A CASE OF CUSHING'S SYNDROME

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In view of the wide interest displayed in the syndrome recently described by Cushing, the following case, presenting the chief signs of that syndrome, may be worth placing on record.

History.—The patient, an unmarried woman of 35, when seen by Dr. Protheroe Smith of Topsham in April, 1934, complained of amenorrhoea for the last four months. The periods had begun at the age of 14 and had been regular, except during the first two gastric attacks referred to later. She also complained of pains, in various parts, of three weeks' duration, and of dyspnoea on going upstairs for the past week. For six or seven years she had had attacks of epigastric pain, vomiting, and occasional haematemesis. Such attacks were always accompanied by wasting and amenorrhoea. In 1928 α rays, test meal, and other investigations did not confirm the diagnosis of peptic ulceration. At that time her complexion was noted to be coppery red. In 1932, when there was another attack of haematemesis, a slight reduction was noted in the urine, and amenorrhoea persisted for nine months after this. In April, 1934, she was seen by one of us (C. M. S.), and the following note was made.

Examination.—A small, stoutly built, somewhat round-shouldered woman, with a thick growth of black hair going grey, a coppery red complexion, and an overgrowth of hair in the beard region, which had been controlled for some years by the daily use of pumice stone. Hirsuties was evident also to a slight extent on the breasts, which were atrophic, and from the umbilicus to the pubis and perineum, where hair was copious; there was a slight growth of hair on the back. Hyperalgesia was present all over, including the scalp and limbs as well as the trunk, being more marked on the left side. The trunk and limbs were pale, save that purpura-like ecchymoses were evident on the lower shins, which were cold to the touch and somewhat bluish. There were typical striae on the abdomen and thighs. The eyes were bright and somewhat exophthalmic, the disks and fundi normal, though the sight has recently become somewhat dim. The heart and lungs appeared to be normal; the blood pressure was 160/112 (previous records gave a systolic blood pressure of 126 in February, 1932). There was great tenderness of the left sacro-iliac joint, and to a less extent of the right joint, and the sciatic test was positive on the left side; there was no tenderness over the sciatic nerve itself. Knee-jerks were present and equal, ankle-jerks absent, and plantar reflexes not obtained. The abdomen was generally tender, but this appeared to be more marked under the right rib margin, where she constantly complained of more pain than elsewhere. The haemoglobin was 112 per cent., red blood cells 5.8 millions, white blood cells 10,000. X-rays showed normal filling of the gall-bladder, with a somewhat remote possibility of a stone in the gall-bladder region; a barium meal showed no abnormality, save for a speck of barium in the duodenum in the four-hour film.

Diagnosis.—These findings led to a diagnosis of chronic appendicitis, to account for her dyspeptic symptoms, and a pituitary basophilism. Before this second syndrome had established itself in our minds, however, an operation was performed in March, 1934, by Mr. Norman Lock, who found the appendix bound down by firm adhesions, but not inflamed. The uterus was infantile and ovaries fibrotic. Unfortunately, the suprarenal glands were not examined. Following this operation the patient's dyspeptic symptoms were for a time very much better. Her other symptoms were unchanged. When seen again in October, 1934, she felt fairly well and continued to be free from dyspeptic symptoms. Her weight was 7 st. 11½ lb. (having been 7 st. 2 lb. on leaving the nursing home). The blood pressure was 156/126. An α -ray of the pituitary fossa at this time showed it to be small, with floor intact, smooth, and of normal outline. She was then put on

menformon injections without effect, save for a transient and abortive menstrual period. In December, 1934, haemoglobin was 122 per cent., red blood cells 6 millions, white blood cells 18,200. She was beginning to vomit more and to have bad headaches. The condition was advancing, and the diagnosis seemed to be between a pituitary or suprarenal lesion. Prior to admission to hospital for further investigation she was seen by another of us (W. L.-B.), who favoured the former diagnosis. At that time the bone and spinal pains were rather severe, and the flattening of the buttocks was marked.

