BASOPHIL ADENOMA OF THE PITUITARY GLAND WITH RENAL CHANGES

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(With Special Plate)

In 1932 Cushing¹ suggested that the multi- (or pluri-) glandular syndrome—obesity, hirsutism, osteoporosis, hyperpiesia, polycythaemia, etc.—was probably due to the excessive secretion of the basophil cells of the pituitary gland, since an adenoma of these cells was a frequent finding in this type of case. His claim has been supported to some extent by reports of cases in which the syndrome has been recognized and the predicted basophil adenoma found in the pituitary.

On the other hand, the association of the syndrome with a basophil adenoma of the pituitary is by no means a constant one. As Leyton² has pointed out, the multi-glandular syndrome has appeared in carcinoma of the thymus and of the bronchus, and in these cases no basophil adenoma was found (although that does not necessarily mean that there was no hypersecretion of the basophil cells). Another objection to Cushing's claim was the knowledge that certain symptoms in the syndrome had been produced by disordered function of other endocrine glands—for example, hirsutism and osteoporosis as a result of the presence of tumours of the suprarenal cortex and parathyroid gland respectively.

Recently Russell, Evans, and Crooke³ reported two cases of basophil adenoma of the pituitary gland, and a review of the published cases led them to conclude that, of the many symptoms of the multiglandular syndrome, persistent high blood pressure and obesity were most commonly associated with this type of pituitary lesion. Cushing¹ himself noted in his original series of cases that a high blood pressure was one of the more constant findings. It would not, however, be correct to make the converse statement—that in cases of high blood pressure a basophil adenoma is frequently found—although it has been claimed that the pituitaries of high blood pressure cases show an increased number of basophil cells (Berblinger, Kraus—quoted by Russell, Evans, and Crooke³). The question of the relation of high blood pressure to basophil cell secretion may have to await final settlement by biochemical methods. Meanwhile, a study of the structural changes in the kidney seems to throw some light on the nature of the basophil cell secretion, and may explain the fact that whereas high blood pressure is a fairly common symptom basophil adenomata are comparatively rare.

MacMahon and others⁴ drew attention to the presence of malignant nephrosclerosis (Fahr) in the kidneys of two cases of basophil adenoma, and in one of the two cases described by Russell, Evans, and Crooke malignant nephrosclerosis was also present; in the kidneys of their other case changes characteristic of benign hypertension only were found. The suggestion has been made, therefore, that the high blood pressure found in cases of basophil adenoma tends to be of the rarer "malignant" type rather than of the more frequent benign type.⁶

The case to be described below is another example of the association in a young person of a high blood pressure, a basophil adenoma of the pituitary, and what is believed to be malignant nephrosclerosis.

History of Case

A single man, aged 27, was admitted to Guy's Hospital under the care of Dr. Poulton on July 16th, 1932, with symptoms of weakness, blurred vision, and epigastric pain. His

parents and brothers are healthy, and none of them has had kidney disease. He himself had had no previous severe illnesses, and was able to work as a builder to within six months of his death. He had acute tonsillitis when he was 19, and many sore throats subsequently. At the age of 23 he contracted gonorrhoea. During the last six years of his life he had often to get up at night to micturate, and on several occasions in the last four years he passed blood in his urine. In his last two years he complained of severe frontal headaches, occasional blurring of vision, vomiting, cramps and constipation. All these symptoms became worse seven months before death. He also became breathless on exertion, and during the fortnight preceding admission he had several attacks of breathlessness at night. He had always been of a nervous, energetic disposition, and his active habits misled the relatives into making light of his symptoms. The portrait here reproduced is from a snapshot taken two months before his death, and shows that he was not obese.

Condition on Admission

On admission the patient was pale and drowsy. Petechiae appeared first on the palate and later in the skin of the chest and forearms. Albuminuric retinitis and haemorrhages into the retinae were seen, and his limbs showed tremors and, occasionally, cramp-like spasms. Haemoglobin was 35 per cent.; blood pressure, 190/150; and blood urea content, 300 mg. per 100 c.cm. The urine contained pus cells and albumin (three parts per 1,000), and had a specific gravity of 1008. He weighed 138 lb. (63 kg.), and his height was 5 ft. 9 in. (175 cm.). The symptoms became rapidly worse, and visual hallucinations, epigastric cramps, and delirium appeared. Finally, he became comatose, and died on July 25th, nine days after admission.

