A PATHOLOGICAL INVESTIGATION OF FOUR CASES OF PITUITARY TUMOUR.

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IN view of the comparative rarity of tumours of the pituitary body and of the interest recently aroused in them, the publication of the pathological investigation of four fatal cases from Guy's Hospital may prove of value. The first two descriptions are taken from cases which

CASE 1.—The patient, a man aged 27, formed one of the cases of pituitary tumour which Mr. Eason showed before the Royal Society of Medicine in May, 1913, at a meeting of the combined Sections of Neurology and Ophthalmology.¹ A short summary of the clinical report is as follows: The patient was short and undeveloped, with a lack of hair about his face and pubes. The voice was half broken and high-pitched. He was extremely drowsy and slept most of his time. Weight 7 st. 10 lb. Looked much younger than his age, being almost boyish in appearance. Examination of his eyes showed complete bilateral temporal hemianopia. The fields of vision are given in Fig. 1. Vision: R., 6/36; L., 6/9. The reaction of the pupils to light on both sides was hemiopic. The Wassermann reaction was positive, but treatment with mercury, iodides, thyroid and pituitary

came to necropsy during the past year. The last two are from specimens in Guy's Hospital Museum which date back to 1883 and 1877 respectively. In the first case advantage has been taken of the fact that a complete examination of the eyes had been made by Mr. H. L. Eason to undertake an inquiry into the extent of the degenerative changes

extracts resulted in no improvement in vision or in any other way, except that the headache was diminished and the weight slightly increased. A skiagram showed some enlargement of the sella turcica. The blood pressure was found to be 100 mm. of mercury. Latterly he had suffered from severe enuresis. The skin was brownish in colour. A condition of semi-coma prevailed during the last three weeks. Pathological examination.—Emaciation was marked. There

FIG. 2.

FIG. 3.

View of the tumour in situ (Case 1).

Mesial section through brain and tumour. The capsule of the tumour lies close up against the corpus callosum. The hemorrhagic cysts are well seen.

resulting in the visual system of nerve fibres and cells. In the second case, also, degeneration has been demonstrated in the optic tracts, but unfortunately in this instance it cannot be correlated with the state of the fields of vision.

were no bony changes, either atrophy or enlargement, present. The heart weighed 190 gm. and showed an early condition of brown atrophy. The liver weighed 1090 gm. It was

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pale yellow in colour, and appeared to contain excess of fat. The pancreas (42 grm.), the thyroid (10 grm.), the spleen (102 grm.), the suprarenals (11 grm.), and the kidneys (294 grm.) all seemed perfectly normal macroscopically. The testes were normal in consistency, but were a little small (abstract from Dr. Herbert French's report).

In the position of the pituitary body was found a bright red irregular tumour, contained in a definite tough capsule, and which had numerous white necrotic areas scattered through it, especially towards the centre. The substance of the growth was soft and hæmorrhagic, and contained several cysts filled with altered blood. The appearance of the tumour is shown in Figs. 2 and 3, reproduced from photographs. It completely occupied the interpeduncular space, extending forwards to reach the orbital portions of the frontal lobes, and spreading laterally over the surface of both temporal lobes. Posteriorly, it separated the crura cerebri widely from each other and then extended over them, covering the upper portion of the pons. A mesial section through the brain and tumour shows the basal ganglia and corpus callosum to be displaced upwards. The superior and inferior walls of the lateral ventricles were in close apposition, their cavities being practically obliterated. The pressure on the base of the skull had resulted in absorption of the original bone forming the sella turcica, and only a thin shell of bone still remained surrounding the greater portion of the tumour. The third, fourth, and sixth nerves on both sides were stretched by the growth. The optic chiasma was broken through in such a way that the right and left optic nerves appeared to be direct continuations of their respective tracts. The degenerative changes found in the optic tracts suggest, however, that this destruction of the chiasma was of comparatively recent date. The brain and meninges appeared perfectly normal macroscopically. It was possible to shell out the tumour quite easily from the bed which it had forced for itself in the base of the brain.