Progress.—She was admitted to hospital in February, 1935. After admission she vomited several times a day, occasionally with blood, and latterly developed photophobia, with misty vision, occasional nystagmus, and double vision when the eyes were directed to the right or left. There was also severe occipital and vertical headache. She was given deep α -ray therapy to the pituitary fossa, but the headache was aggravated thereby, and this treatment was discontinued when about 50 per cent. of the total dose had been administered in small daily instalments. Her headache was somewhat relieved when α -ray treatment ceased. The optic disks were normal. She had always been euphoric, and had some mild delusions. The twenty-four-hour output of urine varied from 14 to 34 oz., averaging about 20; it contained a trace of albumin, a few granular casts, *B. coli*, and occasional small amounts of sugar. Other investigations gave the following results: blood urea, 36 mg. per cent.; Aschheim-Zondek test, negative; serum calcium, 10.2 mg. per cent.; basal metabolic rate, 27 per cent. A sugar curve showed a diminished tolerance, characteristic of this condition. There was no resting hyperglycaemia, but the blood sugar rose to nearly 220 mg. per cent. one hour after 50 mg. of dextrose, returning to normal at the end of two hours, when 0.4 per cent. of sugar was excreted, but no ketones. A further α -ray of the stomach and duodenum showed no sign of ulcer. X-rays of the bones showed no decalcification, but the bodies of the vertebrae were narrowed as if flattened by pressure. No abnormal shadows were seen in renal or suprarenal regions, and the heart and lungs were normal. The cerebro-spinal fluid under normal pressure showed no abnormality, and the Wassermann reaction was negative.

Except for the headaches, her condition is now improving.

Commentary

This case presents the three essential features of Cushing's syndrome—plethoric obesity, hirsuties, and amenorrhoea. It also presents other signs frequently associated with the syndrome, which are of almost equal importance—raised blood pressure, albuminuria (slight here, but accompanied by cylindruria), lowered sugar tolerance, and kyphosis with bone pains. Now that Houssay's observations on the influence of the anterior pituitary on glycosuria have been confirmed we can understand why basophilic adenomas in that gland are so generally accompanied by lowered sugar tolerance and sometimes by frank glycosuria. In a case seen by one of us (W. L.-B.) marked glycosuria requiring forty units of insulin a day occurred before any other evidence of the syndrome, though the full picture subsequently developed. This is unusual. In the present case the blood pressure, though variable, was generally raised, and on one occasion it was recorded at 180/120. High blood pressure is an almost constant feature of the syndrome, and malignant hypertension may close the scene.

Krans (1927) and Berblinger (1932) claim that an excess of basophil cells is found in the pituitary gland in a very large proportion of cases of persistently high blood pressure. In contrast with this Russell, Evans, and Croke (*Lancet*, 1934, ii, 240) have pointed out that in Addison's disease, in which the blood pressure is characteristically low, there is a marked deficiency of basophil cells in the anterior pituitary. The low basal metabolic rate is uncommon. In two cases observed by one of us (W. L.-B.) it was definitely raised, in spite of the patient putting on weight. The Aschheim-Zondek test was negative, as, indeed, it has been in most of the reported cases where the test has been done. This reinforces Woollard's

criticism (*Proc. Roy. Soc. Med.*, 1934, xxvii, 271) that Cushing's syndrome lends no support to the view that the basophil cells are the source of the sex hormone. Certainly hirsuties and amenorrhoea do not suggest that the patient is over-feminized!

It is well known that it is extremely difficult to differentiate between adenoma of the adrenal cortex and pituitary basophilism. It is easier in the present case to exclude a primary thymic carcinoma as the cause of the syndrome, in view of its fairly long duration. The fact that the skiagram showed a small pituitary fossa does not negative the diagnosis of basophilism. The adenoma may be quite small, and has produced no alteration in the fossa in some of the verified cases. The repeated occurrence of haematemesis is of special interest now that E. C. Dodds and R. L. Noble have called attention to the intense haemorrhagic congestion in the acid-producing area of the gastric mucosa, which may result from injection of post-pituitary extracts. Although x-ray therapy produced a temporary aggravation of symptoms, general improvement seems to have occurred later. Marked improvement has been reported by Cushing and by R. D. Lawrence from this method of treatment, and had occurred in two cases recently shown at a meeting of the Association of Physicians in London.

On a balance of the evidence the pituitary seems likely to have been the initial factor here, as, indeed, it is in so many polyglandular syndromes.

PERITONSILLAR ABSCESS IN INFANCY WITH RECORDS OF TWO CASES

BY

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Peritonsillar abscess is a disease which is uncommon in childhood and rare in infancy. The occurrence of two cases in the first year of life is of interest and worthy of comment.

Case I

A boy, born on November 30th, 1933, was quite well until November 30th, 1934, when he became fretful and appeared to have pain in his left ear. On December 1st he was cross and unwilling to take his feeds, and the following day a swelling was noticed below, and in front of, the left ear; saliva issued from the mouth, which was kept open. The family doctor was called in on December 3rd, and administered tablets which produced sweating and promoted a short sleep. In the morning of December 4th the doctor visited the patient again and arranged for his removal to Ruchill Hospital as a possible case of diphtheria.

