Subarachnoid Dissemination of Pineal Germinoma 9 Years After Radiation Therapy without Local Relapse

—Case Report—

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Abstract

A 22-year-old female developed intracranial and spinal subarachnoid metastases 9 years after radiation therapy for a pineal germinoma. Computed tomographic scans showed no evidence of local recurrence. Cerebrospinal axis irradiation achieved total remission. Delayed subarachnoid dissemination may be caused by germinoma cells remaining dormant in the subarachnoid space, outside the radiation field.

Key words: germinoma, subarachnoid dissemination, spinal metastasis, pineal region, radiation therapy

Introduction

Germinomas are highly radiosensitive and are one of the few intracranial tumors controllable by radiation therapy alone.^{1,2,8,10,12,18,21,23,25-28} An inadequate radiation field (local, <30 cm²) or dose (<45 Gy) may cause local relapse.^{1,2,5,10,18,23,28} The optimum dose is 40 Gy to the entire ventricular system, followed by a tumor bed dose of 50–55 Gy.^{12,18} However, subarachnoid dissemination cannot be completely prevented.^{1,2,5,8,10-12,18,23-28} Prophylactic spinal irradiation is recommended in selected cases because of the efficacy, in spite of the complications, particularly in children.^{2,5,8,10,17-19,23}

The risk of meningeal seeding in pineal germinoma is approximately 4–25%.^{1,2,5,8,10,11,18,21,23,25-27} Subclinical metastases detected by computed tomography (CT) occur in more than 60% of cases,^{3,8} as with medulloblastoma.⁷

Subarachnoid dissemination may develop without local relapse. Sung *et al.*²³ reported that of 11 patients with spinal metastases, eight had no local recurrence, two had intracranial metastases, and one manifested spinal metastases during cranial irradiation.

Subarachnoid dissemination usually occurs within 6 months²¹ or a few years²³ of initial diagnosis. A tumor appearing regressive on CT scan after radiation therapy may remain active and seed in the subarachnoid space.^{1,28} Delayed subarachnoid dissemination in intracranial germinoma is rare.^{5,6,14,23}

We present a patient who developed subarachnoid dissemination without local relapse 9 years after initial radiation therapy for a pineal germinoma. The mechanism of delayed presentation is discussed.

Case Report

This patient developed morning headache and vomiting when aged 11 years, and was referred to our hospital in October, 1977. She was alert and oriented with anisocoria (lt > rt), bilaterally sluggish light reflexes, choked discs, left hemihypesthesia including the face, and polyuria (3000 ml/day). The alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), and cerebrospinal fluid (CSF) cytology were not examined. CT scans showed a homogeneously enhanced round mass in the pineal region and hydrocephalus (Fig. 1 upper).

A ventriculoperitoneal (VP) shunt was emplaced. Local irradiation 5020 cGy (⁶⁰Co) by moving beam

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Fig. 1 *upper*: Initial CT scans, showing a homogeneously enhanced round mass in the pineal region and ventriculomegaly. *lower*: CT scans 9 years after initial radiation therapy, showing enhanced mass lesions in the bilateral cerebellopontine angles (*arrowheads*), prepontine cistern, and Meckel's caves (*arrow*). Other areas including both pineal and suprasellar regions are normal.

5 × 5 cm, 25 cm², was given in 46 fractions over 14 weeks. No whole brain or spinal irradiation was performed. Although the shunt controlled the hydrocephalus, diabetes insipidus (urine output, 3000–5000 ml/day) developed during radiation therapy. The tumor was no longer visualized by CT after radiation therapy, which strongly suggested pineal germinoma. She returned to school and did well until readmission. Follow-up was interrupted after 1979.

She developed gait disturbance and pain at the right thigh and hip from a fall when aged 22 years in February, 1987. The progressive symptoms were accompanied by disturbance of mouth opening, facial spasm, hearing disturbance, tinnitus, and impaired urinary and bowel control. Polyuria and polydipsia had persisted since 1978. She was readmitted in October, 1987.