Post-mortem Findings

The post-mortem examination was performed by Dr. C. K. Simpson eight hours after death. The body was that of a muscular young man, and, apart from the pallor and petechiae already noted, showed no abnormal features such as hirsutism, obesity, or wasting. The brain was normal. The trachea and bronchi were clear, and the lungs showed no gross oedema or congestion. There were a few subepicardial petechiae and two ounces of clear fluid in the pericardial sac. The heart showed well-marked concentric hypertrophy of the left ventricle, but no other abnormality. The coronary vessels were healthy and the aorta was mildly atheromatous. There is no record of the weight of the heart. The tonsils were greatly swollen and inflamed, and the crypts contained pus. Numerous petechial haemorrhages were seen in the cardia of the stomach and in the lower end of the ileum, and the entire colon showed many irregular haemorrhagic and ulcerated areas. No abnormality was noted in the thyroid, thymus, adrenals, pancreas, or testes.

KIDNEYS

Both kidneys were shrunken, pale, and mottled. The capsules stripped easily, and the underlying surface was rather coarsely granular. The cortex and medulla were imperfectly differentiated by diffuse scarring, the more severe changes being present in the cortex. There was no macroscopical evidence of ischaemic atrophy or undue prominence of the vessels. For further examination sections of the kidney were referred to Dr. Dorothy S. Russell, who has kindly allowed me to quote from her report as follows:

"The histological changes are characteristic of an advanced stage of chronic insidious Bright's disease or nephritis repens.

The total amount of destruction is very great, the inflammation relatively diffuse, and the inflammatory reaction, as shown by the glomerular changes and the leucocytic infiltration, severe. The amount of ischaemic nephritis is slight, and the degree of vascular hypertrophy only moderate. Many of the vessels show changes of the kind that has been associated by many authorities with malignant nephrosclerosis, though the acute arteriolar lesions that have been described in this condition are remarkably inconspicuous. The histological changes in the kidney as a whole are those of nephritis repens, Type 2."

Professor H. E. MacMahon also examined the kidney sections, and in the summary of his report states that:

"From the standpoint of the kidney the differential diagnosis lies between chronic glomerulonephritis and malignant nephrosclerosis. The widespread destruction of tubules and glomeruli and the diffuse sclerosis would suggest chronic glomerular nephritis. The character of the glomerular lesions and the extent of the vascular lesions within the kidney favour the diagnosis of malignant nephrosclerosis."

PITUITARY GLAND

The pituitary was normal in size and appearance, and was examined in serial sections. The posterior lobe contained many small hyaline bodies, and was not invaded by cells from the pars intermedia. The cleft was greatly distended by colloid material. The anterior lobe appeared to be normal, except for one lateral border, where there was a small adenoma measuring 1.9 mm. by 1.5 mm. and 1.8 mm. in the vertical plane. This small tumour was not encapsuled, but the acini surrounding the margin showed some compression.

The adenoma consisted almost entirely of basophil cells with normal-sized nuclei, but with rather less cytoplasm than is found in the normal basophil cells. They were irregularly arranged, and there was very little stroma to support them. A small recent haemorrhage had occurred in the adenoma. The reproduction in the Special Plate shows the tumour at the lateral border of the anterior lobe of the pituitary.

Remarks

This case is the third to be described in which a basophil adenoma of the pituitary in a male has been identified post mortem. Cushing¹ noted that this type of pituitary tumour seemed to occur with greater frequency in females because the symptoms were perhaps not so easily recognized in a male. Apart from the high blood pressure in a young person, there was no reason to suspect either the syndrome or the pituitary lesion, and the finding of the basophil adenoma was accidental. This case, too, is unlike the others of basophil adenoma so far recorded, in that the kidney was markedly affected by chronic glomerulonephritis. But there is no evidence to suggest that the association of the chronic glomerulonephritis with the basophil adenoma or with the malignant hypertension was other than fortuitous.

Liability to sepsis—another feature noted by Cushing¹—was exemplified in the case here. The patient had had many sore throats in the last eight years of his life, and at the post-mortem examination the foul condition of the tonsils was a striking feature.

