Original Articles.

TUMOR OF THE PITUITARY BODY.

BY G. L. WALTON, M.D.,

Clinical Instructor in Neurology, Harvard University; Physician to Neurological Department, Massachusetts General Hospital,

AND F. E. CHENEY, M.D.,

Assistant in Ophthalmology, Harvard University; Surgeon to Massachusetts Charitable Eye and Ear Infirmary; Ophthalmic Surgeon to Out-patient Department, Massachusetts General Hospital.

PATHOLOGICAL REPORT BY F. B. MALLORY, M.D.,

Assistant Professor of Pathology, Harvard University.

TUMORS of the hypophysis have acquired a new interest since Marie's demonstration of acromegaly a little over a decade ago. The statement made by Rath¹ in 1888, that the function of this organ was unknown, would not be generally accepted to-day, and of late the indirect results of pituitary tumors, through pressure and involvement of adjacent structures, have taken a position of secondary interest as compared with symptoms attributable to disturbance of glandular activity.

The hypophysis, or pituitary body, an organ averaging about half an inch in its anteroposterior diameter, and quarter of an inch transversely, lies in the sella turcica, invested in a fibrous sheath derived from the dura mater, a layer of which (tentorium sellæ turcicæ) roofs over and separates it from the intracranial contents; the infundibulum passes through an opening in this membrane.

The hypophysis consists of two distinct bodies separated only by a fibrous lamina. These two bodies are distinct in structure and function. The posterior lobe represents an outgrowth of the embryonic brain, atrophied in man, and subserving no known nervous function. The chief interest centres in the anterior lobe, which is practically a ductless gland developed from the ectoderm of the buccal cavity. This gland, like others of its class, plays an important part in the economy; its secretion (absorbed by the lymphatics, since in man the duct has disappeared) undoubtedly plays an important part in the nutrition and growth of the body. The exact action of such secretions on the central nervous system is a matter of speculation; Collins² alludes to that of the pituitary gland as either neutralizing waste products, or serving as a trophic agent. Gigantism, acromegaly and allied states seem to stand in a certain relation to disorders of the pituitary gland, though evidence of this relation has by no means proved constant. As Starr puts it, it is not true that a tumor of this organ always produces symptoms of acromegaly, and, conversely, the autopsy does not always show change in the pituitary body in acromegaly.

Few authorities now deny, however, that a relation exists between disease of the pituitary gland and acromegaly, a disease characterized by mental apathy, enlargement of hands, feet and face, vasomotor symptoms, together with loss of sexual power, general weakness, and other signs of perverted growth and disordered nervous function. Arguments are still adduced to show that the diseased gland represents a result rather than the cause of the general perversion of function, but the weight of evidence is in the opposite direction.

The interest in a case of tumor of the pituitary body is now threefold: first, in its bearing upon the anatomy of the chiasm and optic tract, as shown by the various restrictions of the visual field; second, in its symptomatology, as bearing upon early diagnosis; and, third, in its pathology, more particularly with reference to the disturbance of the glandular function.

Vision.—The situation of the gland is such that the optic chiasm is the first important body to be affected by its pressure. The tumor may extend upward either in front of the chiasm or behind it, or both; amblyopia and various forms of visual field restriction follow. Both temporal fields are often lost through pressure upon the chiasm anteriorly; sometimes one eye is completely blind, while the other shows loss of temporal field. In a case recently reported by Leszynsky there was complete temporal hemianopsia in one eye and temporal hemiachromatopsia in the other. Not uncommonly one field is more contracted than the other. Homonymous hemianopsia is sometimes found (as in our case, at a later stage), showing pressure on the optic tract behind the chiasm.

Symptomatology.—The *résumé* of Rath covers this ground, apart from the functions of the gland itself. The symptoms in the order of their frequency and importance are: (1) Headache, generally frontal and temporal; (2) vomiting; (3) vertigo; (4) disturbance of motion, spastic and paretic (pressure on the crura cerebri); (5) disturbance of speech; (6) disordered pupils (mydriasis, myosis, loss of reaction, inequality); (7) paralysis of ocular muscles; (8) diabetes mellitus and insipidus. To these symptoms must now be added those of acromegaly, namely, abnormal development of the hands and feet, large features and prominent brows, large jaws, with separation of teeth, broad nose, thick and long lips, large tongue, thick mucous membranes, doughy tissues, loss of sexual power, weakness and paresthesia.

