MULTIPLE MENINGIOMAS. REPORT OF TWO CASES

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In Cushing’s series of 2,203 verified intracranial tumors, the meningiomas comprised 13.4 per cent. The incidence has been reported as somewhat higher by others (Olivecrona, 15.8 per cent; Craig, 14.9 per cent; Horrax, 19 per cent). Despite its frequent occurrence among brain tumors, the meningioma is rarely seen as a multiple growth unless one includes those cases of centralized neurofibromatosis, a manifestation of von Recklinghausen’s disease, in which the dura is often studded with innumerable small meningiomas. Cushing and Eisenhardt have preferred to designate this condition, which is usually associated with bilateral acoustic tumors, as meningiomatosis rather than to include it in the group of multiple meningiomas. Using this strict classification, they were able to isolate only three examples of true multiple meningiomas from their series of 295 cases of intracranial meningiomas.

The first case of multiple meningiomas reported was that of Anfimow and Blumenau in 1889, who found at necropsy four large and several smaller dural endotheliomas. Similar cases have been reported by others (Krivy, Flick, Upras). Hosoi, who reviewed the subject in 1930, was able to collect 22 cases of multiple meningiomas in the literature. Eleven of these (50 per cent) were associated with other intracranial tumors, chiefly acoustic neuromas, and consisted of a diffusion of tumor nodules over the dura. Cushing would classify these cases as “meningiomatosis.” Hosoi’s case, although not associated with acoustic neuromas, was accompanied by multiple angiomas in the cortex of the right frontal lobe. Frazier and Alpers in their report of 75 verified meningiomas included one example of multiple tumors (Case xiv). Of 60 cases of meningioma reported by Horrax, the growths were multiple in four (no mention is made of associated stigmata of von Recklinghausen’s disease).

The successful removal of multiple meningiomas has been rarely reported. Heuer and Dandy in 1916 reported the first successful removal of two adjacent dural endotheliomas, one having recurred after a preceding operation. Similar cases have been reported by Raaf and Craig, Woltman and Love, Puusepp, Cushing and Eisenhardt, and Echols. In most instances, only two or three tumors were removed. Cushing’s patient underwent five operations over a period of 14 years. One meningioma was removed at each of the second, third and fourth operations. At the fifth operation, numerous small confluent meningiomatous tumors were removed in addition to a large parasagittal growth. In Echol’s case, 9 small ones and 1 large meningioma were successfully removed.

A review of the material at this clinic revealed that 58 patients with in-
tracranial meningiomas were operated upon during the past six years. Of these, four may be considered as multiple growths. Two of these fall into the group of diffuse dural meningiomatosis associated with central neurofibromatosis. One of these two, in addition to bilateral acoustic tumors, displayed at necropsy a generalized neurofibromatosis of the spinal nerve roots and cutaneous evidence of von Recklinghausen's disease. The remaining two cases, the basis of the present report, fall into the group of true multiple meningiomas as delineated by Cushing and Eisenhardt.

CASE REPORTS

Case 1 is of unusual interest not only because 10 meningiomas were removed in 4 successive operations but also because of the graphic histological transition from a benign psammomatous tumor disclosed at the original operation to an unquestionably malignant meningioma when removed at the fourth operation. In Case 2, two distinct meningiomas were successfully removed in one operation. One was a typical left frontal parasagittal tumor arising from the falx, the other a smaller growth in the left inferior frontal region which extended into the lips of the Sylvian fissure.

Case 1. E. L., a 56 year old salesman, was admitted to the Jewish Hospital on January 14, 1940. For 6 months his family had noticed a marked change in the patient's personality.

![Fig. 1. Case 1. Lateral roentgenogram of skull showing dense shadow of calcified meningioma (arrows).](image)

From an alert, aggressive type he had become a quiet, meek, apathetic individual who preferred to sit quietly by himself. Within a short time he found it difficult to concentrate and soon he became slovenly in his habits and careless about his dress. There had been no headache, vomiting or visual disturbances.
Physical Examination. The patient appeared slightly dazed but otherwise was cooperative and well oriented. There were slight disturbances of recent memory. The neurological status was essentially negative except for slight blurring of the right optic disc, complete absence of the abdominal reflexes, and generally overactive tendon reflexes.

Laboratory Data. Roentgenograms of the skull (Fig. 1) revealed a large calcified mass in the anterior portion of the right middle fossa which measured 5 × 6 centimeters in the antero-posterior projection and which appeared to originate from the lesser wing of the sphenoid bone. The mass was thought to represent a calcified meningioma.

