UNUSUAL SIZE AND EXTENSION OF A PITUITARY ADENOMA

CASE REPORT OF A CHROMOPHOB TUMOUR WITH UNUSUALLY EXTENSIVE COMPRESSION OF THE BASE OF THE BRAIN, AND REVIEW OF THE LITERATURE ON THE PATHWAYS OF EXTENSION OF THESE TUMOURS

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Owing to their classical symptoms, adenomas arising from within the sella turcica are rarely permitted to attain any considerable growth before being submitted to operation. This is particularly true of the secreting chromophil adenomata, but the chromophobe variety may grow to a very large size and, in cases of unusual fixation of the optic chiasm, may do so without compressing the decussating optic fibres. In the rare instances where operation has been overlong deferred these neoplasms tend to extend into unusual areas, with the result that diagnosis may become a difficult problem and the predominant symptoms may lead to operation directed against the extension rather than the primary growth. These parasellar extensions not only produce profound alterations in the characteristic clinical syndrome, but complicate the surgeon’s task to a degree where his operative mortality may become prohibitive. In Dr. Harvey Cushing’s series of 338 adenomas (as reported by Henderson) and in Jefferson’s 128 cases, some degree of unusual extension into the parasellar structures occurred in as high a ratio as 22 per cent of the former and 14 per cent of the latter.

To judge from the scarcity of published clinical reports, little attention has been paid to this potential danger. Such complications may result either from failure to establish an early diagnosis, overenthusiastic and prolonged attempts to control the growth by radiation, or procrastination on the part of the physician. Cushing mentioned only 2 specific examples and Henderson, in his detailed study of 338 pituitary tumours operated upon by Dr. Cushing, devoted little space to them and mentioned only four pathways of extension. A brief reference to these unusual extensions in Dr. Cushing’s cases is also made in the survey of the Brigham series made by Dott and Bailey. By far the most important paper on this subject was given by Jefferson in 1940 in his President’s address before the Royal Society of Medicine. Unfortunately this article has been published only in the Proceedings of the Society, so it can have come to the attention of but few medical readers in this country. Jefferson cites three main factors in the production of extrasellar extensions: (a) the growth urge of the adenoma, (b) the state of fixation of the chiasm, and (c) the shape of the pituitary fossa and the nature

* Even the chromophil adenomata may, on very rare occasions, reach a large size and extend into unusual areas, as occurred in a patient of Dr. Cushing’s reported by Dott and Bailey.
of its diaphragm. His paper should be read by all who have to deal with these tumours and are interested in the mechanism of their spread.

Six possible pathways of extension have been found at operation or post mortem after the expanding adenoma has escaped the usual boundaries of the pituitary fossa:

(1) **Pharyngeal extension**: The commonest pathway of growth is downward by bony absorption of the sellar floor, so that the tumour expands into the sphenoid sinus. This situation has long been recognized, as it is easily diagnosed by x-ray. As tumour extension into this area involves no important structures, it produces no outstanding clinical signs unless erosion continues into the nasopharynx. The patient is then likely to complain of discharge and increasing nasal obstruction. A mass can usually be visualized in the roof of the nasopharynx. According to Henderson\(^8\) there were 8 of these complications in Dr. Cushing's series. Bailey and Cutler\(^2\) have recently described such a case where nasal obstruction was the predominant symptom. Resection and biopsy of a "nasal polyp" revealed a chromophobe adenoma of pituitary origin. This woman had unusually extensive destruction of the sella, and at necropsy the tumour was found to have eroded through its floor and the sphenoid sinus directly into the nasal cavity. From its microscopical appearance this tumour was classified as a malignant adenoma. Extensive erosion and rupture into the nasopharynx have also been observed in rare cases of carcinoma of the pituitary, which have been summarized by Ewing.\(^7\)

(2) **Hypothalamic extension**: This is caused by projection of the tumour directly upwards into the third ventricle behind a prefixed chiasm, as is so frequently the case with craniopharyngiomas. Here the usual symptoms, apart from visual disturbances, are headache and drowsiness, with possible evidence of injury to the autonomic centres. Jefferson points out that temperature variations and cardiac or respiratory alterations are not common with tumours that merely indent the hypothalamus without actually invading its walls, but polydipsia and polyuria may be produced by involvement of the supraoptico-hypophysial tract. Since tumour filling the third ventricle blocks the outflow of the cerebrospinal fluid, headache of the severest type with papilloedema may occur in this variety.

