OCCIPITAL EPENDYMOMA WITH EXTRACRANIAL METASTASES*

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(Received for publication March 30, 1954)

Many reports of primary intracranial tumors with extracranial metastases away from the central nervous system have appeared in the literature. Meningeal sarcomas,1 meningiomas,2 pineal tumors,3 hemangioblastomas,4 melanomas,5 and pituitary tumors,6 all have been described as metastasizing tumors. There have been fewer cases of gliomas with metastases reported in the literature. Ependymomas with metastases, a case of which is presented below, are of even more infrequent occurrence.

CASE REPORT

1st Admission, Mar. 21, 1951. A 27-year-old white male entered the hospital complaining of progressive headaches and visual blurring which had been present for the preceding 8 months.

Neurological examination revealed a bilateral papilledema, right homonymous hemianopsia, and right facial weakness. Skull x-rays demonstrated a left occipital calcific mass. EEG revealed abnormal electrical activity in the left occipital area.

Ventriculography and a left parietal-occipital craniotomy were performed on Mar. 27, 1951. A 5 cm. globular tumor was encountered attached to the parasagittal dura mater and invading the left occipital cortex. Because of the dural attachment and the vascularity of the tumor, the surgeon thought it to be a meningioma.

Microscopic examination revealed extensive necrotic areas with surrounding banks of tumor tissue. The neoplasm was felt to be a glioma by all observers, and it was reported as an ependymoblastoma by the Armed Forces Institute of Pathology.

The patient was discharged 3 weeks after operation with residual pressure symptoms.

2nd Admission, Mar. 15, 1952. The patient had had signs of increased intracranial pressure and convulsions for the preceding month. Neurological findings were similar to those during his previous hospitalization. Lumbar pressure was 250 mm. of water with a protein of 140 mg. per cent.

On Mar. 20, 1952, the operative site was reopened; a large intracerebral cyst and several tumor fragments were removed.

The patient was discharged 2 months later after receiving 5265 r to the tumor area, given through three ports—left parieto-occipital, posterior occipital, and vertex. The therapy was administered over a period of 6 weeks in 100–300 r daily doses.

Microscopic examination of the second operative specimen revealed a typical ependymoma pattern.

3rd Admission, July 8, 1953. Six months previously hard masses had developed in the patient’s neck (Fig. 1). He first noticed enlarged nodes in his left lateral cervical region, and later on the right side. For the preceding 2 months, symptoms of increased intracranial pressure had been present.

Examination revealed the scalp overlying the burr opening to be tense and enlarged, as if invaded by the tumor. A 4 × 6 cm. mass occupied the left lateral cervical area. On the right

* This report has been reviewed in the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
side a small 1×2 cm. node was palpable. Chest x-rays and standard laboratory tests were normal.

Removal of the right cervical node revealed tumor identical to the material obtained at the second operation. On July 16, 1953, a ventriculogram demonstrated ventricular displacement to the right. The left occipital horn was enlarged and practically reached the dura mater. Re-exploration of the operative area revealed considerable necrotic cortex extruding through the burr openings. A left occipital lobectomy was performed.

The patient improved temporarily, but progressively became more stuporous and died 2 months later on Sept. 28, 1953. Autopsy was refused.

Microscopic examination of the third operative specimen revealed necrotic and edematous tissue. No tumor tissue was seen.

Microscopic Examinations. The original tumor material demonstrates considerable calcification and necrosis. Figs. 2 and 3 show vascular attachments of elongated cells which are felt to be primitive ependymal cells. Figs. 4 and 5 are views of the same material in another

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**Fig. 1.** Large cervical masses are demonstrated.

**Fig. 2.** Low power view of original neoplasm. Note attachment of cells to the blood vessel. Phosphotungstic acid hematoxylin (PTAH) stain, ×99.
Fig. 3. High power view of original neoplasm. Cells have large nuclei and short tail-like processes. They tend to align in a parallel fashion and attach to the blood vessel. These are early ependymal cells. PTAH stain, $\times 610$.

Fig. 4. Low power view of original specimen in another section. Note tendency to pseudorosette formation. Hematoxylin and eosin (H and E) stain, $\times 99$. 
field and suggest a tendency toward compressed pseudorosette formation.

The tumor tissue obtained from the second craniotomy has a more recognizable ependymoma pattern (Figs. 6 and 7). Pseudorosette formations are more ample and typical. Figs. 8 and 9 show sections of the lymph node biopsy. Under low power examination, the complete replacement of normal lymph-node architecture by tumor tissue can be observed. The capsule and subcapsular areas have been infiltrated by neoplastic tissue. Fig. 9 shows a cellular pattern very similar to that of the tumor obtained from the second operation (Fig. 7).

