Brain metastasis from germinal tumors of the testis

Case report

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Brain metastasis in patients with disseminated nonseminomatous germ cell tumor (NSGCT) has been considered to occur rarely. The authors present the case of a 43-year-old man with an enlarged left testicle, a palpable inguinal tumor, multiple lung tumors, and a large cerebellar tumor. In separate operations, performed 1 month apart, the large cerebellar tumor and the testicular tumor were excised. Elements of teratocarcinoma, embryonal carcinoma, and choriocarcinoma were present in both the brain and testicular tumors. After chemotherapy in which bleomycin, etoposide, and cisplatin were used, the lung tumors and also the surrounding metastasis disappeared; the patient now leads a useful life and remains free from cancer in all organs. The authors suggest that surgical removal of tumor before initiating radiotherapy and chemotherapy for large brain metastasis from NSGCT will produce better results than using the nonsurgical treatments alone.

Key Words • brain metastasis • germ cell tumor • testicular tumor • chemotherapy • etoposide • cisplatin • bleomycin

Brain metastasis in patients with disseminated nonseminomatous germ cell tumor (NSGCT) has been considered to be rare. However, its incidence has increased in association with the improved remission and control of systemic disease. For disseminated NSGCTs, chemotherapy with cisplatin, vinblastine, and bleomycin (PVB), followed by surgical removal of residual tumor, has produced excellent results. However, central nervous system (CNS) metastasis is reported to be resistant to drugs and unresponsive to standard therapy. Nevertheless, we can expect chemotherapy to be efficacious in patients whose original tumors show a complete response to chemotherapy, but who develop a relapse confined to the brain. In these patients, the metastasis of NSGCT to the brain should be treated with aggressive multiagent regimens of chemotherapy combined with suitable surgical procedures. Recently, we successfully treated a patient whose first diagnosis was a large brain metastasis of disseminated NSGCT. In this report, we analyze the treatments of patients with disseminated NSGCT, mainly with regard to CNS metastasis.

Case Report

History. This 43-year-old man gradually developed a headache and vomiting, which first appeared in April 1996. He became lethargic and was hospitalized in September 1996.

Examination. On examination, we found an enlarged left testicle, a palpable inguinal tumor, horizontal nystagmus, left-sided hemiparesis, and other disorders. Magnetic resonance (MR) imaging of the brain revealed a large solid tumor in the left cerebellar hemisphere and obstructive hydrocephalus (Fig. 1 left). Multiple tumors in the right lower lobe of the lung were also detected on chest x-ray films (Fig. 1 right). No metastasis to the other organs could be seen on computerized tomography (CT) scanning. The patient's α-fetoprotein level was 2715.6 μg/L, and his β-human chorionic gonadotropin level was normal. The results of other blood tests showed no abnormality.

First Operation and Postoperative Course. In October 1996, a suboccipital craniotomy was performed and the large cerebellar tumor was completely excised. Postoperatively, the patient's lethargy and symptoms of increased intracranial pressure disappeared, and his left-sided hemiparesis improved markedly.

Second Operation and Pathological Findings. In November 1996, the enlarged left testicle was also excised.
Elements of teratocarcinoma, embryonal carcinoma, and choriocarcinoma were present in both the brain and testicular tumors (Fig. 2).

Chemotherapy. Later in November a regimen of chemotherapy consisting of bleomycin, etoposide, and cisplatin (BEP) was begun. Four courses of BEP therapy were administered to the patient, as outlined in Table 1. In February 1997, the patient’s α-fetoprotein level decreased to 3.2 µg/L and his chest x-ray films appeared to be normal (Fig. 3 left). Follow-up CT scans of the lung and the abdomen also showed no tumors.

Posttreatment Course. The patient was discharged home in March 1997 without any neurological deficits. Since discharge, the patient has progressed well and he has had an uneventful course except for occasional dizziness. His α-fetoprotein and β-human chorionic gonadotropin levels have remained normal since completion of the fourth course of chemotherapy. Recent MR imaging of the brain showed no tumor (Fig. 3 right). As of October 1997, the patient is leading a useful life with no neurological deficits. He remains free from any cancer, showing normal ranges of tumor markers.