(3) **Temporal extension**: A lateral escape of tumour cells between the optic chiasm and the cavernous sinus may result in proliferation of the growth in the middle fossa. It will then compress the optic tract and the medial portion of the temporal lobe. This will result in an homonymous hemianopsia, and frequently in Jacksonian seizures preceded by an olfactory aura. Striking examples are illustrated in Cushing's book\(^4\) and in the more recent articles of Vosskuhler\(^14\) and Jefferson.\(^9\)

Henderson\(^8\) has also mentioned a possible extension into the sylvian fissure, in which the adenoma grows laterally but in a more upward direction

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* This is classified as "thalamic extension" in Henderson's paper, but Jefferson's preference for hypothalamic seems more logical.
than in the typical temporal expansion. He claims that it may thereby destroy the optic nerve. Compression of the frontal and temporal lobes would lead to mental deterioration, seizures with olfactory hallucinations, hemiparesis, and death from increased intracranial pressure (usually, as he pointed out, before vision is lost in the nasal field of the contralateral eye). Jefferson\(^9\) doubts the existence of a true sylvian extension as a solitary feature, and no actual example was described by Henderson.

(4) Invasion of the cavernous sinus: Tumours that invade the cavernous sinus and Meckel's cave have usually broken out of their capsule and taken on certain malignant characteristics, although the tumour cells may still retain a cell type similar to that of the smaller tumours. Jefferson\(^9\) has classified them as "malignant adenomata." When there is invasion of the cavernous sinus, certain classical signs result from compression of the structures that it contains, and there may be further lateral extension with stripping of the dura from the floor of the middle fossa and invasion of the trigeminal root sheath (Meckel's cave). Dott and Bailey\(^6\) in their review of Dr. Cushing's cases recorded 2 particularly striking examples. In one the tumour spread beneath the dura all the way across the middle fossa, eroded the squamous portion of the temporal bone, and appeared outside the cranium beneath the temporal muscle. In the other, the growth surrounded the extradural portion of both internal carotid arteries. An excellent account of tumour invasion of the cavernous sinus has been presented by Weinberger, Adler, and Grant,\(^15\) who described 14 examples from a series of 169 cases of verified hypophysial adenomas in the collection of the Hospital of the University of Pennsylvania. Invasion of the cavernous sinus may be diagnosed from the resultant disturbances of the structures that it contains—palsies of the nerves to the muscles of the eye, irritation of the ophthalmic division of the trigeminal, and engorgement of the orbital veins.

The two remaining pathways of extension are the rarest varieties of adenomatous outgrowth:

