Primary intracranial choriocarcinoma

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The authors report four cases of primary intracranial choriocarcinoma, all in young males. Three tumors occurred in the pineal region and one in the lateral ventricle. Besides the signs of increased intracranial pressure and ophthalmological disorders, skin pigmentation or eruption was observed in three cases and precocious puberty in two cases. Angiography revealed tumor stain with irregular vessels in all cases. Enhanced computerized tomography scans in the last two cases demonstrated a round, lobulated lesion of high density, with relatively low density in the central portion. Hormonal study was carried out in three cases. In addition to high levels of human chorionic gonadotropin (HCG) in the urine and cerebrospinal fluid and/or of plasma luteinizing hormone (LH), LH in the tumor tissue or medium obtained via cell cultures was also high in all three cases, suggesting inherent activity of HCG secretion by the tumor cells. The tumors were relatively demarcated from the surrounding brain. They were very hemorrhagic, and fresh hematoma was identified in the tumor in one case. Good results were obtained in two cases treated with surgical removal followed by simultaneous chemotherapy and 60Co irradiation.

Key Words · choriocarcinoma · hormonal study · human chorionic gonadotropin · luteinizing hormone

Choriocarcinoma occurs in the uterus or ovary, often associated with hydatidiform mole, abortion, or even normal pregnancy. It is a highly malignant neoplasm frequently metastasizing to various organs, including the brain (secondary intracranial choriocarcinoma). Extragenital primary choriocarcinoma is rare, and the mediasinum and intracranium are the usual sites.

This report concerns four cases of primary intracranial choriocarcinoma with a discussion of their clinical features and treatment.

Case Reports

Case 1

This 14-year-old boy was admitted to the University Hospital on May 15, 1972, with a 4-week history of morning headache, increasing gradually in intensity, and later associated with nausea, vomiting, and double vision. Multiple areas of brown skin pigmentation on the chest were also noticed about 1 year before admission.

Examination. On admission, apart from the skin pigmentation, physical examination, including the genitalia, was normal. The patient was slightly lethargic, with signs of increased intracranial pressure (ICP). The left pupil was larger than the right, and neither pupil reacted to light. Both upward and downward conjugate gaze movements were limited, and horizontal nystagmus to the left was seen on left lateral gaze.

Plain skull films showed a pineal calcification that had shifted about 5 mm to the right. Pneumoventriculography showed diffuse enlargement of the lateral ventricles, and a round and slightly irregular mass in the pineal region. Left carotid angiography demonstrated a faint tumor stain, about $5 \times 5 \times 6$ cm in size, which was best seen in the intermediate phase.

Operations. On the 3rd hospital day, a ventriculoatrial shunt was inserted, then irradiation with cobalt-60 ($^{60}$Co) was given in doses of 200 rads/day. Ten days later, the patient suffered severe vomiting and suddenly became comatose. The shunt was immediately revised, but he did not improve. A transcalsal approach was made through a right parieto-occipital craniotomy with the patient in the prone position. Because of swelling, the right occipital
lobe was removed. The parietal lobe was retracted laterally to expose the corpus callosum. A longitudinal incision was made to expose an underlying tumor between the laterally displaced internal cerebral veins. The tumor was dark red, nodular, and soft, and was relatively demarcated from the surrounding brain. It was so hemorrhagic that only partial piecemeal removal was achieved. Postoperatively, the patient remained comatose with decerebrate posture and died on the 8th postoperative day.

Postmortem Examination. Sagittal section of the brain disclosed the tumor filling the posterior portion of the third ventricle. The tumor infiltrated the adjacent tentorium and falx. Otherwise, no tumor was identified within the central nervous system. The organs of the body, including the testes, also failed to demonstrate any evidence of tumor. Microscopic examination of the tumor revealed features of choriocarcinoma, characterized by two distinct cell types: cytotrophoblast and syncytiotrophoblast (Fig. 1).

Case 2

This 11-year-old boy was admitted on September 29, 1975. About 1 year previously, he noticed a change in voice and physical maturity. Three weeks prior to admission, he started to complain of headache and double vision. The headache progressed and was later associated with vomiting.

Examination. On admission, he showed precocious puberty and multiple areas of brown skin pigmentation on the body. He was lethargic, with signs of increased ICP and upward gaze palsy.

Plain skull films demonstrated pineal calcification and shifting to the left. Conray ventriculography revealed hydrocephalus and a mass in the pineal region. Bilateral brachial angiography demonstrated a tumor fed by both anterior and posterior choroidal arteries and the posterior thalamoperforating arteries (Fig. 2). Hormonal study showed excessively high levels of human chorionic gonadotropin (HCG) in the urine (32,000 IU/liter) and cerebrospinal fluid (CSF) (2000 IU/liter). Plasma luteinizing hormone (LH) was also very high (170 mIU/ml), while plasma follicle-stimulating hormone (FSH) was normal.

