Glioblastoma With Metastasis to the Spleen
—Case Report—

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Abstract

A 47-year-old woman presented with headache and left homonymous hemianopsia. T1-weighted magnetic resonance (MR) imaging with contrast medium showed a mass lesion with ring-like enhancement in the right temporo-occipital lobe. The patient underwent surgery, focal irradiation, and chemotherapy. The histological diagnosis was glioblastoma. Four months after the operation, the patient again developed headache and left homonymous hemianopsia in addition to vomiting and mild left hemiparesis. MR imaging showed recurrence of the tumor and hydrocephalus. The patient underwent a second craniotomy and placement of a ventriculoperitoneal shunt. Intraoperative findings revealed that the transverse-sigmoid sinus was occluded by tumor invasion. The patient died of intraventricular dissemination 2 months after the second operation. Autopsy revealed metastases in the spleen and lungs. Glioblastoma with metastases to the spleen is very rare. The prognosis for patients is poor. Excessive therapy should not be used for patients with extracranial metastases from glioblastoma.

Key words: glioblastoma, spleen, dural sinus occlusion

Introduction

Extracranial metastases of tumors of the central nervous system are rare.14) Extracranial metastasis of glioblastoma occurs in only 0.44% of cases,13) and is rare for several reasons.3,6,9,12) Gliomas originate from the ectoderm rather than the mesoderm, where many target organs originate. No true lymphatic vessels are located in the central nervous system. Host tissue responds to glial cells outside the neural tube. The dense dura is resistant to tumor invasion. Small vessels with thin walls and poor support collapse as the tumor develops. Because malignant astrocytomas progress rapidly, patients usually die before there is time for extracranial metastasis.

Metastases from glioblastoma occur in the lung, lymph nodes,9,14) bone,1,2,5,10) bone marrow,6) and liver. Metastasis to the spleen is extremely rare, with only three cases reported.7,9,15) We report a case of glioblastoma with extracranial metastases to the spleen and lung.

Case Report

A 47-year-old woman sought treatment for mild headache at our clinic on February 16, 2001. Neurological examination revealed left homonymous hemianopsia. Magnetic resonance (MR) imaging disclosed a mass lesion with severe edema in the right temporo-occipital lobe, with ring-like enhancement after administration of contrast medium (Fig. 1). Cerebral angiography showed tumor staining and early venous filling corresponding to the mass lesion.

The patient underwent gross total removal of the tumor through a right temporo-occipital craniotomy on February 27. The tumor was gray and bled easily. Histological examination confirmed the diagnosis of glioblastoma based on microvascular proliferation, increased mitotic activity, and necrosis (Fig. 2A). The patient was treated with 60 Gy of external beam radiation therapy (10 MV x-ray tube, field size $13 \times 10 \text{ cm}^2$, 2 Gy/fraction) and two cycles of...
chemotherapy with intravenous nimustine (1 cycle: 100 mg/wk for 2 wks). Her postoperative course was excellent. She was discharged on April 20 with left homonymous hemianopsia and treated once a week with interferon-beta (6 \times 10^6 units) as an outpatient.

The patient was readmitted to our clinic with headache, vomiting, and mild left hemiparesis in addition to left homonymous hemianopsia on June 24, 4 months after the first operation. MR imaging revealed recurrence of the tumor and hydrocephalus (Fig. 3 left). The tumor was growing in all directions from the margin of the first surgical resection.

The tumor was again removed through a right temporo-occipital craniotomy, and a ventriculoperitoneal shunt was placed on July 3. Intraoperative findings revealed that the transverse-sigmoid sinus was completely occluded by the tumor, which was gray, fragile, and bled easily. Although the intraoperative findings differed from the first occurrence, histological examination again confirmed the diagnosis of glioblastoma based on dense morphologic cells and increased mitotic activity (Fig. 2B). The patient’s condition improved for a while, but intraventricular dissemination occurred (Fig. 3 right), and she died on August 9, 6 months after the first operation.

Autopsy revealed a metastasis of 1.2 cm in diameter in the spleen (Fig. 4 left) and multiple metastatic foci (0.5 cm in diameter) in the lungs.
Fig. 3  left: T_{1}-weighted magnetic resonance (MR) image with contrast medium showing recurrence of the glioblastoma and hydrocephalus. The tumor appears as a ring-like enhanced mass beyond the space left by the first resection in the right temporal lobe.  
right: T_{1}-weighted MR image with contrast medium showing ventricular dissemination as enhancement of the ventricular walls.