It must be remembered that these changes are less marked when the disorder appears in adult life after the growth of the patient is established. The fact must also be borne in mind that many persons have some or all of these peculiarities of growth without being deemed abnormal. With regard to such individuals it is worthy of note that Pechkranz³ reports a case of fatal tumor of the hypophysis occurring in a man who showed from youth certain peculiarities of growth and nutrition (hyperplasia of genitals, feminine build of osseous system, etc.). These peculiarities he attributed to congenital anomalous structure of the pituitary body, this anomalous structure forming the basis for the new growth. Of this view our case affords a striking corroboration, as will be seen in the report appended.

Pathology.—The commonest form of new growth appears to partake of the nature of sarcomata or adenomata—tumors rich in cells and vessels. In some cases the gradual passage from gland tissue to irregularly placed cells renders the diagnosis between adenoma and sarcoma difficult, with strong suggestion of adenoma, as illustrated by the case of Hippel,⁴ who asserts that all these new growths start from the anterior lobe.

Burr and Riesmann,⁵ in a recent communication,

¹ *Neurolog. Centralbl.*, 1 März, 15 März, 1899.² *Virch. Arch. f. path. Anat. u. Path.*, 1891., Bd. cxxvi.³ *Journal of Nervous and Mental Diseases*, January, 1899.⁴ Rath: *Ophthalmologische Archiv*, Bd. xxxiv, Heft 4.⁵ *Nervous Diseases*, by American Authors, 1895, p. 893.

have called attention to a probable source of fallacy on the part of those who argue that tumors of the hypophysis without acromegaly negative the implication of this organ in that disease. These writers argue that a very small portion of a ductless gland suffices to perform its function; in evidence they adduce the fact that removal of half of the thyroid gland fails to produce myxedema. In support of their view they report a case of pituitary tumor without signs of acromegaly, careful examination of the tumor showing that a very considerable portion of the glandular structure was intact. Dr. Mallory's findings in our case tend to corroborate this view, for he reports that beyond question a certain part of the pituitary body is present.

The question has not been determined whether the secretion is analogous to that of the thyroid gland, in that by destroying toxins, or otherwise, it checks overgrowth of tissue, or whether, on the other hand, the secretion is itself an irritant acting as a stimulus to growth. The arguments adduced by Brooks⁶ in favor of the latter supposition seem on the whole most convincing, namely, (1) that the pituitary gland has been often completely destroyed without signs of acromegaly; (2) removal of the pituitary body in lower animals does not produce acromegaly; (3) feeding with pituitary extract has no effect upon the disease.

Brooks allows that sarcoma predominates over adenoma in post-mortem reports, but calls attention to the fact that individual observers may be mistaken in the nature of these growths, as he had been himself in his early cases.

Before leaving the question of pathology, it is important to note that optic neuritis is rare, but optic atrophy common. The absence of optic neuritis has been explained by the fact that the tumor, before it has reached great proportions, is separated from the cranial cavity by the tentorium sellæ turcicæ (Pechkranz). Again, when the tumor has become extensive, it shuts off the cerebro-spinal fluid from the sheath of the nerve by pressure (Hippel). In the case of Johnston and Morro⁷ neuritis appeared in one eye and atrophy in the other. Our case comes within the usual rule, in that optic atrophy, without neuritis, was present. This point affords an important aid in diagnosis, for, given general symptoms of tumor of the brain with optic atrophy, attention is at once directed to the hypophysis; if, in addition, loss of temporal fields appear, the diagnosis is made probable.

Dr. G. C. D., a man of exceptional physical vigor, of even disposition, and of mental acquirements giving great promise of success in his chosen field, first consulted Dr. Cheney, July 20, 1895, in regard to his eyes. (He was at that time house officer in the Massachusetts General Hospital, age twenty-six.) His family and previous history were good, with the exception of occasional headaches dating from early life; these headaches were of the nature of migraine and were accompanied by temporary loss of vision on one side (hemianopsia). He was operated on for spina bifida in early infancy. He was a large man with rather heavy gait, with large extremities and features, including, broad nose, large mouth, very thick lips.

⁶ Harlow Brooks: Archives for Neurology and Psychopathology, 1898, vol. 1, No. 4.

⁷ Glasgow Medical Journal, August, 1898.

The tongue was large, the jaws large, the teeth separated. The beard was scant, though he had a fair moustache; the hair was dry and crisp. These peculiarities were not sufficiently noticeable to suggest abnormality, but are mentioned in view of their possible connection with congenital defect in structure of the gland which proved later to be the seat of disease. There was no enlargement of thyroid. He complained to Dr. Cheney of asthenopia, a slight blur in reading, and occasional headaches. The headaches were no more severe than he had been subject to for a number of years.