Operation. On the 3rd hospital day, his level of consciousness suddenly deteriorated. An emergency ventricular drainage was done, followed by a right parieto-occipital craniotomy. Under the operating microscope, the corpus callosum was incised on the midline. The underlying tumor was easily identified and was found to contain fresh blood clot. Gross tumor was removed in piecemeal fashion. Histologically, the tumor was choriocarcinoma combined with teratomatous components. The tumor tissue contained a high level of LH (5500 mIU/gm wet tissue) and negligible FSH.

Postoperative Course. Two weeks after the operation, a ventriculoperitoneal (VP) shunt was inserted for progressive hydrocephalus. Subsequently, his consciousness improved and he became alert. Methotrexate (0.4 mg/kg body weight, intramuscularly) and actinomycin D (10 µg/kg body weight, intravenously) were given once daily for 4 consecutive days, and repeated 3 weeks later. In addition, 60Co irradiation in a total of 4000 rads was given to the pineal region. Postoperatively, urinary HCG levels dropped quickly at first, then gradually fell to normal levels as chemotherapy and 60Co irradiation were given. He was discharged on March 22, 1976.

Four years postoperatively, the patient attends junior high school. He complains of easy fatigability...
and slight recent memory disturbance. The left eye is minimally deviated upward and laterally, and horizontal nystagmus is present on lateral gaze. Computerized tomography (CT) scans demonstrate no evidence of recurrence, and HCG in the urine and CSF has stayed within normal limits.

**Case 3**

This 11-year-old boy was admitted on September 14, 1976. About 5 months previously, he noticed a voice change and hirsutism. Two months later, he developed weakness in the face and the right arm, followed by sensory disturbances.

**Examination.** On admission, precocious puberty and right hemiparesis with hemisensory deficits were found. Plain skull films and cerebral angiography were within normal limits except for a slight elevation of the Sylvian triangle on the left side. Plain CT scanning demonstrated a quite sharply demarcated round region of low density in the left temporal lobe.

**First Operation.** On the 7th hospital day, a left parietotemporal craniotomy was performed. The temporal lobe was slightly swollen. A ventricular needle was inserted to yield a few cubic centimeters of slightly xanthochromic fluid. A cyst in the middle temporal gyrus was explored, and no tumor was identified. Postoperatively, right homonymous hemianopsia was observed in addition to the previous neurological deficits.

After discharge, the patient was well for 9 months, then he gradually developed headache associated with signs of increased ICP. Left carotid angiography showed a large tumor stain with many irregular vessels in the left temporal lobe (Fig. 3). Computed tomography scans demonstrated a large round lesion of high density which enhanced with contrast material (Fig. 4). Hormonal study revealed levels of HCG exceeding 1000 IU/liter in the urine and 20 IU/liter in the CSF. Plasma LH was 448 mIU/ml. He was readmitted on August 15, 1977.

**Second Operation.** On the 3rd hospital day, the previous craniotomy site was reopened. Cortical dissection through the previous operative scar in the middle temporal gyrus revealed a tumor in the posterior portion of the temporal horn extending into the atrium. The tumor was grossly removed and histological examination showed it to be choriocarcinoma. Luteinizing hormone in the tumor tissue was only 32 mIU/gm wet tissue, but it was more than 500 mIU/ml in the medium obtained from the cell cultures. Two weeks later, a VP shunt was inserted.

Subsequently, methotrexate (0.2 mg/kg body weight, intramuscularly) was administered once daily for 5 consecutive days, and was repeated five more times, with a total dosage of 300 mg. Co irradiation in a total of 4000 rads was also given. Postoperatively, urinary HCG dropped to 40 IU/liter, then slowly over 2 months to less than 5 IU/liter. The patient was discharged on November 30, 1977, with bilateral limitation of vertical gaze movements and anisocoria.

He did relatively well until January, 1979, when he gradually developed anorexia associated with gradual increase of urinary HCG. Computerized tomography scans revealed an enhanced lesion in the left frontal lobe.

**Third Operation.** He was again admitted on February 2, 1979. A left frontotemporal craniotomy was carried out, and tumor was removed from the anterior horn through a transcortical approach.
Choriocarcinoma intermingled with teratocarcinoma; LH in the tumor tissue was 650 mIU/gm wet tissue.

Postoperative Course. The patient was comatose with left hemiparesis, more marked on the lower extremity. As he gradually improved, methotrexate (0.3 mg/kg body weight, intramuscularly, and 0.1 mg/kg body weight, intrathecally) was administered daily for 5 consecutive days. He developed severe stomatitis due to pancytopenia, and chemotherapy was stopped. In the second postoperative month, CT scans demonstrated recurrence of the tumor. He died 3 months after surgery, and no autopsy was obtained.

FIG. 5. Case 4. Contrast-enhanced computerized tomography scan showing a round lobulated lesion of high density at the pineal region. Its central portion was relatively low in density.

Postoperatively, methotrexate, 50 mg in total, was administered intrathecally. Urinary HCG decreased to normal levels. He was alert, but the neurological deficits described above were not improved. He was discharged on April 27, 1979, and has since been neurologically unchanged.