**DISCUSSION**

Winkelman and associates\(^2\) recently reviewed the literature and found 48 cases of intracranial tumors with extracranial metastases, 10 of which were gliomas. We have found 3 additional cases, including our own described in this report. Winkelman *et al.*\(^\text{22}\) classified all cases into one of three groups: (1) probably valid; (2) questionably valid; and (3) probably invalid. Their criteria are based upon documentation and description. We feel our case must be placed in the second group because of lack of a postmortem examination. In reviewing the cases reported in the literature, one is impressed with the number of medulloblastomas (Table 1). Three of the 4 cases reported were in adults. Medulloblastomas are not uncommonly confused with neuroblastomas or sarcomas. Pendergrass and Wilbur\(^17\) reported their case in 1928 as a medulloblastoma, but upon review of the material in 1942\(^3\) it was felt that the correct diagnosis was neuroblastoma.
### TABLE 1

**Summary of cases reported in the literature**

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Tumor</th>
<th>Location</th>
<th>Duration of Preop.</th>
<th>X-ray</th>
<th>Post-op. No.</th>
<th>Therapy</th>
<th>Metastases</th>
<th>Postop. Survival</th>
<th>Location of Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>James &amp; Page(^1)</td>
<td>25</td>
<td>F</td>
<td>Oligodendrogioma</td>
<td>Rt. parietal</td>
<td>3 yrs.</td>
<td>2</td>
<td>Yes</td>
<td>2 yrs.</td>
<td>4 yrs.</td>
<td>Nodules in scalp, cervical nodes, rt. lung, rt. femur</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Davis(^2)</td>
<td>31</td>
<td>F</td>
<td>Glioblastoma multifforme</td>
<td>Lt. temporoparietal</td>
<td>3 mos.</td>
<td>2</td>
<td>Yes</td>
<td>4 mos.</td>
<td>6 mos.</td>
<td>Subcutaneous masses, rt. arm, rt. scapula, rt. costal margin</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Mittelbach(^3)</td>
<td>39</td>
<td>M</td>
<td>Glioblastoma multifforme</td>
<td>Lt. parietal</td>
<td>8 mos.</td>
<td>1</td>
<td>No</td>
<td>Found at autopsy</td>
<td>6 mos.</td>
<td>Lung metastases, bilateral node invasion</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Sachs et al.(^4)</td>
<td>38</td>
<td>M</td>
<td>Medulloblastoma</td>
<td>Rt. cerebellum</td>
<td>2 mos.</td>
<td>2</td>
<td>Yes</td>
<td>3 yrs.</td>
<td>5 yrs.</td>
<td>Subcutaneous mass over sternum. Cord implants</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Nelson(^5)</td>
<td>24</td>
<td>M</td>
<td>Medulloblastoma</td>
<td>Rt. cerebellum</td>
<td>6 mos.</td>
<td>2</td>
<td>Yes</td>
<td>Found at autopsy</td>
<td>3 yrs.</td>
<td>Invasion 4 lower T vertebrae. Cord implants</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Köhlmeyer(^6)</td>
<td>38</td>
<td>M</td>
<td>Glioblastoma multifforme</td>
<td>Lt. parietal</td>
<td>1 yr.</td>
<td>3</td>
<td>Yes</td>
<td>3 mos.</td>
<td>4 mos.</td>
<td>Lung metastases, tumor extension into neck. Cervical vein erosion</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Sik(^7)</td>
<td>52</td>
<td>M</td>
<td>Astroblastoma</td>
<td>Lt. frontoparietal</td>
<td>7 mos.</td>
<td>2</td>
<td>No</td>
<td>Found at autopsy</td>
<td>7 mos.</td>
<td>Metastases lung, T4 vertebra, ribs. Invasion bone flap, temporal muscle</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Brandt(^8)</td>
<td>52</td>
<td>M</td>
<td>Glioblastoma multifforme</td>
<td>Lt. temporal</td>
<td>9 mos.</td>
<td>1</td>
<td>Yes</td>
<td>6 mos.</td>
<td>1 yr.</td>
<td>Metastases lung, rt. kidney. Tumor extension around ear and down neck</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Cross &amp; Cooper(^9)</td>
<td>20</td>
<td>M</td>
<td>Mixed type glioma</td>
<td>Lt. temporoparietal</td>
<td>2 mos.</td>
<td>1</td>
<td>No</td>
<td>8 mos.</td>
<td>9 mos.</td>
<td>Metastases lung apex, ant. abdominal subcutaneous area. Invasion scalp, temporal muscle, and around ear</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Maass(^10)</td>
<td>27</td>
<td>M</td>
<td>Ependymoma</td>
<td>Lt. occipital</td>
<td>8 mos.</td>
<td>3</td>
<td>Yes</td>
<td>6 mos.</td>
<td>3 mos.</td>
<td>Bilateral cervical node metastases</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Bailey &amp; Bue(^11)</td>
<td>48</td>
<td>M</td>
<td>Oligodendrogioma</td>
<td>Lt. parietal</td>
<td>17 yrs.</td>
<td>4</td>
<td>Yes</td>
<td>8 yrs.</td>
<td>8 yrs.</td>
<td>Tumor extension into neck</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Wohwill(^12)</td>
<td>90</td>
<td>M</td>
<td>Medulloblastoma</td>
<td>Vermis</td>
<td>—</td>
<td>—</td>
<td>Yes</td>
<td>6 mos.</td>
<td>—</td>
<td>Ganglioneuroma of rt. supraclavicular region</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Pendergrass &amp; Wilbur(^13)</td>
<td>32</td>
<td>F</td>
<td>Medulloblastoma</td>
<td>Rt. cerebellum</td>
<td>3 mos.</td>
<td>4</td>
<td>Yes</td>
<td>4 yrs.</td>
<td>4 yrs.</td>
<td>Multiple bony lesions by x-ray. Tumor later diagnosed neuroblastoma</td>
<td></td>
</tr>
</tbody>
</table>