An examination under homatropine gave the following result: v. o. d. with $+0.50 = +0.50$ cyl. axis $100^\circ = 0.7$, and v. o. s. with $+0.50 = +0.50$ cyl. axis $100^\circ = 1$. There were floating opacities in the vitreous of both eyes, considerably more in the right. Fundus examination negative; glasses correcting the astigmatism were prescribed for constant use. He was seen frequently during the fall and early winter, complaining of various slight asthenopic symptoms. There was some variation in vision from time to time, but there was no falling off appreciable to the patient. On January 21, 1895, with correcting glasses v. o. d. $= 0.6$; v. o. s. $= 1$. With the exception of this slight decrease in sight, and the floating opacities in the vitreous, there was nothing to suggest ocular or general disease.

He was not seen again until April 15, 1896. For some little time he had noticed that people approaching from the left were not seen as readily as those coming from the right, and quite recently everything had looked black and blotted out on the left side of the visual field. There was little or no headache; he felt perfectly well and looked the picture of health. On testing the fields of vision there was found complete left hemianopsia in the left eye for white and colors, the line of demarcation being unusually well defined. He was still able, however, over the central and upper portion of the left field, to distinguish faintly the movements of the hand. The right half of the field was normal for form and color, and the central vision was normal for distance and near point. The field of vision of the right eye was perfectly normal for form and color. The central vision, however, had fallen off to five-tenths and was also defective for near. In June, 1896, Dr. Wadsworth saw the case in consultation and expressed the opinion that both discs were slightly atrophic. Dr. Walton saw him in May, 1896, and at intervals afterwards.

An exhaustive examination from the neurological point of view, October 20, 1896, revealed no disturbance of motion, nutrition, sensation or reflexes, superficial or deep; in fact, the physical examination was absolutely negative except for the pallor of optic discs and loss of visual acuity and field. The only complaint was poor vision and impaired virility, a symptom which attracted no attention at that time, though in strong contrast to his general vigor. In view of the later history it was really of considerable import and should, perhaps, have been more taken seriously into account. The urine was examined a number of times during the summer and fall of 1896, the only result being a well-marked trace of arsenic.

He was attended throughout his illness (except while under the care of Dr. Dennett at Arlington) by his colleague, Dr. Painter, whose records we have utilized in reporting the progress of the case.

The patient began practice in May, 1896, and in the following June took charge of a case which kept him out of town till the 22d of August. During this time he was perfectly well, and though his eyes disturbed him, he succeeded in winning the final prize in two or three golf tournaments. He had to depend upon the caddy to follow the ball, though he had no difficulty in making the stroke. After being at home about two weeks he went away with another patient and did not return till just before his marriage, which took place in September. At this time he reported that there had been a considerable decrease in the vision of both eyes, and he had considerable difficulty in reading. He appeared in excellent condition, had gained in flesh, and felt well physically and mentally. Dr. Cheney's examination at this time showed v. o. d. = 0.2; v. o. s. = 0.5. The fields of vision were unchanged. The right disc was somewhat grayish in tint. On November 12, 1896, v. o. d. = $\frac{2}{8}$; v. o. s. = $\frac{3}{8}$. The fields of vision taken eight days later showed no contraction for form or color in the right eye, and the hemianopic field of the left was practically the same as on previous examination. Both discs were noticeably atrophic in appearance. During the fall and early winter he had an occasional mild headache, not accompanied by nausea or vomiting. In November it was noticed that he was apt to doze off and to sleep unduly. Instead of being ambitious and anxious to do for others, he required constant stimulus even in routine work. His apathy steadily increased. In December, 1896, and in January, 1897, he was distinctly brighter and showed more interest in his work. In January, 1897, Dr. Derby saw the case in consultation, and from this time on the ocular condition was under the observation of both Drs. Derby and Cheney. Headache during the latter part of this time became more frequent and occasionally accompanied by nausea. In the latter part of February he became drowsy and apathetic. Visual examination showed decrease in the right eye to $\frac{2}{8}$, in the left to $\frac{3}{8}$. His weight, which had reached two hundred and sixteen pounds in January, decreased slightly, and his color became poor, his lips particularly showing a waxen pallor. Headaches occurred every three weeks till midsummer, 1897. He grew weaker, finding it difficult to lift the heavy window sashes. His speech also showed less fluency. There was no hesitation for words but they were enunciated slowly. His appetite became very capricious. No diminution was noted in other special senses. His gait was slow and dragging. The features became gradually more heavy and expressionless and the dryness of the hair increased.

