The Problem of Malignancy in Meningiomas*

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From the time of their earliest description in the late 18th century, meningiomas have been considered indolent relatively benign tumors which, when their location is favorable, can be completely removed. Yet Simpson reported recurrences in 21% of 295 surgical cases; half of these were in patients in whom radical removal had been considered complete. He emphasized the invasive properties of these tumors, including limited infiltration of the brain in 4% of his cases, and alluded to two examples of definite malignancy.

This propensity for vigorous activity which may progress to frank malignancy was recognized as long ago as 1858. In 1927, Craig reviewed 56 cases of intracranial meningiomas, and found 11 malignant variants. Cushing and Eisenhardt described six examples in their series of 313 meningiomas. Turner, et al., in a study of 370 intracranial meningeal tumors, found 36 with malignant characteristics.

Moreover, extracranial metastases of meningiomas may occur. Interestingly enough, in some of these cases the microscopic appearance of both the primary and metastatic tumors was that of a benign meningioma. Still another malignant variant of the same fundamental pathological process is the diffuse, generalized, meningeal meningiomatosis.

Our report concerns the solitary intracranial meningioma which, because of its microscopic appearance taken in conjunction with its gross characteristics and behavior, is deemed to be malignant.

Clinical Material

A review of 37 cases of intracranial meningiomas from The Mason Clinic has disclosed six patients in whom a diagnosis of malignant meningioma was made. Two of these cases were unacceptable; one was reclassified as an atypical glioblastoma multiforme, the other as benign. Four patients remain for consideration, (Table 1).

Two patients were women. The ages of the four patients ranged between 40 and 61 years at the time of operation. The durations of symptoms before operation were 3 days, 3 months, 1-1/2 years, and 4 years. All four patients had focal neurological changes of varying degrees. None had signs of increased intracranial pressure. The skull films in one patient showed a large punched-out lytic lesion adjacent to tumor without evidence of bony stimulation. Skull x-rays were normal in the other three cases. The tumor was frontal parasagittal in two patients, parietal parasagittal in another, and arose from the sphenoid ridge in the fourth.

Total removal was believed to have been accomplished in one patient. In two others, a small amount of tumor was left behind. In the fourth patient only a portion of tumor was obtained for biopsy. Three patients were irradiated after operation; only the most recent case was not.

Two patients having what we consider to be low-grade malignancies are alive 5-1/2 and 10 years after the initial operation. The longest survivor in whom tumor was left behind underwent the removal of a neurofibroma of the cauda equina 5 years after the cranial surgery. Then, 2-1/2 years later, an intracerebral clot in the opposite parietal lobe was evacuated; a mercury-203 brain scan 2 years after this was negative.

The second patient in whom biopsy only was carried out had a nearly complete remission of symptoms for almost 5 years following cobalt irradiation. She then rapidly deteriorated, and a radical removal of the tumor was attempted. Except for an extension across the midline, this seemed successful. She continues to improve 5 months after her second operation.

Our third patient, with an advanced malignancy, seemed to be doing well follow-
ing gross total removal of the tumor and cobalt irradiation; he committed suicide 3 1/2 months after surgery and an autopsy was not obtained.

The last patient, who also had an advanced malignancy, did not have irradiation following an incomplete removal. He died of recurrence 5 months after operation.

Pathology

We are aware that our interpretation of malignant changes in the first two cases may be controversial; nevertheless, we consider them examples of early or low-grade malignancy in that each tumor contained areas whose microscopic characteristics were variants of those ordinarily encountered in benign meningiomas. The same can be said for the appearance of these neoplasms at the time of operation.

In our first case, the tumor was a yellow-gray, friable, and somewhat gelatinous tumor that apparently infiltrated the cerebral matter deeper in the midline. Under the microscope, the greater part of this tumor appeared to be typical of a psammomatous meningioma (Fig. 1). There were, however, areas where the architectural pattern was lost and the cells seemed to be less differentiated than those in the more typical regions (Fig. 2).