(5) Posterior subtentorial extension: Examples of extension backwards and downwards beneath the tentorium into the cerebellopontine angle are to be found in Cases 3 and 5 of the series presented by Weinberger, Adler, and Grant. In Case 5 the diagnosis lay between an hypophysial tumour, based on the roentgen findings, or a tumour of the cerebellopontine angle, suggested by the erosion of the petrous tip, cerebellar signs, and unilateral paralyses of the third, fifth, sixth, and eighth cranial nerves. There were in addition bilateral papilloedema, reduced acuity of vision, and absence of any field defect. This led Dr. Charles Frazier to explore the posterior fossa. The patient died soon after the operation, and a post-mortem photograph of the brain shows that the tumour, a chromophobe adenoma, had extended laterally to surround the cavernous sinus and gasserian ganglion. A portion had also extended backwards beneath the tentorium into the posterior fossa to occupy its right cerebellopontine angle (Fig. 1).
Frontal extension: An equally rare pathway of extension is upwards and forwards, so that the tumour either escapes from beneath a post-fixed chiasm or actually surrounds this structure. When the tumour has made its escape in this direction, it extends along the floor of the anterior fossa, separating and compressing the frontal lobes. After going through the Quarterly Cumulative Index from its first volume in 1916 to the present, we have been able to find only 4 cases of this type on record. The first was reported by Müller. His 62-year-old patient had a seven-year history of progressive blindness leading to optic atrophy and finally death from bronchopneumonia. The clinical data on this case are meagre, but there is no mention of seizures or change in personality. Post-mortem examination disclosed a "hen’s egg"-sized chromophobe adenoma, which originated in the sella and compressed the optic and olfactory nerves (Fig. 2). The frontal lobes and corpus callosum were compressed, the septum lucidum and fornix pressed to the left. The tumour encroached upon and was adherent to the floor of the anterior horn of the left lateral ventricle. Jefferson has added 3 more
cases, in which the patients had epileptiform seizures and personality changes characteristic of frontal lobe compression. One of us (J. C. W.) has operated, with temporary success, upon a very similar tumour, which extended forward beneath a post-fixed optic chiasm and thereby brought about severe headaches, personality changes, and epileptiform seizures. This patient showed bitemporal field defects and extensive erosion of the sella turcica. The cerebrospinal fluid pressure was within normal limits, but the protein content was elevated to 90 mm. per cent. Ventriculogram revealed a filling defect at the base of the third ventricle which extended nearly to the interventricular foramina. On transfrontal exposure the tumour was seen expanding upwards in front of the optic chiasm. After section of the right optic nerve it was possible to remove the greater part of the tumour and much of its capsule. There was immediate relief of the epileptiform seizures with a striking improvement in the patient’s mental condition, but this was of short duration. A year later he was hospitalized in a state institution with recurrent convulsive attacks and abnormal behaviour. Removal of this tumour was undoubtedly incomplete, and a further expansion has taken place. Without post-mortem examination no exact knowledge of the
anatomical relationships of this frontally extending adenoma is available, and it therefore does not deserve to be reported at greater length.

We wish to report the following case history of a chromophobe adenoma in detail because of its unusual size and because the post-mortem examination illustrates the two rarest routes of expansion that may take place when a tumour of this type is neglected.

CASE REPORT

William J., a 46-year-old retired chief gunner's mate, began having difficulty with vision in the spring of 1935. He was retired from active service in the U. S. Navy in the same year, but continued to live in China.* In 1938 he first became conscious of restriction in his temporal fields of vision. At this time he was also troubled by diplopia on looking straight ahead, and had to close one eye and use magnifying glasses while reading. He also began to wear dark glasses because bright light hurt his eyes. Following the death of his wife in 1941 he returned to the United States to live with his mother. He then suffered from gradually increasing headaches and more serious loss of vision. He complained not only of constriction of his temporal fields, but also of diminishing acuity, so that he hesitated to go out of the house alone. He also experienced nausea on bending over quickly. His mother noticed a distinct personality change. She was distressed to find that her son, who had always been a “good boy,” was becoming irritable, profane at times, and had no greater ambition than to sit in his room all day listening to the radio.

The course of this illness was very insidious until the night of April 9, 1944. That evening he had complained of nausea and had not eaten his supper. At one-thirty a.m. his mother heard an unusual sound in his room and found him having a convulsion. In a little while he recovered and remembered nothing about it, but at seven a.m. he had a second. This was witnessed by the local doctor, who reported “spastic paralysis, twitching, incontinence, and sonorous breathing.” He recovered from this seizure, but after a third around noon remained in coma, for which he was sent to the U. S. Naval Hospital in Newport.

On admission at six-thirty that evening he was still unconscious. He had wet himself and bitten his tongue in three places. Examination by Lieutenant Commander Hannibal Hamlin (MC) U.S.N.R., showed a semi-comatose patient with essentially normal fundi and neurological findings. He was given barbiturates and remained stuporous and irrational until the morning of April 12. He then became clear mentally and had no further seizures. Lieutenant Commander Hamlin and the Red Cross worker in Newport were able to obtain a very complete family and past history from the patient and his mother. There was no familial history of epilepsy. The patient's past history was not significant. He had never been interested in girls, but married in 1935. There were no children. During the life of his wife he was not impotent, but apparently had reduced sexual desire and never had any sexual experiences after her death in 1941.

On May 2, 1944, the patient was transferred to the Naval Hospital in Chelsea. To avoid unnecessary repetition, the neurological and laboratory findings at the two Naval Hospitals are given together.