CONDITION ON ADMISSION

The patient was admitted to hospital on December 4th, at 1.45 p.m., when his temperature was 99° F., pulse 136, and respirations 38. He was a well-developed child. The pulse was soft and the colour rather grey; the skin was dry. The presence of a little chest retraction indicated respiratory embarrassment. There was slight retraction of the head and swelling and tenderness of the lymphatic gland at the left angle of the jaw. The mouth was open and the tongue dry and coated. The throat was inflamed and the left tonsil very prominent, particularly at its upper pole, from the presence of peritonsillar swelling; the left anterior pillar and the soft palate were oedematous. There did not seem to be any retropharyngeal swelling. Aural and nasal discharge were absent. There was nothing abnormal about the heart, lungs, and abdominal organs, and croup was not noted. Kernig's sign was absent and the anterior fontanelle was soft.

DIAGNOSIS AND TREATMENT

The condition was obviously one of left-sided peritonsillar abscess. The diagnosis was confirmed by aspiration through a hypodermic needle, and later by incision through the left

anterior pillar, when yellowish, foul-smelling pus was obtained. Diphtheria antitoxin 8,000 units and 10 c.cm. (3,000 American units) of scarlet fever antitoxin were injected intramuscularly. On the day following admission the abscess was draining satisfactorily through the wound, but there was an appearance of yellowish membrane over the free surface of the left tonsil. The pulse and colour were improved and the patient slept comfortably and took feeds willingly. The tonsil was still inflamed on December 6th, and was covered with a thin film of greyish mucus; next day the tonsil was clean. Further recovery was uneventful, and the patient was dismissed well, with the throat wound healed, on December 14th. The organism isolated from the pus had the cultural and morphological appearances of *Staphylococcus pyogenes aureus*; throat and nose swabs were examined for *B. diphtheriae* and found negative.

Case II

A boy, born on January 28th, 1934, was well until December 5th of that year, when he became cross and had a convulsion. Next day a swelling was noticed at the right angle of the jaw. When the doctor first visited him, on December 7th, the patient had sore throat, shortness of breath, and a cough; later that day he had another convulsion. As time went on the symptoms continued and the swelling became larger. A throat swab on December 11th failed to yield *B. diphtheriae*. Excessive salivation was noticed on December 12th, and, distress in breathing becoming greater, the doctor was called urgently to see the patient in the early morning of December 14th. He decided to have him removed to hospital as a case of membranous croup.

EXAMINATION

The patient was admitted on December 14th, at 1.30 a.m., with a temperature of 98.4° F., pulse 128, and respirations 28. He was rather thin, but otherwise quite normally developed. The pulse was soft and the colour poor. Croup was absent, but slight chest retraction indicated respiratory embarrassment. The skin was dry, the head retracted, and the right submaxillary lymphatic gland markedly enlarged, the left gland to a less extent. The mouth was held open, and the tongue was dry and coated. There was a large amount of frothy mucus at the back of the throat, and the tonsils and fauces were inflamed, the right tonsil being very prominent from the presence of peritonsillar swelling. The protrusion of the tonsil was most marked at its lower pole, a good view being obtained only by firm depression of the tongue. Retropharyngeal swelling was absent, as were rhinitis and otitis. Kernig's sign was not elicited, and the anterior fontanelle was soft. The heart, lungs, and abdominal organs were normal.

The case was one of right-sided peritonsillar abscess. An incision was made through the right anterior pillar at 1.45 a.m., thick yellowish pus being obtained. The patient was given an intramuscular injection of 4,000 units of diphtheria antitoxin and was allowed to settle down. He remained comfortable until 6 a.m., when signs of shock set in; after making sure that local haemorrhage from the throat was absent, resuscitative measures were employed, and the patient was greatly improved by 9 o'clock. Convalescence was uneventful with the exception of the development of a mild serum rash on December 26th. He was dismissed on December 28th, the throat wound being healed. The pus yielded a pure culture of an organism which had the characteristics of *Micrococcus catarrhalis*; throat and nose cultures for *B. diphtheriae* were negative.

Cases in the Literature

In a search of the literature I have been able to find only one record of typical quinsy occurring in a patient under the age of 1 year—namely, peritonsillar abscess in an infant aged 9 weeks reported by Berman.¹ Coffin published details of a child of 21 months who died from haemorrhage complicating peritonsillar abscess.²

As compared with peritonsillar abscess in adults these cases have several interesting features. The onset of the disease may not be appreciated, the patient being unable to draw attention to his condition. The temperature is