Fig. 4  left: Photograph of the spleen at autopsy showing a round, metastatic lesion about 1.2 cm in diameter at the hiatus.  
right: Photograph of the right lung at autopsy showing two round, metastatic lesions about 5 mm in diameter on the surface.

(Fig. 4 right). Histological examination of these lesions showed highly dense cells and increased mitotic activity similar to the intracranial glioblastoma removed at the second operation (Fig. 2C). Immunohistochemical staining showed that many tumor cells, especially in the lungs, expressed glial fibrillary acidic protein (Fig. 2D) and S-100 protein. None of the tumor cells expressed desmin, α-smooth muscle actin (αSMA), or myoglobin.

Discussion

Risk factors for extracranial metastasis include previous craniotomy, ventricular systemic shunting, high-grade tumor histology, radiation therapy, long interval since the primary therapy, and tumoral relapse. Our patient underwent craniotomy and radiation therapy for histologically confirmed glioblastoma. A ventricular systemic shunt was placed to relieve the symptoms of hydrocephalus. However, the shunt may have facilitated intracranial dissemination and extracranial metastases, although the autopsy showed no peritoneal dissemination.

Malignant glioma rarely invades the dural sinus, probably because of the structure of the venous sinuses, which are enclosed in dense dural tissue. Invasion of the dural sinus may involve several mechanisms: Increasing contact with the dura due to tumor growth; fragility of the sinus wall under certain circumstances; and progression via arachnoidal granulations. Invasion of the dural veins is seen in most cases of extracranial metastases from glioblastoma in patients who did not undergo craniotomy. Spontaneous extracranial metastases might be expected in patients with tumors attached to and invading the dura, such as two cases of the transdural extension of gliomas. Direct contact between the tumor and the basal dura, intracranial hypertension, structural weakness, and surgery can allow tumor cells to migrate through the dura.

In our patient, the intraoperative findings at the second surgery revealed that the transverse-sigmoid sinus was completely occluded by tumor invasion. Cerebral angiography taken before the first surgery revealed that this sinus was patent, so occlusion had occurred during the interval between the operations.

Gliosarcoma has much greater potential to metastasize than other malignant tumors. The prognosis for patients with extracranial metastases from glioblastoma with a sarcomatous component is worse than that for patients with other gliomas. Sarcomatous transformation is believed to occur in the mesenchymal cells of the vascular endothelium. Therefore, gliosarcomas and glioblastomas with a sarcomatous component can metastasize extracranially due to the mixed origin more easily than a glioblastoma without a sarcomatous component.

In our patient, histological examination confirmed that the tumor was a glioblastoma without a sarcomatous component because no tumor cells
Table 1  Reported cases of metastasis to the spleen from glioblastoma

<table>
<thead>
<tr>
<th>Author (Year)</th>
<th>Age, Sex</th>
<th>Site</th>
<th>Metastatic organs</th>
<th>Sinus occlusion</th>
<th>Dissemination (intracranial)</th>
<th>Sarcoma</th>
<th>Therapy</th>
<th>Interval (timing to death)/cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ogata et al. (1987)</td>
<td>68, M</td>
<td>lt fronto-parietal</td>
<td>lung, lymph node, liver, kidney, heart, spleen</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>operation, CT, RT</td>
<td>8 mos/DIC</td>
</tr>
<tr>
<td>Matsuyama et al. (1989)</td>
<td>68, M</td>
<td>rt temporal bone marrow (T-4), liver, spleen</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>operation, RT, CT</td>
<td>5 mos/tumor</td>
<td></td>
</tr>
<tr>
<td>Widjaja et al. (2000)</td>
<td>58, M</td>
<td>rt temporo-occipital</td>
<td>liver, spleen</td>
<td>-</td>
<td>-</td>
<td>+ (component)</td>
<td>operation (twice), RT, CT</td>
<td>unknown (over 15 mos)</td>
</tr>
<tr>
<td>Present case</td>
<td>47, F</td>
<td>rt temporo-occipital</td>
<td>lung, spleen</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
<td>6 mos/tumor</td>
</tr>
</tbody>
</table>

CT: chemotherapy, DIC: disseminated intravascular coagulation, RT: radiotherapy

Metastases in the spleen seldom cause symptoms. Although our patient had one metastatic lesion in the spleen (1.2 cm diameter), she had no symptoms originating from the metastasis.

The present case of a patient with extracranial metastases in the spleen and lungs from a glioblastoma is extremely rare. The prognosis for patients with glioblastoma and extracranial metastasis is poor. Whole body investigation should be considered for such cases. Excessive intervention should not be used unless more efficient therapies are established.

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References

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