Physical and Laboratory Examinations. The patient was 5 ft., 6 in. tall, of medium weight, and of somewhat feminine build. The penis and testicles were smaller than normal, axillary and pubic hair rather sparse, and he needed to shave only every third day. After recovering

* Through the kindness of the Bureau of Medicine and Surgery of the U. S. Navy we have been able to obtain copies of the patient's service health record. This states that vision began to fail in the right eye in April, 1935, and by September was reduced to 10/200. The vision in the left eye was still 20/20. No examination of visual fields was made at that time. The diagnosis was optic neuritis of unknown origin. In December, 1939, however, examination at the Regimental Hospital of the U. S. Marines in Shanghai showed definite bitemporal field defects with atrophy of the nerve heads.
from his seizures, he was at first rather belligerent and profane, but gradually became quite cooperative. His mental reactions did not appear definitely abnormal, but he lacked ambition and seemed to have little insight into his condition. Cerebellar tests were performed normally. The cranial nerves, with the exception of the visual tests, were also normal. His ocular movements and pupillary reactions were in no wise impaired. It is important to stress that ordinary tests for smell brought out no diminution in olfaction, which, although surprising, is in line with Jefferson's findings in two out of his three cases. The superficial and deep reflexes, plantar responses, and tests of motor-sensory activity were all within normal limits. Examination and careful questioning of the patient yielded no symptoms or signs suggestive of autonomic disturbances or emotional changes, which have been reported as occurring from compression of the diencephalic centres (Penfield; Bailey; Alpers; Zimmerman).

Repeated visual examinations showed that his acuity was distinctly reduced: O.D.: Fingers at 1 ft.; O.S.: 20/40. There was a bitemporal hemianopsia with sparing of the macula in the left eye, but not in the right (Fig. 3). The optic discs were slightly pale, but there was no suggestion of papilloedema. The pupils reacted normally to accommodation, but reacted to light only when the beam was projected against the temporal half of the retina (Wernicke's hemianopic pupillary reflex). Action of the external muscles was normal, and there was no limitation of eye movements. There was no engorgement of the superficial veins about the eyes or nose.

X-ray films of the skull disclosed a very large expanding intrasellar neoplasm (Fig. 4). The anterior clinoids were lengthened and tipped upwards and the posterior clinoids greatly thinned and pressed backwards. In addition there was destruction of the dorsum and floor of the sella turcica with erosion into the sphenoid sinus. The pineal body lay in the midline, but was slightly posterior to its normal position.

Lumbar puncture gave an initial pressure of 120 mm. with no cells and a total protein of 53.8 mg. per cent in the spinal fluid.

The electroencephalogram disclosed an abnormal wave pattern. It showed a tendency to moderate slow activity (about 7.5 per second) with marked slow-wave dysrhythmia in the frontal regions. The slow-wave activity in the frontal region was a little more marked on the right than on the left. The moderate slow activity was the same in the parietal and occipital regions, so that there was a definite contrast between these regions and the frontal regions.

The patient's fluid intake and urinary output were within normal limits. Routine blood and urine tests were also normal. The Kahn reaction was negative. The patient's glucose tolerance was within normal limits. Basal metabolism was -15 per cent.
Operations. A diagnosis was made of chromophobe pituitary adenoma with extensive extrasellar extension. Exploratory right frontal craniotomy was carried out on May 9, 1944, through a coronal incision of the scalp. The brain was abnormally tense, but after tapping the anterior horn of the lateral ventricle the frontal lobe was elevated and the floor of the anterior fossa visualized on the right side. The central portion in the region of the olfactory grooves was filled by a well-encapsulated reddish tumour, which extended from the sella turcica between the anterior clinoids and projected forward along the floor of the anterior fossa to the crista galli. The optic chiasm could not be exposed, but the right optic nerve was seen to be greatly compressed by tumour tissue on its medial side. The right olfactory nerve was humped over the dome of the tumour, which expanded upwards at least 3 cm. beneath the frontal lobe. Whether this was an olfactory groove meningioma growing posteriorly into the sella, or an unusual anterior extension of a pituitary adenoma, was not at first clear. The gross appearance of the tumour suggested the first possibility; the ballooned-out expansion of the sella seen in the x-ray and the upward displacement of the olfactory nerves were in favour of the second. A biopsy was taken and a generous flap of frontal bone cut on the left side to permit a secondary trans-midline exposure, with either resection of the right frontal pole or a midline exposure of the tumour from above by separating the frontal lobes. The incision was then closed.