Finally, the absence of cells in the posterior lobe of the pituitary need not be considered abnormal, in spite of Cushing's⁵ recent attempts to attribute the raised blood pressure to the secretion of these cells. If a large series of pituitaries be examined it will be found that the invasion of the posterior lobe by cells growing out from the pars intermedia is comparatively common, particularly in middle-aged subjects, and that marked invasion of the posterior lobe may also be seen in the pituitaries of persons whose blood pressures have been normal for at least several months before death.

Summary

A case of basophil adenoma of the pituitary is described in which the *only* symptom of the many forming Cushing's syndrome was a high blood pressure. The finding of malignant nephrosclerotic changes in the vessels of the kidneys is additional evidence in favour of the suggestion that the hypertension in cases of this pituitary lesion tends to be of the "malignant" type.

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REFERENCES

- ¹ Cushing, H.: *Bull. Johns Hopkins Hospital*, 1932, 1, 137.
- ² Leyton, O.: *Lancet*, 1934, i, 1221.
- ³ Russell, D. S., Evans, H., and Crooke, A. C.: *Ibid.*, 1930, ii, 240.
- ⁴ MacMahon, H. E., Close, H. G., and Hass, G.: *Amer. Journ. Path.*, 1934, x, 177.
- ⁵ Cushing, H.: *Ibid.*, 1933, ix, 539; 1934, x, 145.
- ⁶ MacMahon, H. E.: *Ibid.*, 1934, x, 707.

A CASE OF CHRONIC DISSEMINATED PULMONARY TUBERCULOSIS WITH ERYTHEMA NODOSUM

BY

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(With Special Plate)

The following case is of a type recently reviewed by the *British Medical Journal*,¹ and for which was urged the term "chronic disseminated haematogenous tuberculosis with pulmonary localization." The condition is of great interest in view of the controversial interpretation of such a lesion, and in this case we have, in addition, erythema nodosum. We also have for comparison the original source of infection, a typical case of "tertiary" pulmonary tuberculosis.

Case History

The patient, E. A., a female aged 29, was first seen on May 25th, 1934. She had been ill for two weeks, and on the extensor surfaces of both legs were the characteristic lesions of erythema nodosum. Until the previous week she had been sleeping with her sister, R. A., aged 26, who had been going downhill for about six months, and who was now recognized as suffering from tuberculous infiltration of the right upper lobe, the sputum being positive. E. A. had no cough or sputum, and on examination there were no definite physical signs in the chest, apart from impaired percussion note over the left root. She was then x-rayed, and the film, to our surprise, revealed what appeared to be an acute disseminated pulmonary tuberculosis: the appearances also resembled pneumoconiosis, but this was excluded in view of the patient's work. When she was admitted to the sanatorium on June 23rd the erythema nodosum had cleared up. She was afebrile and, except for an occasional rise to 99°, remained so until her discharge in September. There was definitely no cough or sputum. Unfortunately, through the tactlessness of a nurse, the patient was made averse to any investigations, so that we were unable to do a gastric lavage. Throughout her stay her general condition was very unsatisfactory, and she had lost five pounds during that period. Since her discharge her condition has improved somewhat, and as there are no constitutional symptoms she has decided to return to work.

Discussion

The films of the two sisters are presented for comparison (see Plate). It will be seen that they are each characteristic of the secondary and tertiary stages of Ranke. We have here between two adults the type of contact infection we are accustomed to see between adult and child. The

H. G. CLOSE: BASOPHIL ADENOMA OF THE PITUITARY GLAND WITH RENAL CHANGES

Basophil adenoma at lateral border of anterior lobe of pituitary. Aniline blue only. ($\times 22$.)

A. McNAIR AITKEN: ACUTE IODINE BURN

Acute iodine burn.

SIDNEY DEANER: CHRONIC DISSEMINATED PULMONARY TUBERCULOSIS WITH ERYTHEMA NODOSUM

FIG. 1.—Case "R.A." The radiogram is typical of "tertiary" pulmonary tuberculosis: there is dense shadowing in the right upper lobe with a large cavity at the apex, with drawing up of the thickened interlobar fissure. There is also infiltration in the lower lobe.

FIG. 2.—Case "E.A." This is typical of the "secondary" stage. There is generalized mottling in both lungs, rather coarser on the right side. The root shadows are massive.