Neurological examination revealed hypesthesia in

the left side of the face and bilateral legs, left hearing disturbance, paraparesis, and bilateral straight leg raising limited to 45°. No pupillary abnormalities or Parinaud's sign was noted. Serum AFP, HCG, and carcinoembryonic antigen levels were within normal ranges. The CSF cytology was not unusual. CT scans showed enhanced mass lesions in the bilateral cerebellopontine angles, prepontine cistern, and Meckel's caves (Fig. 1 *lower*). Other areas including both pineal and suprasellar regions were normal. Myelograms demonstrated multiple nodules along the cauda equina with a block at S1 (Fig. 2). Intracranial and spinal subarachnoid dissemination of germinoma without local relapse was diagnosed.

The peritoneal catheter was ligated to prevent systemic dissemination *via* the VP shunt.^{13,16} However, she developed acute hydrocephalus requiring shunt revision. An L4 to S1 laminectomy and multiple subarachnoid nodule biopsy were performed in November, 1987. Histological examination demonstrated pure germinoma (Fig. 3 *left*). Immunohistochemical analysis identified placental alkaline phosphatase (PLAP)²² (Fig. 3 *right*). Whole brain (35 Gy in 19 fractions), cervicothoracic (24 Gy in 16 fractions), and lumbosacral (42 Gy in 28 fractions) Lineac irradiation was given over 7 weeks. No tumor was visible on CT scans after re-irradiation. All symptoms except the left hearing disturbance sub-

Fig. 2 Myelograms, showing multiple nodular defects along the cauda equina with a block at S1.

Fig. 3 Photomicrographs of the tumor. *left*: There are typical features of pure germinoma, including polygonal epithelial and lymphoid cells in the fibrous stroma. HE stain, $\times 200$. *right*: A positive reaction to PLAP is seen. $\times 200$.

sided. Leukocytopenia prevented chemotherapy. There has been no evidence of recurrence for 2 years.

Discussion

Kunishio *et al.*¹⁴⁾ reported a 28-year-old male with mixed germ-cell tumor in the pineal region, who developed spinal metastasis 11 years after initial cranial radiation therapy. They considered that germinoma cells had already disseminated into the subarachnoid space before irradiation, although seeding from a recurrent pineal tumor (mainly teratoma) was also possible. Dayan *et al.*⁶⁾ reported a 21-year-old male with pinealoma who developed spinal metastasis without local relapse 7 years after deep x-ray therapy. Bradfield and Perez⁵⁾ reported a 19-year-old male with pinealoma who developed spinal metastasis without local relapse 4 years after brain irradiation (5850 cGy, 121 cm²). Sung *et al.*²³⁾ experienced a suprasellar and a pineal germinoma which caused metastases 4 and 5 years after initial irradiation, respectively.

What then are the factors controlling subarachnoid dissemination of germinomas? Germinoma, like medulloblastoma, has no adhesive factor preventing tumor cell dissociation into the subarachnoid space. It does have stromal fibronectin which accelerates the attachment of migrating tumor cells to new sites.¹⁵⁾ Pineal teratoma or mixed germ-cell tumors only disseminate germinomatous components.^{14,24)}

The labeling index of testicular seminomas is 11%,²⁰⁾ comparable to medulloblastomas (12%).⁹⁾ The labeling index of intracranial germinomas is presently unreported. However, germinoma cells demonstrate lower proliferation and malignancy than

medulloblastoma.⁴⁾ Delayed subarachnoid dissemination and/or local recurrence may be caused by germinoma cells remaining dormant for many years in the subarachnoid space, outside the radiation field.^{5,6,14,23)} Our patient developed diabetes insipidus in an early stage, suggesting that germinoma cells had already disseminated into the intracranial and spinal subarachnoid spaces before initial radiation therapy, although not demonstrated conclusively by CT.

Spinal axis irradiation after manifestation of spinal metastases may achieve long-term control. 45% of patients with spinal metastases survive more than 2 years following spinal cord radiation therapy.²³⁾ Aida *et al.*²⁾ achieved control of spinal metastasis for 11 years after re-irradiation. However, some spinal metastases have recurred after spinal irradiation.^{1,5,6)} Craniospinal irradiation may develop complications, particularly in young people,^{17,19)} so cis-platinum multidrug combination therapy is now the treatment of choice for both primary and recurrent germinomas.^{3,13,16)}

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