The patient made a very smooth recovery, marred by the opening of a small sinus over a buried silk suture, which required over a month to heal. Microscopical examination established the diagnosis of chromophobe adenoma.

The second-stage attack on the tumour was undertaken on July 12, 1944, under intratracheal ether anaesthesia. The previous coronal scalp incision was reopened and the right-sided bone flap turned down. Next the bone on the left was removed, and the bridges across the longitudinal sinus rongeured away. By cutting and elevating the dura right up to the longitudinal sinus and dividing the anterior bridging veins, it was possible to elevate the right
frontal lobe more freely than before. When the tumour was exposed anteriorly, it proved to be much larger than supposed on the previous inspection. It extended posteriorly from the crista galli to a point well behind the right anterior clinoid and far laterally over the lesser wing of the sphenoid. After resecting the tip of the right frontal lobe to obtain a better exposure, we began to scallop out tumour tissue with the electro-cautery loop. This worked nicely and there was at first little bleeding. The compressed right optic nerve was cleared at its origin and tumour tissue removed from the olfactory groove and crista galli on the right side, but it proved impossible to develop the chiasm or the left optic nerve. Although the patient did not lose any unusual amount of blood, and in spite of transfusion, his blood pressure fell to 50/?. Satisfactory haemostasis was secured by placing small patties of fibrin foam wet with thrombin solution over the tumour bed. When the blood pressure failed to recover, the bone flaps were replaced and the incision closed.

**Course.** During the evening the blood pressure rose to 110/70, the pulse fell to 100, and respirations to 20, but the patient did not recover consciousness. The vital signs remained satisfactory until six a.m., when there was a sudden change in colour and fall in blood pressure. Death occurred at six-forty-five.

**Post-mortem Examination.** This was performed eight hours after death by Lieutenant Commander John L. Tullis (MC) U.S.N., and one of us (S. W.). Examination was restricted to the head. Externally, the body was essentially normal. The scalp was shaved, and a clean, sutured surgical incision ran from above and anterior to each ear over the vertex. A large bilateral frontal bone flap was exposed on opening the incision, and beneath this was a slight amount of fresh epidural and subdural haemorrhage.

The frontal lobes were displaced upward by a firm, bulging mass arising from the sella turcica. The anterior and posterior clinoid processes were flattened. The tumour ballooned...
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out in all directions, compressing and depressing the temporal lobes, bulging between the hemispheres, and extending into the left orbit. The brain and tumour together weighed 1590 grams, the tumour by itself about 150 grams. The roof of the ethmoid and sphenoid sinuses was extremely thin, but not invaded. The tumour was firm, smooth in contour, and slightly granular.

After formalin fixation further inspection of the tumour was carried out. Posteriorly the undersurface presented a mass of firm, white, coarsely nodular tissue covered with a filmy translucent membrane. This extended posteriorly to the anterior margin of the left cerebellar peduncle and to the right anterior border of the pons. It communicated anteriorly with a larger nodular mass showing dark haemorrhagic foci. The total mass extended 9.7 cm. antero-posteriorly and 6 cm. laterally (Fig. 5). As 2 cm. of the anterior pole in the region of the crista galli had been removed at operation, the original over-all length of the tumour was nearly 12 cm. Both temporal lobes were in contact with the mass but were not adherent. Both frontal lobes were molded outward from the midline to accommodate the tumour. On the left the meninges were intact, but displaced; on the right previous surgical removal of the mesial portion of the frontal lobe had exposed the tumour. This region of the tumour presented a raw gray to black granular surface in contrast to the smooth surfaces elsewhere. The left frontal lobe at the point of greatest lateral extent of the tumour was 3.5 cm. thick, while the right at a similar point measured 1.8 cm.

On elevating the tumour posteriorly, the posterior portion of the circle of Willis was clearly seen and was normal, aside from some atrophy of the communicating branches. Both carotid arteries and their cerebral branches were uninvolved, passing lateral to the tumour mass. The right anterior communicating artery entered the tumour mass; the left was free.