His interest lagged even in matters pertaining to his profession. In the early part of the spring, while away with a patient, he attempted to perform transfusion, and experienced great difficulty in finding the vein. Muscular weakness, somnolence, and lack of interest increased. An examination of vision made by Dr. Derby in June showed improvement in the right eye to $\frac{4}{8}$ and the left to $\frac{4}{8}$. During a remission he amputated a breast, obviously handicapped by poor vision. Finding the same difficulty in another operation he abandoned general surgical work. During June and July, he showed evident signs of exhaustion. His appetite was poor, he had lost a number of pounds in weight, his muscular strength was at a very low ebb, and he was somnolent much of the time.

Examination by Dr. Derby in June showed left

homonomous hemianopsia, and an examination by Dr. Walton in September showed, in addition, loss of color sense in the otherwise normal half field of the right eye. At the examination in September he had lost thirty-four pounds, weakness was marked, speech was slow, and he seemed quite sluggish in grasping directions, for example, in the use of the perimeter, though his answers regarding the vision were definite and constant in several trials. The absence of color fields in the right eye and the normal boundaries of the color fields in the left eye were established with special care by repeated tests. Five days later he had a sudden attack of numbness and prickling in the left arm and left side of the face and tongue, of short duration.

The 1st of October he was persuaded to give up his work. After going into the country he apparently improved for a time. Since July his headaches had come at rather shorter intervals, and the frequency of the nausea had also increased.

After an interval of comparative comfort and enjoyment he was confined to his bed by a severe headache with extreme prostration, and after a period of somnolence, died December 29, 1897.

PATHOLOGICAL REPORT BY DR. F. B. MALLORY.

The sella turcica is involved by a discrete, lobulated, encapsulated tumor measuring 2.7 centimetres from front to back, 3.5 centimetres in width, and three centimetres in vertical diameter. The tumor has led to the disappearance of the olivary process, and of the base and posterior portions of the sella turcica. On section of the growth, after fixation in formaldehyde, the growth appears soft and granular; for the most part dark grayish in color, but in the posterior half there is a whitish area and also several translucent light grayish masses resembling cartilage but softer. Two or three septa extend part way in from the fibrous capsule and to some extent divide up the growth.

Microscopic examination shows the growth to consist mainly of delicate blood-vessels surrounded by walls of round cells, which are, for the most part, epitheloid in type. The vessels can be teased out readily, like the tubules of a testicle. The transparent areas resembling in gross hyaline cartilage consist of masses of colloid material. The darker areas in the growth are due to hemorrhage. Along one of the septa of fibrous tissue is an area which presents a different appearance from the rest of the growth. It consists of narrow compressed tubules, some of the cells of which tend to take on eosin stain, as do many of the cells in the anterior portion of the normal pituitary body after fixation in Zenker's fluid. A number of these tubules are dilated and contain colloid material. This area is probably the remains of the anterior part of the pituitary body.

Diagnosis. — *Perithelial angiosarcoma* (endothelioma).

To summarize the case, we have a patient with peculiarities of growth suggestive of congenital defect of the pituitary gland. Attacks of migraine accompanied by hemianopsia had existed so long as to at first exclude an organic basis. Later, we find a persistent defective field involving primarily the temporal field of one eye only; later, an extension to the nasal field of the other eye, producing homonomous hemianopsia; still further we have a loss of color field

on the otherwise unaffected side of one eye (hemianchromatopsia). During the progress of the case we find loss of sexual power, diminution of vision and optic atrophy, the ocular symptoms with the persistent headaches first establishing the diagnosis of tumor. Toward the end appeared vasomotor symptoms, somnolence, physical weakness and apathy and lack of mental grasp.