At the initial operation in our second patient, soft, friable, purplish tumor was encountered just beneath the dura. At the time of the second operation, soft gelatinous tumor had extruded through dura and bone and was found just beneath the scalp. The main mass of tumor deeper within the brain had the gross characteristics of a typical meningioma. Microscopically, the more friable areas of tumor showed mild pleomorphism, loss of architecture, and increased cellularity (Fig. 3). In addition, there was invasion of the brain (Fig. 4). Invasion of the brain by tumor must be distinguished from extension of tumor into the brain along the Virchow-Robins' spaces (Fig. 5) since this latter characteristic in no way suggests malignancy. The remainder of the tumor had
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Fig. 1. Photomicrograph of the tumor, Case 1. This section is representative of the more benign portions of neoplasm, typically a psammomatous meningioma. H. & E., ×225.

Fig. 2. Another section of the tumor, Case 1. There is increased cellularity, loss of tissue architecture, and dedifferentiation. H. & E., ×225.

Fig. 3. Photomicrograph of the tumor, Case 2, showing mild pleomorphism, loss of architecture and increased cellularity. H. & E., ×225.

the microscopic appearance of a meningotheliomatous meningioma.

We considered our last two cases definitely malignant, showing marked pleomorphism with multinucleated giant cells, mitoses, and invasion of the brain (Figs. 6 and 7). In the last patient there was, in addition, an intense glial reaction of the invaded brain (Fig. 8). This finding, together with the extensive pleomorphism, made it difficult to distinguish these tumors from atypical glioblastoma multiforme. The use of special stains in both cases disclosed abundant amounts of reticulum which seemed to confirm their true source (Figs. 9 and 10). Reticulum formation does not usually occur in tumors of glial origin.1,19 There was no evidence of it in the glial reaction in our last case (Fig. 11).

Discussion

The term “malignancy” as applied to meningiomas suggests a quality not ordinarily encountered in these usually indolent tumors. Such increased activity may be predicted from their microscopic appearance.
Fig. 4. Another section of tumor, Case 2, showing invasion of the brain. H. & E., X225.

Fig. 5. Extension of meningioma in Case 2 into the Virchow-Robins' space. This does not denote a malignant change. H. & E., X225.

Fig. 6. Photomicrograph of the tumor, Case 3, showing marked pleomorphism, multinucleated giant cells, and mitotic figures. H. & E., X225.

Fig. 7. Photomicrograph of the tumor, Case 4. Some organization is present but there is marked pleomorphism, and mitotic figures are evident. H. & E., X95.
Kernohan and Sayer\textsuperscript{15} base their criteria for malignancy purely on histologic grounds: giant cells, cellularity, mitoses, and tumor architecture. Turner, \textit{et al.},\textsuperscript{26} found that the early low-grade malignant characteristics of certain meningiomas were reflected in the
tissue architecture rather than the cell type, these tumors being highly cellular with little variation in size of cells or nuclei, and with little change in structure. Well-advanced malignant meningiomas exhibit dedifferentiation, pleomorphism, mitoses, and giant cells. When invasion of the brain has occurred, the neighboring glia may undergo proliferative changes in excess of ordinary gliosis.24

Simpson25 has made no attempt to separate the biologically malignant meningiomas purely on their microscopic appearance. He found that even the most benignappearing meningiomas were capable of infiltrative growth and could invade dura, dural sinuses, bone, temporalis muscle, paranasal sinuses, ears, and, finally, the brain itself. Henschen26 found no constant relationship between clinical course and histology. Russell24 and Robertson22 mention the remarkably benign or typical microscopic appearance that is seen occasionally in meningiomas with extracranial metastases. They cite invasion of the central nervous system as a malignant trend important in prognosis.

The ability to predict the malignant potential of meningiomas prior to operation would be most helpful since, if the probabilities of recurrence were high, a more radical excision would seem justified. In addition, these patients may benefit from a full course of irradiation therapy in spite of the fact that such treatment is deemed ineffective in most meningiomas.9,10,23

Two clinical inferences are worth noting. The likelihood of recurrence25 and malignant change seems greatest in parasagittal meningiomas. The presence of destruction rather than stimulation of the adjacent skull suggests malignancy.25

It is doubtful whether radical excision followed by prophylactic irradiation is anything but palliative in the meningiomas of high malignancy. On the other hand, such an approach may be effective in meningiomas of low-grade malignancy, and, in our opinion, the prognosis is not necessarily grave in such cases.

Summary

We have discussed four malignant meningiomas and have emphasized the clinical and histological means of identifying this unusual variant of a relatively benign tumor. We believe this recognition is important, since some of these patients may benefit from radical excision followed by radiation therapy.

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References

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