The left optic nerve was greatly thinned and so stretched that it could be followed 3.5 cm. forward over the superior and lateral aspect of the tumour. The right optic nerve could be identified at its origin from the brain, but disappeared into a semi-necrotic portion of the tumour, to reappear at the anterior border of the tumour 5.3 cm. anteriorly. Its fibres could not be distinguished in the tumour. The optic chiasm was lost in the tumour.

The left olfactory lobe was thinned, elongated, and stretched 5.3 cm. along the superior lateral margin of the tumour. The right olfactory lobe was similar, measuring 3.8 cm.

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Fig. 6. Sagittal midline section of brain. The anterior, darker portion of the tumour formed the floor of the right lateral ventricle. The posterior, lighter portion extended downwards beneath the brain stem to the pons.
On sagittal section the surgical defect in the right lower frontal lobe was clearly visible. A well-demarcated tumour mass rose from the floor of the anterior fossa to a height of 3.3 cm. (Fig. 6). Its upper surface formed a granular floor 3.5 cm. in diameter to the right lateral ventricle and a portion of the third ventricle. The hypothalamus was displaced superiorly and posteriorly, with marked concavity. The left lateral ventricle was compressed but not invaded. The basal ganglia on the left were displaced upward.

Microscopical examination revealed a tumour made up of uniform compact cells with but little stroma. Foci of necrosis and haemorrhage were present. The cytoplasm of the cells was scanty and neutrophilic. The nuclei were regular and occupied up to one-half or two-thirds of the cells. The chromatin was evenly scattered in fine mass. Mitoses were not present. Rare eosinophilic cells were scattered among the chromophobe cells.

Anatomic diagnosis was as follows: Chromophobe adenoma of hypophysis, with compression of hypothalamus, cerebral hemispheres, olfactory lobes, optic nerves, clinoid processes, and right anterior communicating artery; also invasion of right lateral ventricle and optic chiasm.

DISCUSSION

Although the tumour in our patient was much larger than in the cases reported by Jefferson, many of the symptoms and signs produced by it were very similar. The irritability, distaste for company, and loss of ambition, as well as the extreme loss of vision and central scotoma in the right eye, in the presence of normal cerebrospinal fluid pressure but elevated protein, are all similar to Case 2 from the Manchester Royal Infirmary. Jefferson points out that central scotoma and elevation of the protein content of the cerebrospinal fluid are indications of unusual extension of a pituitary tumour. The wide extension of this tumour and its inclusion of the optic chiasm with a portion of the right optic nerve, as well as the right anterior cerebral artery, made it inoperable. The unusual fall in blood pressure, which occurred at an early stage of the final operation before any undue amount of blood had been lost, was undoubtedly due to disturbance of the contiguous autonomic centres in the walls of the third ventricle. Operative manipulation in the region of the anterior commissure and just posterior to it commonly results in profound changes in pulse rate, blood pressure, level of consciousness, and other vital signs (Dott, White). On thinking back over this case, it would certainly have been wiser to have performed a preliminary ventriculogram. Jefferson has advocated this procedure in all cases in which there is anxiety as to the size of the tumour, and we shall insist on its use in all future cases in which an unusual extension of a pituitary tumour is suspected. Such was obviously the case here, in view of the severe generalized epileptic seizures. In addition, we should have suspected frontal lobe compression had we received in time the social worker’s report of the patient’s personality changes, which was obtained from his mother. However, even if air studies had been made, the fear of total blindness would have made

* Bilateral central scotomata signify a large retro-chiasmal expansion, since the macular fibres appear to decussate in the posterior part of the chiasma (Henderson). A unilateral scotoma is caused by abnormal localized herniation of the adenoma impinging on an optic nerve (Jefferson).
operation very difficult to refuse. A preliminary ventriculogram, however, would have disclosed the extreme compression of the third ventricle and served as a warning to institute temporary catheter drainage of the lateral ventricles as a post-operative safeguard. This step might have prevented fatal cerebral compression from the wave of oedema which so often follows partial removal of such a large tumour.

