Case Report

A coloured houseboy aged 30, of simple, facile, cheerful, and deceitful character, came to hospital complaining of a vague respiratory illness. He had always been of small stature: height, 58½ in. (149 cm.); span, 60½ in. (154 cm.); lower segment, 29 in. (74 cm.); upper segment, 29½ in. (75 cm.). His neck was markedly webbed (Fig. 2). There was no cubitus valgus. His muscles were very well developed—a midget "Mr. Universe." Sexually he also appeared fully equipped (Fig. 1), yet he denied having ever experienced sexual feelings of any kind and stated he had never had an erection or an emission. (Curiously, one of the few reported male cases had an enlarged phallus (Greenblatt and Nieburgs, 1948) as a possible additional congenital abnormality.) We were unable to obtain a specimen of semen. There was some disagreement regarding the size and consistency of the testes—possibly smaller and firmer than usual. The prostate was small. The blood pressure was 145/75 mm. Hg.

FIG. 1.—Short and muscular, with masculine stature and well-developed phallus.

Radiographs showed mild generalized osteoporosis. The 17-ketosteroids were 5.9 mg. per 24 hours (single estimation—method of Holtorff and Koch, 1940). The Wassermann reaction was negative. Urinary gonadotropins: 96 units per 24 hours (method of Klinefelter, Albright, and Griswold, 1943).

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Summary

We have observed a case representing Turner's syndrome in the male—the homologue of ovarian agenesis

FIG. 2.—Note webbing of neck.

with short stature and congenital anomalies. We have made this an excuse for a consideration of what the male homologue should be and for a comparison of this with the Klinefelter-Reifenstein-Albright syndrome.

We conclude that the absence of homogeneity in the various reports of these conditions is due to the separation of endocrinal and germinal tissue in the male gonad,

whereas in the female gonad one single tissue—the Graafian follicle—serves both endocrinal and germinal functions.

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ELECTROLYTE IMBALANCE AFTER OPERATION FOR PITUITARY TUMOUR

BY

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A proportion of patients who have a pituitary adenoma or cyst present clinical evidence of hypopituitarism. Further light has been shed on this syndrome by Sheehan (1939) and Sheehan and Summers (1949), and by the development of biochemical tests of endocrine function.

In patients undergoing surgical treatment a hypopituitary crisis may be precipitated by the stress of the operation and by disturbance of function of the remaining pituitary tissue. This may prove fatal. Grant (1948), in his series of 71 cases, reported three in which a relatively simple operation was followed by stupor, coma, and death on the fifth, ninth, and twelfth days. At necropsy on two of these atrophy of the gonads and adrenal and thyroid glands was demonstrated.

The crisis may present with a variety of endocrine and biochemical disturbances, but is commonly characterized by the gradual onset of drowsiness progressing to stupor and coma, usually over a number of days. It is sometimes preceded by convulsions (Sheehan and Summers, 1952).

The management of hypopituitarism has advanced considerably in recent years. A combination of testosterone, thyroid, and deoxycortone acetate (D.C.A.) as substitution therapy is usually employed (Robertson and Kirkpatrick, 1951a), but cortisone and adrenocorticotrophic hormone (A.C.T.H.) have been used with more striking effect (Robertson and Kirkpatrick, 1951b; Summers and Sheehan, 1951; Rolland and Matthews, 1952).

Treatment of the emergency of hypopituitary coma has been discussed by Sheehan and Summers (1952):

intravenous glucose, testosterone, thyroid, and the control of hypothermia, if present, are all of value. Allott and Simmons (1951) describe a case which rapidly improved with cortisone. Caughey, James, and Macleod (1952) describe four patients who passed into a state of stupor following removal of pituitary adenomas, associated with a low blood sodium and chloride. In two cases cortisone was given with good effect, and subsequent substitution therapy with testosterone, thyroid, and D.C.A. was used.

The following case is one of a series in which A.C.T.H. is being employed pre- and post-operatively in patients with pituitary tumours who show clinical or laboratory evidence of pituitary hypofunction.

Case History

A man aged 41 was first seen in March, 1950, complaining of headaches and impaired vision for the previous three months. He had also noticed impotence and loss of libido for about a year, and had come to dislike cold weather intensely.

On examination he was found to be of normal physique. His skin was soft and pale, with absence of pigmentation. The facies was flabby, with pallor of the cheeks; his speech was quiet and slow. Scalp hair was fine and silky and pubic hair was present, but the axillary hair and beard were scanty; he shaved twice a week. The thyroid was not palpable, and there was marked atrophy of the testes. The blood pressure was 100/70 mm. Hg. There was early optic atrophy. Perimetry showed an early incomplete bitemporal hemianopia. The lumbar cerebrospinal fluid (C.S.F.) pressure was normal, and the protein 65 mg. per 100 ml. A radiograph of the skull showed an enlarged pituitary fossa with preservation of the posterior clinoid processes.

During the next month the headaches became less severe and his vision returned to normal. Surgical intervention was deferred. After a few months of relief, however, his headaches returned, and during the latter part of 1951 his vision became steadily worse. He also suffered from intense lassitude and the facial hair became sparser.

