Intracranial and Intraspinal Dissemination from Pineal Yolk Sac Tumor Treated by PVB Therapy
—Case Report—

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Abstract
A 15-year-old male was admitted because of diplopia and persistent headache. Postcontrast computed tomography (CT) revealed a homogeneously enhanced large mass, 3 × 4 cm in size, in the pineal region and moderate obstructive hydrocephalus. A right ventriculoperitoneal shunt was installed. At that time, the serum α-fetoprotein (AFP) level increased to 23,036 ng/ml, but the level of serum β-subunit of human chorionic gonadotropin was less than 0.2 ng/ml. These data indicated the tumor to be a pure yolk sac tumor. Following cisplatin-vinblastine-bleomycin (PVB) therapy and whole-brain irradiation (50 Gy), the tumor disappeared on CT, although the AFP level did not return to normal. Eight months after the completion of initial therapy, he had lumbago. Spinal magnetic resonance imaging revealed a metastatic mass at the L5-S2 levels, which was subtotally removed and histologically diagnosed as yolk sac tumor. Postoperative local irradiation (30 Gy) was performed. Seven months after the operation, spinal dissemination at the Th7 level occurred and, 1 month later, intracranial dissemination in the left cerebellopontine angle was detected. He died 25 months after the first admission. PVB therapy did not prevent spinal dissemination in this case.

Key words: germ cell tumor, yolk sac tumor, chemotherapy, spinal dissemination

Introduction
Pure yolk sac tumor appears to be very rare among primary intracranial tumors, despite occasional reports of yolk sac tumors in young patients. We encountered a case considered to be pure yolk sac tumor originating in the pineal region which metastasized to the intraspinal and intracranial cavities. This case is described with emphasis on the clinical course and autopsy findings.

Case Report
I. First hospitalization
A 15-year-old male was admitted to our department on September 3, 1986, with chief complaints of headache, vomiting, and diplopia. He had first experienced intermittent pulsating headache of the entire head in about August, 1984, but had not consulted a physician because of its transient nature. He had noted diplopia in about the middle of August, 1986, and had consulted the ophthalmological department of our hospital, where a computed tomographic (CT) scan demonstrated a mass in the pineal region. There was no relevant clinical history.

On admission, he had a clear consciousness and showed no anisocoria, but his pupils were oval and reacted sluggishly to light. His eyegrounds and optic discs were normal. Parinaud's sign and vertical nystagmus were present during upward gaze.

A precontrast CT scan demonstrated an isodense mass with partial calcification in the pineal region, and a postcontrast CT scan revealed it to be a homogeneously enhanced mass 3 × 4 cm in size. Moderate dilatation of the ventricles was also observed (Fig. 1A, B). Serologic examination revealed a considerable increase of the α-fetoprotein (AFP) level to 23,036 ng/ml. However, the β-subunit of human chorionic gonadotropin (β-HCG) (<0.2 ng/
ml) and the carcinoembryonic antigen (CEA) (1.7 ng/ml) levels were low.

Since symptoms of increased intracranial pressure such as headache and vomiting persisted, a right ventriculoperitoneal shunt was emplaced on September 4, resulting in alleviation of the symptoms. The cerebrospinal fluid (CSF) obtained at this time showed a cell count of 1/3 and a protein content of 26 mg/dl, and cytological examination disclosed no tumor cells. From the data of tumor markers above, a diagnosis of pure yolk sac tumor of the pineal body was made, and PVB therapy (cisplatin 20 mg/m²/day, vinblastine 3-5 mg/m²/day, bleomycin 10 mg/m²/day) combined with whole-brain irradiation was initiated on September 13. The AFP level increased temporarily to a maximum of 33,446 ng/ml, but decreased to 194 ng/ml after completion of whole-brain irradiation of 50 Gy and three courses of PVB therapy. The tumor volume also increased temporarily to a maximum of 27.3 ml and decreased to 1.2 ml; nearly complete remission was achieved (Fig. 1C). He was discharged on November 27, 1986.

II. Second hospitalization

From January 2 to February 8, 1987, the first maintenance PVB therapy was carried out. During this period, AFP level was slightly higher at 93-147 ng/ml.

III. Third hospitalization

On March 28, 1987, he was readmitted for the second maintenance PVB therapy. There were no marked neurological changes, but the AFP level had remained above 1000 ng/ml since admission. Therefore, local irradiation of 20 Gy was applied to the pineal region. Spontaneous pain and numbness from the left hip to thigh had occurred since early May, but were left untreated. He was discharged on May 24, 1987.