Operation I. On January 19, 1940, under avertin and ether anesthesia a right fronto-

![Fig. 2. A. Case 1. Photomicrograph of psammomatous meningioma (H.E. ×100) removed at first operation. B. Same ×350.](image)

temporal craniotomy was performed. A large encapsulated tumor, arising from the lesser wing of the sphenoid, was removed piece-meal. The mass was firmly adherent to the base of the skull. After its removal, the bed of the tumor was cauterized to destroy any fragments of tumor which remained.

Histology (Fig. 2). The tumor was a typical benign meningioma. The sections showed a large number of psammoma bodies, some of which coalesced to form areas of calcification of considerable size. Fewer areas consisted of predominantly elongated cells, closely packed, and frequently describing curves with some whorl formation. There were no mitotic figures. The cells were all uniform in size and shape.

Course. The post-operative convalescence was uneventful except for a right external rectus palsy and a right peripheral facial weakness. He was discharged on the nineteenth post-operative day. Roentgenograms of the skull taken before discharge revealed complete disappearance of the pre-operative calcification.

Interval Note. Following operation the patient remained mentally sluggish and apathetic. He spent most of the time in bed. Because of slow recuperation he was referred back to the hospital for study.
Second Admission. March 26, 1940. The patient remained in the hospital for three weeks during which he was given a high caloric diet with supplementary vitamin B complex and liver. At the time of discharge, he showed marked improvement.

Interval Note. During the next two years, the patient was completely asymptomatic. He returned to work and was able to conduct his business as well as formerly. In June, 1942, however, there was a recurrence of the same personality deficits noted prior to his first admission. He began to complain of pain about the right eye and cheek and noticed that his left arm was weaker than formerly.

Third Admission. July 9, 1942. Examination at this time revealed the patient to be quite dull mentally. He was slightly disoriented and showed disturbance of recent memory. There was a left homonymous hemianopsia. The optic discs were pale. There was a left hemiparesis, an exaggerated left knee jerk, a left Hoffman sign but no Babinski. Position sense, vibratory perception, 2-point discrimination were all impaired in the left upper limb. There was astereognosis on the left.

A pneumoencephalogram was made on July 15, 1942. This revealed a failure of the right ventricle to fill with gas. The left ventricle, however, was enlarged and was definitely displaced to the left. In some views the third ventricle was visualized and also appeared displaced to the left.

Operation II. On July 17, 1942, the previous bone flap was re-elevated. A spherical, encapsulated tumor mass about 3 cm. in diameter was found in the anterior portion of the middle fossa in the region of the outer third of the sphenoid wing. The tumor was attached to the lateral dura and not to the base of the skull as in the previous operation. Nevertheless the tumor was thought to represent a recurrence of the original growth.

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Fig. 3. A. Case 1. Photomicrograph of cellular fibroblastic meningioma with occasional psammoma body removed at second operation (H.E. X100). B. Same X350.
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Histology (Fig. 3). The tissue was quite cellular consisting of sheets of cells with poorly defined cell borders. There was some tendency to whorl formation and an occasional psammoma body was seen. The cells in some areas showed slight variation in size and shape. There was slight tendency toward nuclear clumping but true multinucleated cells were not visible. No mitotic figures were seen. Laidlaw’s connective-tissue stain revealed an extensive reticulin and collagen network throughout the tumor. In many areas the cells were spindle-shaped and clearly of fibroblastic type.

Course. The immediate post-operative reaction was satisfactory. The patient, however, continued to exhibit marked disturbance of sensorium. He developed bowel and bladder incontinence. Gradually these symptoms improved. He was allowed out of bed on the twelfth post-operative day and discharged on the twenty-first post-operative day. At the time of discharge, the incontinence had disappeared and the patient was oriented and alert.

Interval Note. The patient continued to improve at home but within two months, he again presented himself for admission because of severe headache and increasing weakness of the left upper and lower limbs.

Fourth Admission. October 11, 1942. Examination at this time again revealed slight disturbances of orientation and memory. The left hemiparesis had increased slightly. It was difficult to conceive of another recurrence in so short an interval. Nevertheless another pneumoencephalogram was made. This revealed a tremendous shift of the ventricular system to the left. Operation was advised but the family did not consent and the patient was discharged to a nursing home on November 18, 1942.

Interval Note. He continued to go downhill. The mental symptoms and the hemiparesis increased. Because of the rapid progression, he was brought back for operative intervention.

Fifth Admission. December 30, 1942. Examination was similar to that of the previous admission except for the increase in the mental deficit and progression of the hemiparesis.

Operation III. On January 4, 1943, the previous bone flap was re-elevated. Anteriorly where the previous tumor had existed, there was a large empty space filled with clear fluid.

