. RUSSELL FRASER: The tufting gets less, just as does the cortical bone thickness.

DOCTOR FROM AUDIENCE: One test of the various hypotheses about the cardiomegaly would be to ask Dr. Lewis whether, if he had known nothing of the clinical findings, he could have diagnosed acromegalic heart disease from the histology?

DR. LEWIS: No. Published pathological findings on acromegalic heart disease are not comprehensive. Hypertrophy is the commonest microscopic change recorded in the muscle, with some cases showing fibrosis, but there is no constant picture, and no definitive source of reference either.[6,7]

DR. OAKLEY: It is not all that obscure. We know that growth hormone increases the size of the cardiac fibres. There is no evidence that function is impaired more than that of any other hypertrophied myocardial fibres—for example, in hypertrophy secondary to obstruction of a valve. Hypertrophied muscle works almost as well as normal muscle but under stress it fails and its velocity of shortening is slower. This bulky muscle may have a precarious blood supply, and if we also throw in an increased after load due to increased blood pressure and increased output associated with expansion of red cell and plasma volume then we may expect failure.

The next point is the one that Dr. Pallis raised—which is why with no pituitary in the sella for 10 years did the patient go on and get heart failure? Extreme cardiac hypertrophy never regresses after removal of the cause, and in any case he had developed quite severe hypertension *after* the pituitary ablation.

DR. PALLIS: But was there extreme cardiac hypertrophy? The heart size on the early *x*-ray films was normal.

DR. OAKLEY: I am sorry, but you cannot appreciate cardiac hypertrophy on radiography—only cavity dilitation. There was, I am sure, a great increase in muscle bulk at the time of those radiographs but cardiac function remained good, so there was no detectable increase in cardiac dimensions.

PROF. RUSSELL FRASER: Dr. Pallis, we must not ignore the probability of his having been acromegalic for a decade at least, before losing all his growth hormone; that may have been enough to lead to eventual failure.

REVERSIBLE HYPERTROPHY

DR. D. J. EVANS (7): Could I ask if there is any evidence that the cardiac hypertrophy could be reversible? With other organs, particularly the liver, hypophysectomy will considerably reduce the proportion of the liver weight to the body weight. I am not sure whether a growth-hormone-stimulated hypertrophy is strictly comparable with that produced by a valvular obstruction.

PROF. RUSSELL FRASER: If, for example, you produce hypertrophied hearts by administration of thyroid hormone, when you stop the thyroid hormone it takes a very long time to regress if it does at all. In the same way I think it is true with overgrown hearts from injections of growth hormone. But whether it would fully regress eventually, I think, is a doubtful question.

DR. EVANS: If you are postulating ischaemia, are you surprised to see no electrocardiographic evidence of ischaemia?

DR. OAKLEY: I agree that most of his failure may have resulted from the increase in heart work, but the electrocardiogram is a crude tool. In the presence of marked hypertrophy it may not be possible to recognise ischaemia.

DR. EVANS: There is one other point about this patient, and that is the gross disparity between the severe atheroma present in the aorta, and the minor atheroma in the coronaries. This is a good reason why one should not use incidents of cardiac infarction as an index of severity of atheroma.

DR. JOPLIN: Could we postulate that at the time he had his operation only a small reduction in myocardial efficiency existed, and was directly attributable to a deleterious effect of high growth hormone levels. At that particular time, when he was younger and fitter, the pump was strong enough for his way of life. If there is no possible repair of efficiency of the fibres after pituitary implantation, then over the years this would present exactly the same stimulus for sustained and continued hypertrophy as any other mechanical defect such as aortic valve obstruction. So he could go on increasing his heart size indefinitely, even although the cause of the initial damage has been eliminated. To avoid this train of events one would need to prevent the initial myocardial weakening by operating much earlier in the disease.

DR. LEWIS: Yes, that is a good suggestion. You could even postulate, for the sake of argument, that the growth hormone triggers the adventitial cells, or the cells which are going to make new muscle fibres, from a G_0 into a prolonged G_1 phase —in other words, it puts them into a potentially mitotic state.

DR. JOPLIN: The other thing is that I am sure we can drop the necessity for regarding hypertension as an essential factor in the production of his heart disease. A few years ago we did a clinicopathological conference on a young acromegalic aged 34. He died of intractable heart failure without having any pituitary treatment at all. He had an enormous heart, like to-day's patient, and yet his E.C.G. was virtually normal. At necropsy there was not the slightest sign of coronary artery disease or myocardial ischaemia. He had a normal blood pressure documented frequently for a year before he died. So we need not bring blood pressure into the reconstruction of the present patient's story at all, although it was a fact that he had moderate hypertension, and hypertension is more common in acromegalics than in the general population.

PROF. RUSSELL FRASER: But the hypertension is not entirely a red herring, is it? Our analysis of the incidence of hypertension in acromegaly as against the normal population, by decades and sex, shows clearly that there is more hypertension among acromegalics than among the normal population. So it is one factor; maybe a small factor.

TRIGLYCERIDES IN ACROMEGALY

DR. B. R. TULLOCH (8): In their paper on the natural history of acromegaly Wright and his colleagues[1] found ischaemic cardiovascular disease to be the commonest cause of death. Raised fasting triglycerides are a known risk factor for vascular disease and fig. 6 shows the fasting triglyceride levels in 25 acromegalic patients from our series treated by pituitary implant. The mean value (147 mg/100 ml) is just above the upper limit (140 mg/100 ml) of the normal range for this hospital, and in the nine cases re-studied three months post-implant fasting triglycerides were significantly reduced.