IV. Fourth hospitalization

The AFP level increased to about 5000 ng/ml in June, 1987, but no recurrence of the pineal tumor was observed by CT. One month later, hypesthesia from the left thigh to shank developed, and he began to drag his left foot during walking. He was readmitted on July 21. A T₁-weighted spinal magnetic resonance (MR) image showed a high-intensity mass at the L5–S2 levels, and spinal dissemination was suspected (Fig. 2A). The third maintenance PVB therapy was initiated on July 24, but the AFP level remained above 20,000 ng/ml.

On September 1, a L5–S2 laminectomy and subtotal removal of the tumor were carried out. Epidural fat tended to be reduced, and the surface of the dura was discolored to reddish brown, suggesting the tumor invasion immediately below the dura. Detachment of the tumor, which tightly adhered to the dura and readily hemorrhaged, was difficult. In addition, the tumor surrounded the nerve roots, making its total removal impossible. The tissue specimens obtained during this operation contained many periodic acid-Schiff (PAS)-positive cells and, in some parts, ductal structures. Immunohistological examination using the peroxidase method showed that the tumor cells were positive for AFP but negative for β-HCG. From these findings, the mass was considered to be a metastatic pure yolk sac tumor.
tumor (Fig. 3). Intraoperative CSF analysis showed a normal cell count of 4/3 but an increase in the protein content to 125 mg/dl.

After the operation, the AFP level decreased to above 10,000 ng/ml, half the preoperative level, but no further reduction was observed. Local irradiation of 30 Gy was applied to the spine at the L5–S2 levels from September 18. The AFP level began to decrease rapidly during the radiation therapy, and reached 101 ng/ml on December 4, 1 month after the completion of irradiation. The fourth maintenance PVB therapy was performed from December 8, and the AFP level was controlled to below 100 ng/ml. Both β-HCG and CEA levels were within the normal ranges. He was discharged on January 8, 1988.

V. Fifth hospitalization

The AFP level increased to 816 ng/ml in late February, 1988. Muscle weakness of bilateral lower extremities (MMT, 2/5 on the right side and 4+/5 on the left) and amblyaphia and analgesia below Th7.

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Fig. 2 A: T₂-weighted spinal MR image obtained at fourth admission, showing a high-intensity mass at the L5–S2 levels. B: Spinal MR image taken 8 days after fifth admission, revealing a metastatic mass at the Th7 level.

Fig. 3 Photomicrographs of surgical specimens of the lumbosacral tumor. ×400. A: HE staining shows perivascular rosette formation. B, C: Many AFP- (B) and PAS-positive (C) cells are shown. D: There were no β-HCG-positive cells.
level developed, and he was readmitted on March 28. A spinal MR image obtained on April 5 disclosed a new metastatic mass localized at the Th6-Th7 levels (Fig. 2B). Ascending myelograms demonstrated a complete block at the lower margin of Th7. Simultaneous CSF analysis showed a normal cell count of 3/3 but a remarkable increase in the protein content to 1903 mg/dl.

On April 12, a Th5-Th8 laminectomy and total removal of the tumor were carried out. The dura tended to be tense and to expand on the right side. An epidural tumor localized at the Th6-Th7 levels was detached under the operating microscope and aspirated as completely as possible using an NIH ultrasonic surgical aspirator. A few nerve roots at the Th7 level, which were surrounded by the tumor, had to be transected. After the operation, CSF pulsation was confirmed at the site of the tumor removed. Histological examination indicated a tumor with generally clear epithelial features: irregular, solid cell aggregation exhibiting a columnar formation. This mass was considered to be a metastatic yolk sac tumor, as with the lumbosacral lesion.

Postoperatively, the AFP level remained high and began to exceed 10,000 ng/ml from early May. The fifth maintenance PVB therapy was initiated on May 23, but had to be discontinued due to a reduction in white blood cells (WBC) to 800/mm³. During the same period, left peripheral facial paralysis and hearing impairment on the left side developed, and a CT scan and an MR image showed a tumor in the left cerebellopontine angle (Fig. 4). The AFP level had increased linearly from late June, with a proportional enlargement of this tumor. However, the pineal tumor showed no changes or recurrence. On September 2, he suffered digestive bleeding and aspiration pneumonia followed by disseminated intravascular coagulation syndrome, and died on October 1, 1988.