Microscopical examination.—Sections were examined of portions of the thyroid, pancreas, suprarenals, liver, and testis. Thyroid: The alveoli appeared well formed and contained the normal amount of colloid. There was no

FIG. 4.

The upper portion of the field shows the edge of the growth. The lower portion shows up the capsule being invaded by groups of tumour cells. (Case 1.)

evidence of cell proliferation, and the interstitial tissues were normal in appearance. Pancreas and suprarenals: The structure of these organs was that of normal functioning glands. Liver: Extensive fatty change was present throughout the section, and was confined to the peripheral portions of each lobule. The cells in the centre of the lobule were

normal in appearance and there was no cirrhotic change. Testis: The seminal tubules were normal in number and in character. There was a slight increase in the interstitial connective tissue, indicating a very early fibrotic change. Sections were examined with special reference to the condition of the interstitial testicular cells. These were markedly deficient in number. Several sections were examined from various parts of the testicle. Stained with Herxheimer's stain the few interstitial cells present were found to be in a somewhat atrophied state. The pituitary tumour itself under the microscope was seen to be made up of large

FIG. 5.

View of tumour in Case 2. The cyst has been distended with cotton wool to its normal size.

polyhedral cells, the protoplasm of which stained a faint pink and the nuclei a dark blue with the ordinary hæmatoxylin and eosin method. The chromatin granules show up distinctly in these latter. The cells themselves are arranged in long columns, with occasionally a tendency to alveolar grouping, the whole appearance closely simulating the structure of the anterior glandular portion of the pituitary. No colloid material was discovered, and nothing corresponding to the posterior lobe was seen. The vascular spaces characteristic of this organ were well marked, and towards the centre of the tumour they became large hæmorrhagic cysts in which red blood cells were mixed with necrotic tumour cells. Towards the periphery, however, they became smaller and smaller, until when the capsule was reached they ceased to exist. The capsule was thick and consisted of dense fibrous tissue. In numerous places the cells of the growth were extending into the capsule along the lymph channels. (Fig. 4). Its appearance, therefore, was that of a malignant epithelial tumour of the pituitary gland. The entire absence of secondary deposits is noteworthy.

CASE 2.—The patient, an unmarried woman, aged 27, was admitted into Guy's Hospital under the care of Mr. L. A. Dunn. She had had continuous headache for the previous three weeks accompanied by vomiting. The left eye was completely blind, and the vision in the right eye was markedly defective. Both eyes reacted to light and accommodation, but the reaction of the left was very deficient. The patient was seriously ill and died shortly after admission, so that a detailed examination of the eye condition was impossible. She was extremely lethargic. Pulse 56 and low tension. Temperature subnormal. The left eye showed

a definite degree of exophthalmos as compared to the right. Further details have been kindly supplied by Dr. H. J. Henderson and Mr. L. C. D. Irvine, of Amersham, who attended the patient in private. They state that, in spite of her age, menstruation had never occurred. The breasts were undeveloped, and there was complete absence of pubic and axillary hair. Nothing is known of the sugar tolerance, but for some time past she had shown a great partiality for sweet things, and had been used to taking bread and butter thickly coated with brown sugar. A year ago Mr. Arnold Lawson had examined the eyes and found advanced optic atrophy in the left eye. This was confirmed on the examination of the patient here. There was no sugar or albumin in the urine.

Post-mortem examination.—With the exception of the tumour nothing abnormal was found in any of the organs (Dr. Herbert French's report).