When readmitted to the neurosurgical unit in February, 1952, his visual acuity was 6/9 partly for both eyes, there was marked bilateral optic atrophy, and the bitemporal hemianopia had increased. The blood pressure was 114/90 mm. Hg; plasma cholesterol, 290 mg. per 100 ml.; and the C.S.F. protein had increased to 120 mg. per 100 ml. Laboratory tests of metabolic and endocrine function confirmed the clinical evidence of a severe degree of pituitary hypofunction. The glucose-tolerance curve was "flat" (rising to 100 mg. per 100 ml. one and half hours after 50 g. of glucose by mouth), and a fractional test meal showed a low gastric acidity. The Kepler test for adrenocortical insufficiency gave a coefficient A of 10.8 (normal over 30). The plasma chloride level was 605 mg. per 100 ml., and the urinary chloride concentration during the Kepler test was 11 g. per litre.

Pre-operative A.C.T.H. substitution therapy (40 mg. daily intramuscularly) was begun 12 days before operation. This produced improvement in his physical energy, and he felt less lethargic than for many years. The laboratory tests were repeated after a week of treatment and significant changes in the results were noted. The glucose-tolerance curve assumed normal proportions (rising to 182 mg. per 100 ml. one and half hours after 50 g. of glucose) and there was an increase in the gastric acidity. The Kepler coefficient A was now 25.5 and the plasma chloride 630 mg. per 100 ml. During the test the urinary chloride concentration was 2.3 g. per litre.

A right frontal craniotomy was performed on April 15 by Mr. D. G. Phillips. Elevation of the frontal lobe revealed a rounded swelling arising from the pituitary fossa and displacing the optic chiasma forwards. Aspiration produced 4 ml. of dark-brown fluid containing cholesterol

crystals. This was enough to decompress the chiasma, and after removal of a fragment of cyst wall the wound was closed without drainage.

The immediate post-operative period was without incident. The blood pressure was maintained, and there was a rapid return of consciousness. A.C.T.H. (40 mg. daily) was continued for the next six days, being reduced to 20 mg. over the final 48 hours. The urinary output remained within normal limits (1–1.5 litres a day) and there was no polydipsia. Two days after A.C.T.H. had been discontinued the patient vomited twice and the urinary chloride concentration was found to be 11.8 g. per litre. He became rather lethargic and disinterested and continued so for the next few days.

Twelve days after the operation he vomited again and complained of numbness in the left hand. He was found to have a hemiparesis affecting this side. Next day (April 28) the lethargy and drowsiness were more evident, and there was a marked generalized muscular weakness. The blood pressure was 100/80 mm. Hg, pulse rate 92, and temperature 98.6° F. (37° C.). Testosterone, 100 mg., D.C.A., 5 mg., and thyroid, $\frac{1}{4}$ gr. (16 mg.), were given daily.

During the next 48 hours the blood pressure fell to 90/65 mm. Hg, the stupor and hemiparesis became worse, and he had a number of epileptic attacks affecting the left side. Because of this, on April 30 the craniotomy wound was reopened under local analgesia. Apart from a small subdural blood clot and a localized collection of C.S.F. in the region of the optic chiasma, nothing abnormal was found. There was no significant brain oedema and it was doubtful if the findings adequately accounted for the late deterioration. The wound was resutured with drainage, the bone flap being removed as a precautionary measure lest brain oedema occur. Penicillin, 100,000 units, was given four-hourly.

On return to the ward the blood pressure fell to 80/65 mm. Hg, and the pulse rose to 140. Blood transfusion and intravenous "methedrine" (30 mg.) had no effect on the hypotension. Estimation of the blood electrolytes revealed that there was a severe *sodium and chloride deficiency*. The plasma sodium was 287 mg. per 100 ml., plasma chloride 539 mg. per 100 ml., and serum potassium 18 mg. per 100 ml. (normal ranges being 310 to 345 mg., 590 to 625 mg. as NaCl, and 17 to 20 mg. respectively).

A.C.T.H., 60 mg., was given intramuscularly, together with 30 g. of sodium chloride—20 g. as a hypertonic solution intravenously, and the remainder, with 5 g. of potassium chloride, by oesophageal tube. Within an hour of the saline administration the blood pressure rose to 100/75 mm. Hg, and remained at this level; the patient also became more alert and easily roused to take fluids by mouth.

Throughout the next day his improvement continued and the hemiparesis was now only just perceptible. Estimation of the blood chemistry showed that the plasma sodium was 306 mg. per 100 ml., and the chloride and potassium 585 mg. and 18.4 mg. per 100 ml. respectively. The blood sugar was 164 mg. per 100 ml. Substitution therapy with 80 mg. of A.C.T.H. per day was continued, plus supplementary sodium chloride by mouth to balance the urinary loss.

His relative well-being was short-lived; four days later he again became drowsy and unresponsive to questions. This was accompanied by pyrexia and signs of pneumonia. The penicillin was stopped and chloramphenicol, 1 g. six-hourly, substituted. He remained very ill during the next two days, and developed slight oedema of the hands and sacral region; because of this the supplementary oral salt was reduced. An electrocardiogram at this stage showed low-voltage waves, but no evidence of hypocalcaemia or hyperalkalaemia or of hypocalcaemia or hypercalcaemia. The jugular venous pressure was not visibly raised.