If Jefferson’s\textsuperscript{9} valuable paper had come to hand before this patient’s operation, we should have realized from his greater experience that the best solution was to leave such a large growth respectfully alone. In it Jefferson stated that in most cases of pituitary tumours with unusual extensions operation is a course of doubtful wisdom. While his mortality was only 2 per cent for the usual small adenoma, 4 out of 12 patients with extrasellar extensions died.\textsuperscript{*} Finally, operation on long-standing massive tumours is not often profitable for the patient, “as the severe changes in the chiasma brought about by prolonged and increasing compression are irremediable.” When confronted by an unusual tumour of this sort in the future we shall first attempt to estimate its size by pneumography. When discretion is judged the better part of valour, radiation therapy can be pushed to the limit, although the chances of a satisfactory response in such widely extending adenomas composed of chromophobe cells are not very bright (Sosman\textsuperscript{12}). With continued growth progressive blindness may be unavoidable, but surgical intervention will not become imperative before the advent of obstructive hydrocephalus. Ventricular drainage by catheter passed beneath the scalp from the posterior horn of a lateral ventricle to the cisterna magna, as described by Torkildsen,\textsuperscript{13} can then be used as a palliative procedure. After this operation White and Michelsen\textsuperscript{17} have found that patients with inoperable brain-stem tumours may live in relative comfort for a period of months to years, until direct compression of vital centres ultimately results in death.

A final point which deserves comment is that the cells of this enormous tumour, which had grown around the optic chiasm and the right anterior communicating artery, showed no evidence of malignancy. Jefferson\textsuperscript{9} has pointed out that neither size nor unusual extension are proofs of malignancy, which can only be diagnosed when the pituitary tumour has broken through its capsule and actually invades the surrounding structures. This is the case with the adenomata that invade the cavernous sinus and Meckel’s cave, or cause extensive erosion of the cranial base with extension into the nasopharynx, as in the case reported by Bailey and Cutler.\textsuperscript{2} In our patient the capsule of the tumour was everywhere intact, and the damage to surrounding structures was caused by simple compression.

\textsuperscript{*} All three of Jefferson’s patients with frontal extension survived the operation and appear to have done well, so we do not intend to draw the conclusion that operation should be withheld in all cases when this diagnosis is made. Actually the resection of a small frontally expanding adenoma is liable to be less difficult than that of the more common examples of temporal lobe or hypothalamic extension, particularly if a maximum exposure is ensured by partial resection of the frontal lobe.
SUMMARY AND CONCLUSIONS

1. This article reviews the common pathways of extension of chromophobe adenomas of the pituitary. Aside from the very common invasion of the sphenoid sinus, which causes no injury to the brain or cranial nerves, these include extension upwards into the third ventricle, laterally into the temporal lobe, or into the cavernous sinus.

2. In the two rarest types of extension the tumour may expand down through the incisura of the tentorium to compress the peduncles, pons, and the cranial nerves that arise from this region; or it may work its way upwards into the anterior fossa of the skull, with compression of the frontal lobes.

3. The history of a case is given in detail that illustrates both of these rare types of expansion. During the tumor's ten-year growth it attained a weight of over 150 grams and a length of nearly 12 cm., extending from the crista galli beneath the brain stem to the pons.

4. It produced the classical evidence of compression of the optic chiasm, with nearly total loss of vision in the right eye. In addition, there were clear-cut signs of cortical irritation (generalized epileptiform seizures) and frontal lobe involvement. In spite of its great size and nearly complete compression of the third ventricle, the intracranial pressure remained within normal limits, but the protein content of the cerebrospinal fluid was elevated to 53.3 mg. per cent.

5. At operation the extent of the tumour and its inclusion of vital structures made its removal impossible. Death followed from compression of the autonomic centres in the brain stem.

6. Post-mortem examination showed a chromophobe adenoma of unusual size and extension, with compression of the hypothalamus, cerebral hemispheres, olfactory lobes, optic nerves, and right anterior communicating artery, and with invasion of the lateral ventricle and optic chiasm.

7. In planning operative intervention on hypophysial tumours with signs that suggest compression of structures beyond the optic chiasm, the surgeon should bear in mind the possible pathways of extension that may be followed by slowly growing tumours after rupture of the diaphragma sellae or invasion of the cavernous sinus. Successful surgical removal of the growth under such circumstances is likely to be extremely hazardous and often impossible. A preliminary ventriculogram should facilitate the exposure and aid in determining the operability of such a growth.

REFERENCES