The tumour: In the position of the pituitary body, filling up the interpeduncular space, there was a cystic tumour, the relations of which are shown in Fig. 5. It measured $\frac{3}{4}$ inch antero-posteriorly and $1\frac{1}{4}$ inches from side to side, and was almost exactly the size of a golf ball. On removal a deep hollowed-out depression was found at the base of the brain. The sella turcica, on which the tumour had rested, was flattened into a shallow concave surface. The vessels of the circle of Willis were present on the lateral walls, indicating that the original cyst had been small enough to be within the circle, and that as it enlarged the vessels became stretched on its outer walls. The optic chiasma lay stretched over the antero-inferior portion of the tumour, and had apparently given way through its centre. The right optic tract and nerve were not much damaged, but the portions of the left optic tract and nerve near the chiasma were pressed out into a wide thin band. The tumour was pressing them down on to the hard bone at the base of the skull. On the other hand, the third and fourth cranial nerves, lying between the tumour and the soft structures forming the base of the brain, showed little or no flattening. On being cut through the tumour was seen to consist of one large cyst composed of two loculi, which communicated freely with each other, and they contained a thin reddish fluid. The wall of the cyst was tough and fibrous, and scattered over its surface there were four or five small masses of a reddish glandular substance closely similar in appearance to the anterior pituitary lobe. The largest was of the size of a pea and the smallest about half this size. In addition there were still smaller masses of the same nature to be found scattered over the surface. The larger ones are shown in Fig. 6, which is about natural size. It also shows

FIG. 6.

From a photograph (actual size) of the tumour in Case 2, showing the glandular masses in the capsule.

the division into two loculi—the large one which formed the main portion of the cyst, and the smaller one which occupied the right anterior angle of interpeduncular space.

Macroscopically the brain was normal in every way, with the exception of a slight degree of dilatation of the lateral ventricles. Under the microscope the cyst wall was seen to consist mainly of laminated fibrous tissue. Everywhere between the laminae were to be seen small collections of cells, which in places were aggregated to form the red

glandular masses already referred to. The arrangement and character of these cells to all appearances were those of the anterior lobe of the pituitary. Large spaces packed with red blood corpuscles lay between the columns into which the cells were arranged, and in places large hæmorrhages were present. The cells themselves were polyhedral or oval in shape, and had large dark nuclei. The majority were chromatophobes, but several approximated to the chromophilic type. More externally they showed the same tendency to infiltrate the layers of the cyst wall, as was seen in the first tumour. It can only be described, therefore, as of the same nature—viz., a malignant epithelial tumour of the pituitary gland, with complete absence of secondary deposits.

CASE 3 (Specimen No. 2876 in Guy's Hospital Museum).—The patient was a male, aged 23, who died in 1883. He had been under the care of the late Dr. F. W. Pavy and Dr. Frederick Taylor. There was a history of a head injury

FIG. 7.

FIG. 8.

Mesial view of No. 2876 showing the capsule of the tumour lying just beneath the corpus callosum as in Case 1.

View of the left half of the brain, No. 2876, showing the position and appearance of the tumour.

and concussion 15 years previously. Three years before admission he had had vertigo and frontal headache, and for the last 18 months the vision in the left eye had been failing. On admission the left eye was completely blind, and there was also partial loss of vision in the right eye. He was a dark muscular man, but no mention is made as to sexual development. Apart from headache, there were no other symptoms.

Post-mortem examination (by Sir James F. Goodhart).—The pituitary fossa was enlarged to form a diamond-shaped space, in which lay a soft lobulated tumour. This occupied the position of the pituitary body and extended forwards over the ethmoid; laterally it overlapped the temporo-sphenoidal lobes, and posteriorly it covered over the upper part of the pons. On the left side the optic nerve and third, fourth, and fifth nerves were pressed into flattened bands. On the right side the optic nerve and third nerve were lost in the tumour, while the fourth and fifth nerves were stretched over it. The other cranial nerves were unaffected. (Figs. 7 and 8.) The tumour itself was more or less circular in outline and measured $2\frac{1}{2}$ inches across. On section, thick cream-like material oozed away, leaving numerous cystic cavities with ragged walls.

Under the microscope the tumour was found to consist mainly of cellular elements, the cells being the chromophilic type, though somewhat smaller than the cells in the two previous tumours. With the exception that there is much less stroma present, the general appearance, however, closely approximates to them. There is the same tendency for the cells to form columns and an alveolar arrangement, and also for those on the periphery to infiltrate the layers of the capsule. (Fig. 9.) With the other two, therefore, it must

FIG. 9.

