Extraneural metastasis of choriocarcinomatous element in pineal germ-cell tumor

Case report

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Case Report

This 23-year-old man came to our attention in April, 1983, complaining of headache, vomiting, and an upward gaze palsy.

First Admission. A computerized tomography (CT) scan showed dilated third and lateral ventricles and a mixed-density mass with calcifications in the pineal region that enhanced irregularly with contrast medium (Fig. 1A). He was diagnosed as having a pineal tumor and obstructive hydrocephalus, and a right ventriculoperitoneal shunt was placed on April 28. Laboratory examination revealed that the specific tumor-marker levels in the serum were high, with HCG at 110 ng/ml, and AFP at 743 ng/ml (normal range in our institute: HCG < 1 ng/ml and AFP < 20 ng/ml). Cerebral angiography demonstrated a faint tumor stain in the pineal region, 3 × 3 × 3 cm in size, supplied by the thalamo-perforating arteries.

A germ-cell tumor was diagnosed, and radiation therapy was started on May 27, 1983. With a linear accelerator, a total dose of 2000 rads in 10 fractions was given over 14 days to two parallel opposed lateral fields of the pineal region, and the whole brain was subjected to a total dose of 3000 rads in 15 fractions over 20 days. Just after the termination of irradiation, the headaches and Parinaud's sign were improved. A month after irradiation was concluded, serum HCG and AFP levels had decreased to a normal range (Fig. 2), and the...
FIG. 1. Computerized tomography scans. A: Scan obtained on admission after injection of contrast medium showing an irregularly enhanced mass with calcification in the pineal region. B: The enhanced mass was reduced 1 month after radiation therapy. C: There was no enhanced lesion 3 months after the termination of radiation therapy, but the calcified mass in the pineal region remained.

FIG. 2. Summary of the patient’s clinical course showing the alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) levels and tumor size and therapeutic interventions. The tumor-marker levels fell to the normal range following radiation therapy. The onset of metastatic pulmonary tumor on December 3, 1983, was determined by retrospective analysis of chest x-ray films. Serum HCG levels are related to the growth of the metastatic tumor. OP = operation; MTX = methotrexate; CDDP = cisplatin; PEP = peplomycin sulfate; ACNU = nimustine hydrochloride; VCR = vincristine sulfate; VBL = vinblastine sulfate.
Choriocarcinomatous metastasis from germ-cell tumor

tumor size was reduced on CT scanning (Fig. 1B). On July 26, 1983, the patient was discharged without neurologic symptoms.

Second Admission. On September 9, 1983, the patient's serum HCG and AFP levels began to increase again, although CT showed that the tumor remained small (Fig. 1C). On November 2, he was readmitted with headache and double vision. A 4-week course of chemotherapy was initiated on November 9, with 40 mg cisplatin and 15 mg peplomycin sulfate per week; however, the serum HCG and AFP levels continued to rise, and the pineal mass gradually increased in size (Fig. 2). On December 12, cerebral angiography showed a larger pineal mass; the inferior sagittal sinus, the great vein of Galen, and the straight sinus were not visualized, although they had been clearly seen on angiograms obtained at the previous admission.

Operation. On December 20, 1983, a partial removal of the pineal tumor was performed via a right occipital craniotomy with the patient in the sitting position. The tumor was soft and necrotic, invading and occluding the internal cerebral veins and the great vein of Galen. Histological examination of the operative material revealed massive necrosis containing a very small portion of choriocarcinoma.

Postoperative chemotherapy with nimustine hydrochloride (ACNU) and vincristine sulfate, followed by cisplatin, peplomycin sulfate, and vinblastine sulfate, failed to reduce the tumor size. On March 22, 1984, the patient died of respiratory failure due to brain-stem involvement of the pineal tumor and multiple pulmonary metastases that, judging by retrospective analysis of chest x-ray films, had developed prior to removal of the pineal tumor.

Postmortem Examination. Autopsy was performed only on the intrathoracic organs and demonstrated multiple metastases in both of the lungs and the hilar lymph nodes. Microscopic examination of the metastatic tumor showed nests of cytotrophoblasts and syncytiotrophoblasts in the necrotic tissue. Immunohistochemical staining revealed HCG in the syncytiotrophoblasts, but no AFP was found in any part of the pulmonary tumor. The AFP and HCG levels were measured in homogenized tissue from the pulmonary metastases and revealed AFP 95 ng/gm and HCG 152,466 ng/gm. By contrast the final serum levels were: AFP 710 ng/ml and HCG 16,000 ng/ml.

Discussion

Germ-cell tumors usually arise in the gonadal organs and midline structures, including the suprasellar or pineal regions, of the young. Neoplasms of germ-cell origin were precisely classified according to comparative morphology and ontogenesis by Teilum. Specific types of germ-cell tumors manufacture biological markers, such as HCG and/or AFP. Alpha-fetoprotein is produced by the yolk sac in the early stage of development, and HCG is synthesized by the chorioepithelium, both extra-embryonic structures. Choriocarcinomas produce HCG, and AFP is a specific tumor marker of yolk-sac tumors (endodermal sinus tumors). Less differentiated germ-cell tumors containing multiple differentiated extra-embryonic structures produce both HCG and AFP, and such tumors are called "embryonal carcinomas." The correlation between tumor marker and germ-cell origin supports the classification by Teilum. Embryonal carcinoma has the potentiality to differentiate to mature or immature teratoma, teratocarcinoma, choriocarcinoma, or yolk-sac tumor. This multipotentiality of a single embryonal carcinoma cell was experimentally verified by Kleinsmith and Pierce using an in vitro cloning technique.

In this case, the pineal tumor produced both HCG and AFP, and was diagnosed as a germ-cell tumor which had the components of a choriocarcinoma and a yolk-sac tumor. The metastatic tumor was a choriocarcinoma, producing only HCG. In the early stage of this case, AFP was predominant relative to HCG, but after development of the metastases, HCG levels increased (Fig. 2). The postmortem pathology revealed that the pulmonary tumor was a choriocarcinoma consisting of cytotrophoblasts and syncytiotrophoblasts. On immunohistochemical staining, HCG was positive in the syncytiotrophoblasts and AFP was negative. The HCG content of the pulmonary tumor was extremely high, while the AFP concentration was relative to serum levels.

Yolk-sac tumors sometimes disseminate along CSF pathways and may metastasize to the peritoneal cavity via a ventriculoperitoneal shunt. Choriocarcinomas tend to metastasize hematogenously, especially after surgical intervention such as biopsy or removal of the tumor. In this case, only the choriocarcinomatous component of the multipotential germ-cell tumor in the pineal region metastasized via the blood to the extraneural organs, probably by venous invasion before surgical removal of the pineal tumor.

References