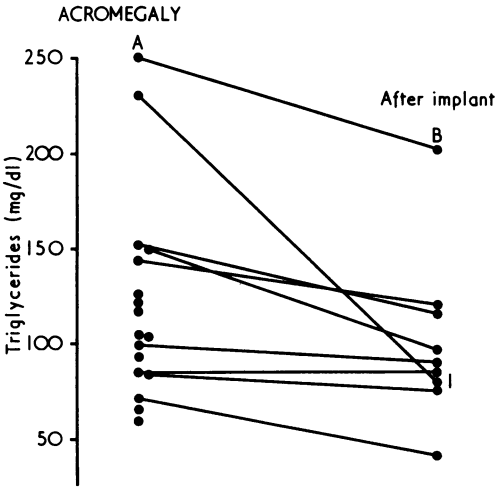

FIG. 6—Fasting plasma triglyceride values in a series of patients with acromegaly. Column A: before implant; mean 147 mg/100 ml. Column B: 3 months after ^{90}Y pituitary implant; mean 103 mg/100 ml. ($p < 0.001$ on paired pre-treatment values).

In the fasting state plasma triglycerides are synthesized by the liver and are cleared peripherally by the enzyme lipoprotein lipase. Our studies in nine subjects using Boberg's fat tolerance tests[9] have indicated that following pituitary implant the fall in fasting triglycerides is accompanied by a decreased rate of triglyceride clearance. This would suggest a mechanism for the acromegalic hypertriglyceridaemia to be an increased liver output of lipoproteins.

DR. B. PIMSTONE (9): No one has mentioned the problem of sodium retention. Some acromegalics are similar to patients with primary hyperaldosteronism, with an expanded and fixed plasma volume. The exact mechanism is ill-understood but may be relevant to the pathogenesis of hypertension in

acromegaly. Is the lipid abnormality caused directly by the high levels of growth hormone, or is this due to the well-known disturbance in insulin metabolism?

DR. TULLOCH: Our group of acromegalics was selected for study to exclude those with an abnormal glucose tolerance test. There is little information about how metabolic changes secondary to growth hormone could be differentiated from the associated plasma insulin increase. We once studied a single case of pan-hypopituitarism due to a craniopharyngioma, and recorded an increase of fasting plasma triglycerides from 70 to 120 mg/100 ml after six days' treatment with human growth hormone (10 mg/day).

PROF. RUSSELL FRASER: Well, evidently we still do not know the mechanism of this heart disease which afflicts a high proportion of acromegalics. This problem remains for future study.

This conference was recorded and edited by Dr. G. F. Joplin.

APPOINTMENTS OF SPEAKERS

(1) Dr. G. F. Joplin, Senior Lecturer in Clinical Endocrinology and Consultant Physician, Royal Postgraduate Medical School, and Hammersmith Hospital.

(2) Dr. F. H. Doyle, Reader in Diagnostic Radiology, Royal Postgraduate Medical School.

(3) Dr. Celia M. Oakley, Consultant Cardiologist, Royal Postgraduate Medical School, and Hammersmith Hospital.

(4) Professor Russell Fraser, Professor of Clinical Endocrinology and Consultant Physician, Royal Postgraduate Medical School, and Hammersmith Hospital.

(5) Dr. P. D. Lewis, Lecturer in Histopathology, Consultant Physician and Histopathologist, Royal Postgraduate Medical School, and Hammersmith Hospital.

(6) Dr. C. A. Pallis, Reader in Neurology, Royal Postgraduate Medical School.

(7) Dr. D. J. Evans, Senior Lecturer and Consultant Histopathologist, Royal Postgraduate Medical School and Hammersmith Hospital.

(8) Dr. B. R. Tulloch, Wellcome Senior Clinical Research Fellow and Honorary Lecturer in Clinical Endocrinology, Royal Postgraduate Medical School.

(9) Dr. B. Pimstone, Visiting Colleague (endocrinology).

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Contemporary Themes

Social Effects of Genetic Counselling

ALAN E. H. EMERY, MURIEL S. WATT, ENID CLACK

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Summary

In a follow-up study of 104 subjects referred for genetic counselling between 1965 and 1969 all were at risk of having children with a variety of serious genetic disorders. Most subjects were in social classes III and IV, were married, in their late 20s, and already had an affected child. Sixty-three per cent. were referred by hospital consultants, 27% by their general practitioners, and 10% were self-referrals. All of those counselled appeared to have appreciated the genetic implications, although four overestimated the risks and 11 underestimated the risks.

Of those at high risk (greater than 1 in 10) of having an affected child 10 out of 55 couples "planned" further pregnancies despite the risks. In two this was because they had been unable to adopt a child, in four because they had no living children and the disorders in question usually resulted in stillbirth or death in infancy so that the "burden" of an affected child would be of relatively short duration, and one mother had had antenatal diagnosis and selective abortion. Most of the couples in the low-risk group (less than 1 in 20) were reassured and planned further pregnancies.

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Introduction

An increasing proportion of morbidity and mortality, particularly in childhood, can be attributed to genetic factors. For example, in a recent survey in Newcastle upon Tyne, no less than 42% of childhood deaths in hospital could be attributed to disorders which were largely or even entirely genetically determined.[1] The prevention of such disorders lies within the province of genetic counselling whereby the risks of recurrence are explained to prospective parents. If the risks are high and the disorder in question is a serious one the parents may decide to have no further children and rely on contraception or one of the parents being sterilized. More recently antenatal diagnosis with selective abortion of affected fetuses has become possible in chromosomal and certain metabolic disorders. A follow-up study from this department of women referred for genetic counselling in families with Duchenne type muscular dystrophy showed that some women at high