Reproduction of a photomicrograph of No. 2876 showing cells at the edge of the growth infiltrating the capsule.

be classed as a malignant epithelial tumour of the pituitary gland, showing no tendency to form secondary deposits.

CASE 4 (Specimen No. 2875 in Guy's Hospital Museum).—The patient was a male, aged 45, who died in Stephen Ward in 1877. He had been under the care of Dr. Samuel Wilks. He was a thin, wasted man. Three weeks before admission

FIG. 10.

Reproduction of a drawing of the brain by Mr. Hamersley in the original post-mortem report (No. 2875). The tumour is largely hidden by the two swollen optic nerves.

he was seized with fits which were followed by left hemiplegia. On admission there were loss of memory, occipital headache, and nausea, but no vomiting. The vision was dim, but no definite optic neuritis or optic atrophy was

present. The left external rectus muscle was paralysed. The patient was often delirious.

Pathological examination.—The ventricles of the brain were slightly dilated and contained turbid fluid. At the base of the brain was a large gelatinous tumour which was in direct continuation with a somewhat enlarged pituitary body. The bone in the pituitary fossa is flattened out and partly absorbed. The tumour measured $1\frac{1}{2}$ inches long by 1 inch broad and 1 inch thick. The optic commissure is stretched over it anteriorly, and the optic nerves, as seen in Fig. 10, are swollen up into two large swellings half an inch in diameter. Laterally and posteriorly the tumour is bounded by the crura cerebri. There was a patch of growth in the apex of the lower lobe of the left lung consisting of spindle cells arranged in loculi. Histologically the tumour showed a relatively large amount of fibrous stroma in which lay groups of cells, the majority of which were columnar in shape, a few being polyhedral. There was much mucinous material scattered through the section and several goblet cells were to be seen, which would suggest a possible origin from nasal mucous membrane. Its characters were those of a malignant columnar-celled growth. The secondary deposit present in the apex of the lower lobe of the left lung showed similar histological appearances.

The examination of the visual system of nerve fibres and cells.—The left side of the brain in Case 1 was sectioned and utilised for this purpose. A reference to Fig. 1 illustrating the fields of vision will show that the optic fibres destroyed by the tumour are confined to the nasal half of the retina—i.e., the temporal half of the field of vision. And, further, that a portion only of these fibres are affected. From this it might be expected that the degeneration present in the optic tracts would be extremely limited and circumscribed.

The optic tracts.—The accompanying drawings (Fig. 11) of the left optic tract, however, made from

FIG. 11.

Posterior portion. Anterior portion.
Left optic tract, Case 1. Weigert-Pal preparation.

Weigert-Pal preparations, illustrate the condition actually found. A narrow band of fibres (A) occupying the outer portion of the tract alone stain normally. Two other bands of fibres (B) and (C) also stain, only less distinctly. The remainder of the tract is completely degenerated. The degenerated area can be described as occupying mainly the central and lower part of the tract. This agrees with Henschen's conclusions as to the position of the nasal fibres in the optic tract. The fibres which stain normally (A), however, which are from the temporal side of the retina, are found lying in the external and lower portion of the tract and not in the superior and external position which he describes.

A comparison of the two drawings will further show that the relative position of the fibres remains approximately the same along the whole length of the tract. The first section is taken from the anterior part of the tract and the second from the region of the external geniculate body. Sections taken through the subthalamie region still showed

the degeneration in the optic tract fibres as they entered the external geniculate body and the pulvinar. In this region no particular zone was degenerated; the affected fibres seemed to be scattered amongst those which stained normally. Preparations stained by Marchi's method show the presence of early degeneration amongst those fibres which stain normally with the Weigert-Pal method.