Perhaps the most interesting feature of the case is the anomalous distribution of visual field impairment, an impairment difficult to explain even with the pathological findings before us. In the first place, the recurring attacks of hemianopsia extending over a long period of time are perfectly consistent with functional disorders of the visual centres (migraine). It is difficult to believe that they could have been produced by pressure upon an optic tract persisting for so great a length of time and yet producing no permanent defect in the field or other sign of intracranial pressure. The next point of interest is the appearance of achromatopsia in one of the otherwise unaffected half fields. Achromatopsia is a rare condition, if we may judge from the lack of reported cases; it is, however, possible that the condition would be oftener found if oftener sought. Enough cases are already on record to establish the occurrence of loss of color sense in a field which shows no change in the perception of objects. The disturbance has hitherto been regarded as one of central origin, Gowers, for example, stating that it probably depends upon disease of a part of the occipital lobe, in which lies a separate color centre; Villebrand regards this centre as lying in front of the apical region, through which impressions pass, however, to reach it. According to this author, disease of the apex itself causes loss of form and color sense only in the corresponding half fields. This view would certainly be in perfect analogy with that of other cerebral symptoms, and yet our case forces us to recognize the possibility, at least, that achromatopsia may result from peripheral lesion. The case recently reported by Leszynsky points in the same direction.

It is not improbable that when the patient was first seen (July 20, 1896), that the slight defect of sight in the right eye was due to pressure on the nerve fibres supplying the macular region, and not, as was then supposed, to the floating opacities in the vitreous. Nine months later the central vision of the right eye has decreased to five-tenths, while the field for form and color remained perfectly normal, and in connection with this a well-marked temporal hemianopsia had developed in the left eye, but the macular fibres not being involved, central vision was unimpaired. From this time on there was a gradual failure of central vision in both eyes, with very little change in the visual fields for at least a year. Three months before his death, a well-defined nasal hemianopsia had developed in the right eye, giving a left homonymous hemianopsia indicating conclusively pressure on the right optic tract.

It should be noted also that while the temporal field of the right eye was normal for form at this time, the color field had entirely disappeared. The earlier visual fields showing monocular hemianopsia and a perfectly normal field for form and color of the other eye, with defective central vision, were difficult to account for, or rather it was not easy to understand at just what points pressure was exerted to give this result. The optic tract and chiasm were not removed

with the growth, and as the writers were unfortunately absent from the autopsy, the exact points of pressure are still more or less theoretical. The chiasm would seem to be the only point where pressure could have been exerted on the macular fibres independently. These fibres are of course at the outer surface of the nerve just after their exit from the globe, but approach nearer its centre as they progress backward and are entirely central at the optic foramen. In front of the chiasm the bundles form a horizontal oval. Entering the chiasm they almost reach the periphery — and interlace — the macular fibres being both crossed and uncrossed at about the centre of its dorsal surface. In the tract they again become too deeply seated to suffer independently of the other nerve bundles. The crossed fibres to the left eye might perhaps have been involved just as they left the chiasm to join the right optic tract, and the later development of a left homonymous hemianopsia would certainly favor this view if the early and extensive involvement of the macular fibres of the other eye could be ignored. The visual condition is best accounted for by supposing the crossed fibres to have been pressed upon, either at the anterior or posterior part of the chiasm, probably the latter and to the right, just before joining the uncrossed fibres to pass to the tract. A small nodule of the growth involved first the macular fibres of the right eye, before they had reached the point of separation into crossed and uncrossed, and later those of the left, probably near the centre of the chiasm. Later, the growth seems to have extended backward and to the right, exerting enough pressure on the crossed fibres of the right eye to destroy the color perception, but not the field for form, while the complete destruction of function of the uncrossed fibres of this eye was probably due to extension into the right optic tract.

CONCLUSIONS.

(1) Congenital peculiarities in growth resembling those of acromegaly, but occurring in otherwise healthy individuals, may point to structural defect of the pituitary gland, a defect sometimes furnishing the starting-point for new growth later in life.

(2) The occurrence of pituitary tumor without definite symptoms of acromegaly does not necessarily disprove a connection between this organ and this disease, for the persistence of even a small amount of healthy gland tissue is sufficient fairly to carry on the function of the pituitary body.

(3) The combination of general symptoms of new growth with optic atrophy and loss of temporal field of vision makes the diagnosis of pituitary tumor almost certain.

(4) Hemianchromatopsia is not necessarily of central origin.

SPECIAL PREPARATIONS OF PATIENT, SURGEON, INSTRUMENTS, SUTURES, ETC., AND POINTS IN TECHNIQUE OF OPERATIONS FOR HERNIÆ.

BY J. COPLIN STINSON, M.D., C.M., SAN FRANCISCO, CAL.

As the excellent results obtained in operations for the cure of hernia depend partly upon aseptic and antiseptic technique, etc., I shall briefly describe and concisely review the several points in the preparation of the patient, surgeon, instruments, etc., as they apply more especially to hernia operations.