The urinary output, which had been balancing his fluid intake, fell on May 5 to 0.5 litre. Accompanying this, the

plasma sodium increased to 414 mg. per 100 ml. and the chloride to 719 mg. per 100 ml. There was a fall in the serum potassium to 14 mg. per 100 ml. These figures show sodium and chloride retention. Oliguria persisted for a further three days, his oedema became worse, and his general condition deteriorated still further. Intake of fluids meanwhile was 2-3 litres a day. Urea, 60 g. a day, was then given as a diuretic for three consecutive days, and produced a good response. The urine output increased to 3 litres a day and the oedema lessened. The blood electrolytes fell to normal limits.

With the return of his blood chemistry to normal, his condition began to improve steadily; his temperature settled and the antibiotic dosage was reduced. Nine days after the second operation testosterone and thyroid were started, while the A.C.T.H. was gradually reduced in dosage each day, being finally discontinued two weeks later. During the following month his fluid and electrolyte balance remained satisfactory with a normal diet, and blood electrolyte estimations from time to time showed normal figures. Testosterone and D.C.A. were continued, but he remained lethargic and rather uncooperative in spite of his hormone treatment. Cortisone was not available.

Discussion

In this case A.C.T.H. substitution therapy appeared to be successful in tiding the patient over the stress of the operation on the pituitary cyst. After cessation of the treatment he slowly lapsed into the form of stupor characteristic of "endocrine failure." This was accompanied by a fall of blood pressure and loss of body sodium and chloride; in fact, a high concentration of chloride in the urine together with a normal fluid excretion had been observed during the period before the collapse, but the significance of this was not then recognized. Daily estimations of the amount of salt excreted therefore appear to be important in such a case.

Concurrently with his deterioration the patient developed a hemiparesis of the side opposite to that of the surgical approach. Focal epileptic attacks followed. These phenomena may have been due to local thrombosis, but it is strange that they improved so suddenly once the electrolyte balance was restored and A.C.T.H. recommenced.

Re-exploration of the operation field did not reveal adequate cause for the late deterioration, and failed to produce an immediate improvement. The level of consciousness and the blood pressure improved after the replacement of body salt and the administration of A.C.T.H.

The second relapse was associated with elevation of plasma sodium and chloride, oedema, and respiratory infection. This responded to restriction of salt and the use of a diuretic and antibiotics.

An abnormal water and electrolyte metabolism is often found in hypopituitarism, and is essentially similar to that occurring in Addison's disease and in adrenalectomized animals; there is failure of normal water diuresis, deficiency of sodium and chloride, and accumulation of potassium in the body. These features were present in the case described. Although the secretion of the electrolyte-regulating hormones of the adrenal cortex is not under the influence of the anterior pituitary to the extent, for example, of the hormones controlling carbohydrate and protein metabolism, in the absence of the adeno-hypophysis the adrenal cortex is unable to regulate the reabsorption of electrolytes by the renal tubules so as to preserve the constancy of the internal environment when confronted by physiological changes, variations in diet, and stress (Sayers, 1951). An interesting feature is that throughout the period of observation of this patient in hospital before and after operation, and also while he was being given A.C.T.H., most of his urine was passed at night, a reversal of the normal diurnal rhythm. This is in keeping with previous observations in hypopituitarism (Robertson, 1951).

Summary

A case of hypopituitarism due to a pituitary cyst is described in which A.C.T.H. was given before and after operation.

Several days after cessation of treatment with A.C.T.H. the development of hemiparesis, epileptic attacks, and stupor was associated with sodium and chloride depletion.

Rapid improvement followed correction of the electrolyte depletion and resumption of A.C.T.H. therapy.

Onset of respiratory infection and oedema, with sodium and chloride retention, was associated with a relapse. This was relieved with antibiotics and induction of a diuresis.

The pituitary-adrenal relationship is discussed.

It is concluded that constant attention to electrolyte balance is important in the management of such a case.

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MYOCARDIAL CALCIFICATION ASSOCIATED WITH PITUITARY ADENOMA AND OBESITY

BY

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Myocardial calcification without evidence of extensive tuberculous, rheumatic, or ischaemic heart disease is not common, and few cases have been reported. In the following case the gross obesity and large pituitary tumour add to the interest.

Clinical History

A woman aged 64 was admitted to hospital on a Saturday afternoon and died 36 hours later, before radiological or pathological investigations could be undertaken. Owing to her poor mental state an accurate history was out of the question, but her relatives said that her legs had been swollen for some 30 years and that more recently she had been short of breath. Nevertheless, in spite of her increasing disability—she had virtually been confined to bed for two years—she had refused to allow her doctor to see her. She had not had diphtheria or tuberculosis, nor had she been abroad. There was a family history of obesity, both parents and three siblings being overweight, and two of these had died of heart failure.

Examination was made difficult on account of her vast size and rather bovine mentality. Her weight was estimated