Discussion

Brain metastasis in patients with disseminated NSGCT has been reported to be unusual, occurring in 15% of progressive testicular tumors and in 0.7% of metastatic brain tumors. Because of the development of modern diagnostic techniques and the prolonged survival times of patients, CNS involvement appears to be increasing in patients with disseminated NSGCT. The general outcome of patients with NSGCT that is confined to the testis and surrounding organs is improving because of more effective chemotherapeutic protocols. In addition, chemotherapy alone has proved to be an effective treatment for primary and metastatic lesions. Central nervous system involvement by disseminated NSGCT, however, is a complication with high rates of morbidity and mortality, and the therapeutic principles that are applied to disseminated non-CNS disease should not be applied to CNS disease. Although metastasis of cancer to the brain indicates that a cancer is widely disseminated and the patient’s prognosis may be poor, disseminated non-CNS NSGCT can usually be cured by a combination of chemotherapeutic proce-
Brain metastasis from germ cell tumor

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Chemotherapeutic regimens and physiological indicators in a patient with brain metastasis of NSGCT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy &amp; Laboratory Results</td>
<td>Times of Treatment &amp; Testing</td>
</tr>
<tr>
<td>drug regimen (mg/day [no. of days])</td>
<td>11/96</td>
</tr>
<tr>
<td>etoposide</td>
<td>150 (5)</td>
</tr>
<tr>
<td>cisplatin</td>
<td>30 (5)</td>
</tr>
<tr>
<td>bleomycin</td>
<td>30 (3)</td>
</tr>
<tr>
<td>laboratory results</td>
<td></td>
</tr>
<tr>
<td>white blood cells (per mm³)</td>
<td>6500</td>
</tr>
<tr>
<td>α-fetoprotein (µg/L)</td>
<td>2258.1</td>
</tr>
</tbody>
</table>

* — = not given.

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dures, and small brain metastasis can often be cured by chemotherapy and radiotherapy. Because NSGCT is radiosensitive, radiotherapy for these tumors seems to be effective in eliminating small tumors.\(^2\) Chemotherapy consisting of PVB is reported to be useful for treating the central portion of a brain metastasis and radiotherapy is efficacious for treating the periphery.\(^6,7\) Other reports, however, indicate that this type of chemotherapy alone is ineffective for brain metastasis because the blood-brain barrier can provide a sanctuary from the effects of PVB within the brain.\(^5\) The effectiveness of chemotherapy is also influenced by the size of brain tumors.\(^3,8\) Furthermore, the toxic chemotherapeutic programs designed to overcome the sanctuary effect of the blood-brain barrier may lead to serious complications associated with these treatments. In disseminated non-CNS disease, surgical removal of tumor before initiating chemotherapy is not suggested and curative surgery on residual masses after chemotherapy is recommended. However, this principle should not be applied to brain metastasis for various reasons. Spontaneous hemorrhage is known to occur frequently in NSGCTs,\(^3,9\) and choriocarcinoma also appears to have a greater predilection to metastasis to the brain than other germ cell tumors.\(^10,11\) Surgical removal of a large brain metastasis can improve the neurological symptoms of a patient and can eliminate the complication of hemorrhage.\(^12\) Our case shows that patients with brain metastasis from NSGCT can be cured if there is an effective treatment for the disseminated cancer. In our experience, BEP chemotherapy has been effective for patients with disseminated NSGCT without causing any adverse side effects. Four courses of intensive BEP chemotherapy were given to the patient described in this report and the serum level of α-fetoprotein decreased to normal. This BEP chemotherapy is, therefore, also expected to be useful as a maintenance chemotherapy for patients with disseminated NSGCT. Finally, curative treatment should not be withheld from a patient with NSGCT simply because the brain metastasis is large, multiple, or inoperable. In conclusion, we propose that surgical removal of large brain metastases before radiotherapy and chemotherapy will produce better results than currently prescribed nonsurgical treatments.

References