Fig. 4. Case 1. Three meningiomas removed at third operation.
In the posterior inferior half of the exposure, there was a rather large encapsulated tumor adherent to the tentorium in the region of the lateral sinus. It measured approximately 5 cm. in diameter. It was necessary to extend the cranial defect posteriorly to attack this mass. The tumor was removed completely and its bed coagulated. With this out of the way, there came into view another tumor in approximately the same region of the tentorium but more medially placed. It was smaller than the first, measuring about 3 cm. in diameter. This tumor was removed in a manner similar to the first. With this accomplished, a third tumor came into view even more medially placed than the second. This too was excised and after careful inspection revealed no further tumor masses, the procedure was terminated (Fig. 4).

![Image](50.png)

**Fig. 5.** A. Case 1. Photomicrograph of meningiomas removed at third operation (H.E. X100). Appearance essentially similar to Fig. 3 except that cells are slightly more variable, areas of necrosis are present; occasional mitotic figures; disappearance of psammoma bodies. B. Same X350.

**Histology** (Fig. 5). Sections taken from different portions of the 3 tumors showed essentially the same microscopic appearance. The tissue was fairly cellular, the cells being irregularly round, oval, or elongated and of medium size. In some areas they showed a moderate degree of variation in size and shape. An occasional mitotic figure was seen. Some areas showed definite whorl formation. There were focal areas of necrosis scattered throughout the tumors and these areas contained numerous fat-filled cells and granular debris. In some areas finger-like projections of tumor were present in the adherent brain. The tumor was permeated by a rich reticulin and collagen stroma. The tumors resembled those previously removed although there was more variation in the cell type on this occasion.

**Course.** Post-operative convalescence was slow. The patient ran an unexplained spiking temperature for three weeks during which his mental status became even more deteriorated. At this point the temperature gradually returned to normal and coincidentally his sensorium cleared. The hemiparesis began to improve. He was discharged on the fifty-first post-operative day.
Interval Note. The improvement was short-lived. Five weeks after discharge, the patient developed persistent hiccough and progressive jaundice. He was referred for admission to the medical service.

Sixth Admission. March 27, 1943. Examination revealed in addition to generalized jaundice, a large tender liver, a palpable spleen and a temperature of 101°F. Four days after admission he had a massive hematemesis. The hemoglobin fell to 44 per cent. He was treated with repeated transfusions. The jaundice and fever gradually receded and he was discharged to a nursing home on April 13, 1943. The episode of jaundice was interpreted as due to acute hepatitis.

Interval Note. The patient continued to improve during the months of April, May and June. He became mentally alert and, according to the family, was again his "former self." He soon began to walk with the aid of a cane. Again our optimism was to no avail for in July, six months following the third operation, there were again symptoms of recurrence. His sensorium became cloudy and he began to complain of severe headaches over the right half of the head. He became increasingly drowsy and soon sphincteric incontinence appeared.

Seventh Admission. October 20, 1943. A pneumoencephalogram was made on October 22, 1943, and revealed once more a shift of the lateral and third ventricles to the left. In addition gas in the fourth ventricle appeared displaced to the left. In view of our previous experience, there was every indication that we were dealing with one and probably multiple recurrent tumors.

Operation IV. November 1, 1943. Upon re-elevating the original bone flap once more a
large empty space filled with clear fluid could be seen through a defect in the dura. This space represented the site of removal of the previous tumors. The dural defect was enlarged and four small meningiomas came into view. One was over the convexity of the brain, two were attached to the sphenoid wing, and a fourth occupied the base of the skull in the anterior part of the middle fossa. This last tumor eventually proved to be a large growth extending through the base of the skull. Further search revealed a fifth and even larger tumor attached to the tentorium in the region of the petrous bone. This mass was found to extend medially through

the tentorium into the posterior fossa (Fig. 6). Chronologically this tumor was removed first separating it from the surface of the cerebellum and pons. Then the three superficial tumors were removed. Finally the fourth, extending through the base of the skull, was attacked. This could not be removed cleanly but what shaggy remains were seen were thoroughly coagulated.

*Histology* (Fig. 7). Sections taken from different portions of the various tumors showed a variable microscopic appearance. In some sections there were numerous whorls and some psammoma bodies. In most of the sections there were moderate numbers of mitotic figures. In sections taken from two of the tumors, there was considerable variation in the size and shape of the cells, which presented no definite architectural pattern. The cells were, for the most part, of medium size with round or oval nuclei and usually without nucleoli. The cytoplasm was rather ill-defined and there was some tendency toward nuclear clumping. Blood vessels were moderate in number and their walls were well formed.