VI. Autopsy findings
A partly degenerated tumor remained in the pineal region. A reddish brown tumor, 4 x 4.5 x 3.5 cm in size, was observed in the cerebellopontine angle, and a metastatic tumor extending from L4 to S3 vertebra surrounded the cauda equina. Histologically, the tumor cells in the cerebellopontine angle were cuboidal- or polygonal-shaped, and were frequently arranged in papillary or cobblestone patterns. This papillary structure often resembled a Schiller-Duval body. Hyaline bodies were also occasionally noted (Fig. 5). A large number of hemorrhagic and necrotic foci were observed within the tumor. In the pineal lesion, necrotic foci containing cholesterol crystals were surrounded by xanthoma cells. Metas-

Fig. 4 Postcontrast CT scan (A) and coronal MR image (B) obtained after third operation, showing a metastatic mass (arrow) in the left cerebellopontine angle.

Fig. 5 Photomicrographs of autopsy specimens of the cerebellopontine angle tumor. A: x 200, B: x 400. HE staining shows a typical Schiller-Duval body (arrowheads) and a hyaline body (arrow).
tases to the cerebellopontine angle and the spinal cord had occurred primarily by extramedullary invasion probably via the subarachnoid space. The bone marrow was markedly hypoplastic and mostly replaced by fat. The seminiferous tubules mostly consisted of sertoli cells, without germ cells.

**Discussion**

Intracranial germinoma is encountered more frequently in Japan than in Europe or America and reportedly accounts for about 5% of all brain tumors. In our present case, serum AFP level was very high, but serum β-HCG and CEA levels remained within the normal ranges throughout the course. Schiller-Duval and hyaline bodies were histologically observed, and the localization of AFP in tumor cells was demonstrated by the immunostaining technique. These findings indicated pure yolk sac tumor.

The spinal metastasis of yolk sac tumor was described in detail by Ihara et al., who reported that the site of the primary lesion was the posterior portion of the third ventricle or the pineal region in nine of 11 cases, and the symptoms due to spinal metastasis appeared within a few months from the initial treatment in nine. Only one case was previously reported, in which whole-brain irradiation combined with PVB therapy was carried out, but this treatment did not prevent spinal metastasis as in the present case. It appears that this treatment does not decrease the incidence of spinal metastasis as compared to whole-brain irradiation with or without other chemotherapies. In addition, our case received whole-brain irradiation of 50 Gy and five courses of PVB therapy when the symptoms due to spinal metastasis appeared. These results support the earlier observation that the transport of cisplatin into the CSF is very poor and so it is not useful to prevent spinal metastasis.

Retrospectively, the changes in the serum AFP level are considered to have most accurately reflected spinal metastasis (Fig. 6). The maximal AFP level was 147 ng/ml during the second hospitalization, but had increased to 1400-1500 ng/ml during the third hospitalization, suggesting the inadequacy of the second maintenance PVB therapy. Since no marked changes were observed on head CT scans at this time, local irradiation of 20 Gy was applied to the pineal region, but the procedure is not considered to have been highly effective. During the fourth and fifth hospitalization, the AFP level exceeded 10,000 ng/ml, when obvious metastatic lesions were noted in the lumbosacral spine, thoracic spine, and cerebellopontine angle. PVB therapy had little effect on the metastatic spinal tumors, and the AFP level
reduced only after tumor removal and spinal irradiation.

The protein content in the CSF may be another index useful for the detection of spinal metastasis. In our case, the protein content was 26 mg/dl at the first admission, but increased to 125 mg/dl at the removal of the lumbosacral lesion, and reached 1903 mg/dl before the removal of the thoracic lesion. However, tumor cells could not be demonstrated by cytological examination of the CSF at these times.

Leukocytopenia is the greatest problem when PVB therapy is combined with irradiation. In our case, also, the WBC had already been reduced to below 2000/mm³ at the initial remission. It decreased to below 800/mm³ during the fifth maintenance PVB therapy, making discontinuation inevitable. The autopsy revealed marked hypoplasia and remarkable fatty vacuolar degeneration of the bone marrow, suggesting severe suppression. Metastases to the intraspinal and intracranial cavities in our case occurred by dissemination of the tumor cells via the subarachnoid space, as in earlier reports. On the other hand, the primary pineal lesion became necrotic and did not recur. In our case, the intraspinal and intracranial metastases were the decisive factor in survival, as suggested by Nakagawa and Matsumoto. The development of radical therapies to prevent the formation of metastatic lesions is required.

References


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