In some of the reports shown in Table 1, it was stated that the intracranial tumor extended through the operative bony opening into the neck.\(^5,6,8,12,13\) In 2 cases, invasion of the temporalis muscle was demonstrated.\(^6,19\) Köhlmeyer\(^13\) found a cervical vein with intraluminal tumor extension from a glioblastoma multifforme extending into the neck. James and Page\(^12\) demonstrated metastases to cervical node and scalp. In most of the cases, there were multiple operations and in 3 cases the bone
Fig. 6. Low power view of neoplastic tissue removed at second craniotomy. Note the more typical pseudorosette formation. H and E stain, ×99.

Fig. 7. High power view of same tissue as in Fig. 6. Note pseudorosettes. H and E stain, ×610.
flap was removed, providing ample opportunity for extracranial extension.

The higher incidence of non-gliomatous tumors associated with extracranial metastases is felt to be ascribable to hematogenous spread arising from invasion of the dural sinuses. Towne reported a case of a meningioma that invaded the inferior longitudinal sinus and followed the venous pathway into the neck. Tumor tissue was removed from the internal jugular vein. Tompkins et al. described a pineal tumor that invaded the straight venous sinus and gave rise to lung metastases. Gilmour also reported an adenocarcinoma of the pituitary gland which invaded the cavernous sinus and gave origin to extracranial metastases.

Winkelman et al. suggested that metastases from gliomas are infrequent because: (1) it is difficult for soft gliomatous tissue to penetrate the dural sinuses; (2) the cerebral veins that are thin-walled and held relatively loosely by the brain tend to collapse before allowing the entrance of tumor tissue; and (3) extracranial tissues are poor media for glioma growth.

MacCarty quoted Penfield as stating, "metastases outside of the central nervous system are rare because of the astrocytic barrier around blood vessels. The same wall of astrocytic feet is thrown up against pia as well. But this latter barrier does not prove to be impassable.”

Penfield in 1937 stated that one element in the failure of metastases is the absence of lymphatic vascular connections within the pachymeninges.
felt that absence of lymphatics as well as a tendency for the tumor cells not to invade the blood vessels accounted for the lack of metastasis. MacCarty, in studying metastasis of gliomas to the subarachnoid and ventricular spaces, concluded that the pia and subpial glia, ependyma and subependymal glia offered barriers to implantation in these spaces. Zimmerman and Maier, who have produced experimental gliomas in mice, feel that there is no mesodermal resistance against metastatic gliomatous growth. They also postulate that failure of gliomas to invade vessels and the absence of lymphatic connections with intracranial structures account for the infrequency of metastases.

When extracranial metastases do arise from intracranial gliomas, there appear to be several possible routes. Invasion of the scalp or muscles attached to the skull will soon be manifested in the cervical lymph nodes. Direct tumor extension into the neck may also produce infiltration of nodes through lymphatic invasion or erosion into cervical veins. After implantation into the nodes, hematogenous seeding may occur. A third route of metastasis may be produced by the rare occurrence of gliomas arising from cell rests (heterotopic glial nests) in the dura mater, leptomeninges, or in mesodermal tissue outside the central nervous system. Dural tumors, as proved by their reported frequency (14 cases in Winkelman's series), are more prone to extracranial metastases. There is also the possibility that introduction of a tumor embolus into a dural sinus or cerebral vein during an operation could produce metastases.
SUMMARY

1. A case report of an occipital ependymoma with evidence of cervical metastases has been presented.
2. The literature concerning extracranial metastases from intracranial gliomas has been reviewed.
3. Theories explaining the rare occurrence of extracranial metastases from intracranial gliomas have been discussed and possible routes of metastases have been suggested.

The author would like to express his appreciation to Dr. Nathan Malamud for his assistance in reviewing the microscopic examination of the material in this case.

REFERENCES