The cortical visual fibres.—Attention was next directed to the state of those fibres which after the relay of the optic tract fibres in the external geniculate body continue the visual impulses to the occipital cortex. No change could be demonstrated. The sections through the optic radiations, stained by Weigert-Pal, were quite normal. Similarly, no change could be found in these fibres when traced to their termination in the cortex surrounding the calcarine fissure. Sections of this cortex were then stained by Nissl's method and the large stellate cells in the fourth layer—i.e., those concerned with the reception of the visual impulses—were examined. It cannot be said that there was any deficiency in the number of these cells or in their size. It was, however, found that a certain proportion of them exhibited chromatolytic changes, but this did not occur in any definite grouping.

FIG. 12.

Left (A) and right (B) optic tracts in Case 2. Weigert-Pal preparations.

The fibres concerned with the reaction of the pupils to light.—The presence of the hemiopic pupil suggested that this case might throw some light on the question of the course which these fibres take. Serial sections of the posterior thalamic region and the mid brain were accordingly cut and compared with normal preparations. The path described by Meynert—i.e., fibres running dorsally to the anterior corpora quadrigemina, relaying in these bodies and continuing by means of new fibres which end in the oculomotor nucleus—did not give any evidence of degeneration. Similarly, the investigation of the path described by Darkschewitsch and Mendal—i.e., fibres running to the ganglia habenulæ and continuing by new fibres which reach the oculomotor nucleus *via* the posterior commissure—also led to negative results. As, however, the majority of pupil fibres were unaffected in this case, and, further, that

either theory states that the degenerated fibres end in cell relay stations in the neighbourhood of the primary optic ganglia, this result is not surprising.

In Case 2 the optic chiasma, although severely compressed, was not broken through as in Case 1. Primary optic atrophy had been observed clinically in the left eye but not in the right. The condition of the optic tracts was as follows. The left optic tract was quite normal with the exception that a few degenerated fibres were found occupying its lower border. This area is indicated in Fig. 12. The right optic tract, on the other hand, was found to show marked degeneration very similar to that present in the other case. A band of fibres situated in the outer and lower part of the tract are seen to be unchanged, although even they do not take the stain as well as do perfectly normal fibres. The remainder of the tract is completely degenerated.

Conclusions.—The only change, therefore, which it has been possible to demonstrate in the visual fibres as a result of a lesion of the optic chiasma—which had caused eye symptoms in both cases for upwards of two years—is a degeneration in the optic tracts. This degeneration was not found extending further back than the primary optic ganglia. The amount of change present in one case was more than was indicated by the visual loss. The statement that certain optic fibres reach the occipital cortex without relaying in the cell stations in the primary optic ganglia would appear to be refuted by the fact that no degeneration was found in the optic radiations and the fibres entering the calcarine cortex. Finally, both cases show that the uncrossed visual fibres tend to occupy the outer and lower portion of the optic tracts.

REMOVAL OF A FOREIGN BODY FROM THE LARYNX BY SUSPENSION LARYNGOSCOPY.

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THE patient, a little girl aged 2 years, was sent to the Central London Throat and Ear Hospital on May 22nd, 1914, by Dr. A. G. Stewart, of Paddington Infirmary, on account of laryngeal obstruction. The history was that one day, four months previously, the child made a grab at a piece of rabbit on her mother's dinner-plate and tried to bolt it. The mass stuck and the child "choked." But a neighbour woman rushed to the rescue and promptly hooked the meat out of the child's throat with her finger and breathing was re-established. Not only so, but, according to the mother, the respiration was then quite free and unimpeded. Next morning, however, the mother noticed that the breathing had become loud and stertorous again and she thereupon took the child to a hospital where during the next three months she was treated as an out-patient for bronchitis. At about 10 o'clock one evening in the middle of April the patient had another severe attack of asphyxia and she was then taken to the Paddington Infirmary under Dr. Stewart's care. Here she did have genuine bronchitis, being laid up with it for about a month, and during this illness she was also for several days unable to swallow and had to be fed with a nasal tube. While in the infirmary a search was made for a foreign body in the larynx with X rays (screen examination), but nothing definite could be made out.