Case 4

This 22-year-old man was admitted to the Fukuyama National Hospital with a 4-month history of progressive headache and difficulty in hearing on the left side. He was found to have a pineal tumor. A VP shunt was placed, and 5050 rads of 60Co irradiation was given over a 5-week period. Suddenly he developed complete bilateral ptosis, accompanied by headache, nausea, and vomiting. Conray ventriculography showed the tumor had grown in spite of radiation therapy. He was transferred to the University Hospital on August 8, 1977.

Examination. On admission, he was drowsy. There were numerous areas of skin eruption, and almost complete ptosis of both eyes. The pupils were anisocoric and reacted to light very sluggishly. Both upward and downward gaze movements were completely paralyzed, and the right medial rectus was weak. In addition, hearing and taste sensation were markedly disturbed on both sides. Plain skull films showed pineal calcification shifted to the left. Computed tomography scans demonstrated an enhanced lesion in the pineal region (Fig. 5). Left vertebral angiography showed a tumor stain, and hormonal study demonstrated a slight increase of urinary HCG (50 IU/liter).

Operation. On the 14th hospital day, the tumor was removed through a right parieto-occipital transcallosal approach. The histological report was choriocarcinoma intermingled with teratocarcinoma; LH in the tumor tissue was 650 mIU/gm wet tissue.

Discussion

The incidence of primary intracranial choriocarcinoma is rare. Hasegawa, et al., reviewed the literature up to 1974, and found only 34 cases reported. The tumor usually occurs in the pineal region, but also less frequently in the parasellar region and in the lateral ventricle. Extracranial metastasis, mainly to the lungs, has been reported occasionally. The pathogenesis of so-called "pinealomas," including choriocarcinomas, has been debated. Russell postulated that many of them were atypical teratomas. Friedman considered them germinal in origin since they were histologically classified as types of germinal tumors, namely, germinoma, embryonal carcinoma, choriocarcinoma, and teratoma. On the other hand, endodermal sinus tumor (yolk sac carcinoma) has been reported only rarely as a specific germinal growth. A pure form of choriocarcinoma is rare; it is usually seen with other types of germinal tumors, such as embryonal carcinoma and teratoma. Furthermore, a case of choriocarcinoma reported by Giuffre and Di Lorenzo was differentiated from teratoma a few months after intracranial surgery.

In our four cases, all three pineal region tumors demonstrated calcification radiographically. Angiography showed tumor stain with irregular vessels in all cases, best seen in the intermediate phase (Figs. 2 and 3). The angiographic picture was not specific as to the type of germinal tumor. Computerized tomography scanning in Cases 3 and 4 showed some features. In Case 3, the plain scan on first admission showed a quite sharply demarcated round region of low density. Nine months later, the diminished absorption was completely replaced by a large lobulated mass. The major peripheral portion was of high density which enhanced well by contrast material, while the eccentric central area was of relatively low density (Fig. 4). In Case 4, the plain scan showed an irregular lesion of high density at the pineal region. Following contrast infusion, it enhanced to reveal a round, lobular shape. The central portion was of relatively low density (Fig. 5).

Hormonal study was done in three cases. Human chorionic gonadotropin in the urine and CSF was...
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### TABLE 1

| Case No. | HCG (IU/liter) Plasma | LH (mIU/ml) Tumor Tissue* Medium |
|----------|----------------------|----------------------|----------------------|
| 2        | 32,000               | 170                  | 5500                 | not done          |
| 3        | 1000                 | 448                  | 32                   | 500               |
| 4        | 50                   | 4.6                  | 650                  | 3.3               |

*HCG in tumor tissue is mIU/gm wet tissue.

The results of the hormone studies are summarized in Table 1. The glycoprotein hormones (HCG, FSH, LH, and thyroid-stimulating hormone) have an almost identical alpha chain, while the beta chain is specific. However, the beta chains of HCG and LH are quite similar and cross-reaction between them is common. Therefore, the high levels of LH in the plasma, tumor tissue, and/or medium obtained via cell cultures of our cases were considered due to a high level of HCG. High levels of HCG in plasma, urine, and CSF of primary intracranial choriocarcinomas have been well documented, and are a good landmark for its diagnosis and follow-up management. These levels are usually due to secretion by tumor cells as demonstrated in our cases. The correlation between primary intracranial choriocarcinoma and precocious puberty, often associated with high gonadotropin secretion levels, has often been reported. However, in some patients, no correlation was reported, even with significant amounts of gonadotropins detected.

Since the effects of methotrexate were reported by Li, et al., and actinomycin D by Ross, et al., these two medications have been a standard treatment for genital trophoblastic diseases, including choriocarcinoma. For secondary intracranial choriocarcinoma, Stilp, et al., emphasized a combination of surgical extirpation, chemotherapy, and irradiation. Among our four cases, Co irradiation was given before craniotomy in two cases (Cases 1 and 4) and was found ineffective. Chemotherapy (methotrexate and actinomycin D, or methotrexate only) and Co irradiation were given postoperatively in two cases (Cases 2 and 3). In both cases, the patients are doing relatively well 5 years and 3/2 years since the onset of the symptoms.

As a conclusion, we suggest that primary intracranial choriocarcinoma should be treated surgically to decrease its size, followed by simultaneous chemotherapy and irradiation.

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### References


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