These sections differed strikingly from those of the previous tumors. The first specimen showed a predominance of psammoma bodies and whorls. This tendency gradually became less marked. There was no doubt, in reviewing the various sections of all the tumors, that
there had been a progressive tendency toward a malignant change with some of the last tumors being obviously malignant.

Course. The immediate post-operative reaction was satisfactory. However, the patient failed to regain consciousness. His breathing became rapid and stertorous, he sank deeper into coma, and despite supportive measures, expired forty-eight hours following operation.

Necropsy. The dura over the right frontal parasagittal region contained several pea-sized nodules (Fig. 8). In addition a flat tumor mass was present between the leaves of the tentorium cerebelli on the right side. No tumors were found on the left side of the brain and none were present in the posterior fossa. There was no evidence of von Recklinghausen’s disease.

The second case was much less dramatic, but since two separate and distinct tumors were found at operation, we believe it should be included as another example of multiple meningioma in the absence of von Recklinghausen’s disease.

Case 2. B. G., a 45 year old insurance broker, was admitted to the neurosurgical service of the Jewish Hospital on June 2, 1942. Eight years previously he had noticed a lump in the left temple which was accompanied by periodic sticking pains in that region. He was seen by
a general surgeon at that time, and following numerous roentgenograms of the skull and other bones of the body, a biopsy of the lump was taken. Apparently a definite histological diagnosis could not be made. The final opinion, however, was fibrosarcoma. Because of this, thirty x-ray treatments had been given over the region of the tumor. Four years prior to admission, the patient had two spells of unconsciousness of short duration. Neither was witnessed. In October, 1941, he developed progressive weakness of the right lower limb, affecting chiefly the foot. Two weeks before admission he noticed a hard lump over the vertex of the skull to the left of the midline. This had not been present before.

**Fig. 9.** Case 2, showing two halves of the larger tumor and half of the smaller one. Also the bone flap where involvement by the parasagittal tumor is seen in the inferior portion of the photograph and the Sylvian tumor in the superior portion of the photograph of the flap.

*Physical Examination.* The skin over the left fronto-temporal area was scarred and atrophic due to the extensive radiotherapy. Beneath the atrophic skin an irregular hyperostosis was palpable. There was, in addition, a hard bony lump in the left parasagittal region above the scar. The general examination was otherwise normal. The neurological survey revealed moderate weakness of the right lower limb, most marked in the dorsi-flexors of the foot, hyperactive right knee and ankle jerks, and a positive right Babinski sign.

*Laboratory Data.* Roentgenograms of the skull revealed a large area of decalcification in the left fronto-temporal region. In addition there was an area of hyperostosis in the outer table near the vertex just behind the coronal suture. This corresponded to the bony lump felt on examination of the head.

*Operation.* On June 9, 1948, a left fronto-temporo-parietal craniotomy was performed.
When the bone flap was turned, tumor was seen extruding through the dura and into the bone both along the parasagittal region and in the region of the pterion. The bone flap was so extensively involved with tumor that it was thought unwise to replace it and it was, therefore, removed early in the operation. Additional bone which was also involved by tumor was rongeured away. A small tumor, measuring 4×1.5×.5 cm., was encountered in the fronto-temporal region involving the dura and extending into the lips of the Sylvian fissure. This was excised completely. The dura was then opened superiorly toward the parasagittal region. Here a second and larger tumor, measuring 7×5×4 cm. and weighing 72 grams, was discovered. This was found to be adherent to the superior longitudinal sinus for a considerable distance. The tumor was removed without undue difficulty (Fig. 9).

*Course.* The patient’s post-operative convalescence was very satisfactory. There was a transient mild aphasia and a right hemiparesis, both of which cleared rapidly. At the time of discharge on the fifteenth post-operative day, the patient was completely asymptomatic except for slight hesitancy in speech. It is now 18 months since operation. The patient is back at work and in excellent health.

*Histology.* The tumors were clearly meningiomas whose microscopic appearance varied considerably in different regions. In some areas the appearance was that of a psammomatous type of meningioma with whorls predominating. In other areas the fibroblastic elements were conspicuous and in still other places, the appearance was suggestive of a hemangioblastoma. There was no evidence of malignancy in any of the sections. The tumors were classified as meningiomas of mixed type.

**COMMENT**

Multiple meningeal tumors, as previously stated, occur either alone or in combination with centralized neurofibromatosis. Usually no attempt has been made to segregate the two types. In the von Recklinghausen type, the growths usually consist of a diffusion of meningeal tumefactions, small in size, and scattered over a wide area of the meninges. The familial nature of multiple neurofibromatosis has long been recognized (Harbitz, Preiser and Davenport, and Schaltenbrand). More recently Gardner and Frazier have shown that bilateral acoustic tumors, a special form of centralized neurofibromatosis, is also a familial and hereditary disease.

Usually no such diffusion of tumors and no such familial or hereditary relationship has been shown to exist in those cases of multiple meningiomas without the stigmata of von Recklinghausen’s disease. For this reason, it seems best in the present state of our knowledge to consider them, as Cushing has done, in a separate category. The cases reported here belong to this group.

In Case 1, ten meningiomas were removed from the right hemicranium over a period of three years. The patient was under constant clinical observation throughout his illness and neither during life nor at necropsy could any of the stigmata of von Recklinghausen’s disease be found.

Cushing stated that the meningiomas “rarely, if ever, change their histological type and that a given tumor of sarcomatous type has been sarcomatous from the outset.” He cites three of his cases in which there was no appreciable change after 12, 13 and 17 years respectively, despite frequent recurrences. In the successive tumors removed in our Case 1, however, there can be no doubt that there was a transition in histological form. During the three year period, there was a remarkable transition from a benign psam-
momatous meningioma removed at the first operation to an unquestionably malignant tumor at the fourth operation. Sections taken from the original tumor were unmistakably those of a psammomatous meningioma, considered to be perhaps the most benign of the meningeal tumors. At the second operation, the tumor had become more cellular, there had been a marked decrease in whorl formation, and only an occasional psammoma body was seen. The picture undoubtedly represented more rapid growth. At the third operation, the general appearance of the tissue was similar to that of the previous tumor but for the first time, one began to see some variation in the size and shape of the cells and an occasional mitotic figure. There were also small areas of focal necrosis in various portions of the tumors. At the fourth operation, two of the tumors were obviously malignant, showing marked variation in the size and shape of cells, unusually large forms, giant cells, and numerous mitotic figures. The general impression was one of increasingly rapid growth in each successive tumor.

Turner, Craig and Kernohan\(^8\) have recently studied the pathology of malignant meningomas. In their review of 370 meningeal intracranial tumors seen at the Mayo Clinic they found 36 (approximately 10 per cent) malignant growths. Applying their histological criteria, the tumors removed at the third operation in Case 1 would be considered of low grade malignancy while two of those removed at the final operation would be of pronounced malignancy. These authors cited no examples of benign meningiomas becoming malignant at subsequent operations for recurrence. That this transition occurs in certain of the gliomas has long been known. Bailey\(^2\) has shown that a typical protoplasmic astrocytoma removed at a primary operation was transformed into a glioblastoma multiforme at a secondary operation a few years later. The changes in our case may be considered analogous to the dedifferentiation of the astrocytoma. To our knowledge there has been no similar case reported in the literature. Perhaps a more careful study of recurrent meningiomas will lead to similar cases showing different degrees of anaplasia from one operation to the next.

In reviewing the progression of events in this case, one is struck by the limitation of the meningeal growths to the right hemicranium. Both during life and at necropsy there was no evidence of involvement of the left side of the brain. The thought occurred that the multiplicity of the recurrent tumors in our case was due to spreading by implantation at the time of operation. However, Cushing\(^8\) was aware of this hemicranial distribution of the tumors in most of the cases of true multiple meningiomas reported in the literature but he offered no explanation for it. It is to be contrasted with the meningeal tumefactions seen in cases of centralized neurofibromatosis where the distribution is practically always bilateral. Because of this and the absence of a familial or hereditary transmission in these cases, it would appear that multiple meningeal tumors are not necessarily an expression of von Recklinghausen’s disease, where the defect is said to be a congenital abnormality of the ectoderm, commonly familial and often inherited as a Mendelian dominant.
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In Case 2 two separate and distinct meningiomas were removed at one operation. The case is recorded merely as another instance of successful removal of multiple meningiomas. Here, as in Case 1, the tumors were limited to one side of the brain and there was no clinical evidence of von Recklinghausen’s disease.

SUMMARY AND CONCLUSIONS

Two cases are presented, the one with ten meningiomas confined to the right hemisphäre, removed at four operations; the other with two meningiomas removed from the left side of the brain.

In the first case the original tumor was a benign psammomatosus lesion. With each episode leading to reoperation, the tumors showed a progressive tendency to more rapid growth, until one of the last tumors was definitely sarcomatous. This change appeared analogous to dedifferentiation in gliomatous tumors from more benign to more malignant types.

The absence of neurofibromatosis in these two cases leads us to classify them as cases of multiple meningioma as distinct from meningiomatosis seen accompanying von Recklinghausen’s disease.

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