Choriocarcinoma brain metastasis in a patient with viable intrauterine pregnancy

Case report

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We now report such a case, with particular emphasis on the surgical and medical management of this extremely rare event.

**Case Report**

**History.** This 27-year-old woman (gravida 3, para 2) in her 30th week of pregnancy was admitted to the emergency department with a complaint of severe and unremitting headaches, nausea, and progressive somnolence. Her last pregnancy had ended in spontaneous vaginal delivery of a healthy infant and placenta 27 months earlier, with no evidence of retained tissue or other complications. Ultrasoundography performed 10 days before admission confirmed the gestational age and viability of the fetus, and revealed no abnormal intrauterine masses or placental abnormalities. The patient had complained of headaches for several weeks before this admission and had been evaluated 1 week earlier at another emergency room for similar but less severe complaints. While in the emergency department, she became obtunded and minimally responsive to painful stimuli.

**Examination.** Physical examination demonstrated bilateral papilledema, a minimally reactive 6-mm right pupil with a reactive 3-mm left pupil, and abnormal flexion to painful stimuli. The patient was administered intravenous

Abbreviations used in this paper: β-HCG = human chorionic gonadotropin–β subunit; CT = computerized tomography; MR = magnetic resonance.
mannitol (1 g/kg over a 15-minute period), which prompted rapid reversal of her neurological deterioration. Her right pupil decreased to 3 mm and became reactive to light, and her level of consciousness returned to a mild stupor within 20 minutes. Computerized tomography scanning of the brain revealed a 6 × 5–cm hemorrhagic mass in the right occipital region with associated vasogenic edema, subfalcine herniation, right-to-left shift of midline structures, and brainstem compression (Fig. 1 upper left). The mass enhanced heterogeneously after administration of contrast agent (Fig. 1 upper right). The patient was admitted to the intensive care unit and a high-dose corticosteroid regimen (6 mg intravenous dexamethasone every 6 hours) was initiated. Consultations were obtained with the obstetrics and neonatology services. Continuous monitoring of fetal heart sounds and fetal heart rate was also initiated. A pelvic and uterine ultrasonographic study was performed, verifying the presence of a viable 30-week-old fetus and the absence of any abnormal masses. Coagulation parameters, electrolytes, and blood pressure were all within normal limits.

The patient remained clinically stable overnight and the next morning an MR image of the brain was obtained, confirming the CT findings of a 6 × 5 × 3.5–cm, partially hemorrhagic, solitary tumor in the right occipital region, with surrounding vasogenic edema (Fig. 1 lower left and right). The lesion was believed to represent either a primary brain tumor or metastasis from an unknown primary tumor. The serum β-HCG level was markedly elevated at 865,000 ng/ml. The serum α-fetoprotein level was normal. A series of CT scans of the chest, abdomen, and pelvis revealed multiple pulmonary nodules, which were also suggestive of a metastatic process.

A tentative plan was made for elective delivery of the fetus with the aid of a cesarean section, to be immediately followed by biopsy sampling and resection of the brain lesion. Members of the neonatology service proposed a 48-hour delay before surgery so that dexamethasone therapy could be continued to facilitate fetal lung development. In the next 36 hours, the patient suffered two episodes of increased obtundation. During both episodes she responded promptly to mannitol-induced diuresis, but at the time of the second episode a decision was made to proceed directly to surgery as a life-saving measure.

Operation. The patient was brought to the operating room and intubated. A cesarean section was performed during which a viable 30-week-old fetus was delivered; the infant was noted to have excellent lung sounds and Apgar scores of 6 at 1 minute and 9 at 5 minutes following delivery. Manual and visual inspection of the uterus, pelvis, and abdomen did not reveal any abnormal masses. The patient next underwent a right occipital craniotomy.
On exposure of the brain, a large, firm, fibrous mass admixed with areas of focal hemorrhage was identified and removed in a piecemeal fashion. The tumor was well circumscribed and easily separated from the surrounding hemosiderin-stained brain. Once the tumor had been removed, there was immediate relaxation of the brain, normalization of vital signs, and prompt hemostasis.

Postoperative Course. Following surgery the patient experienced a profound improvement in neurological function and level of consciousness. She was transferred to a regular ward 1 day after surgery and made a complete neurological recovery within 4 days, with the exception of persistent mild visual blurring in her right eye. A postoperative CT scan revealed markedly diminished mass effect and gross-total removal of tumor.

After consultation with specialists in medical and radiation oncology, the patient began high-dose chemotherapy with etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine 5 days after surgery, along with whole-brain radiotherapy to a dose of 30 Gy in 10 fractions. The patient was discharged from the hospital on postoperative Day 10. She completed six cycles of chemotherapy and, at her latest follow-up examination 1 year following admission, there is no evidence of disease. Her child is healthy and does not display any appreciable deficits.

Pathological Findings. Pathological examination of the brain tumor (Fig. 2 upper) revealed a hemorrhagic mass with the classic histological pattern of metastatic choriocarcinoma, characterized by the dimorphic arrangement of cytotrophoblasts and syncytiotrophoblasts. Gross examination of the placenta revealed two small areas of hemorrhage and necrosis, 1 and 1.4 cm in diameter, respectively. Histological examination of the placenta (Fig. 2 lower) demonstrated multifocal choriocarcinoma arising from mature placenta without forming space-occupying masses. The tumor cells merged with adjacent normal placental tissue and involved less than 5% of the entire placenta. The pathological appearance of the placental tumors was indistinguishable from the brain lesion. The absence of any large tumor nodules within the placenta also correlated with the normal findings on ultrasonograms observed during the pregnancy.

Discussion

Choriocarcinoma is generally detected several months after an identifiable gestational event such as a hydatidiform mole, an abortion, or a full-term gestation. Current pathological evidence demonstrates that choriocarcinoma arises from the trophoblasts of stem cell villi within the uterus22 and, thus, is frequently identified when dilation and curettage is performed after a nonviable pregnancy. In the past, it generally has been viewed to be incompatible with a coexistent viable pregnancy. We are aware of only three other cases of choriocarcinoma that have been reported to be associated with concurrent pregnancy. Barghorn, et al.,3 reported a case identified following a cesarean section without evidence of metastases. Steigard and associates4 reported a case in which there was antepartum hemorrhage due to a vaginal metastasis without disseminated spread. Dana and colleagues6 reported the only other case of cerebral metastasis from a choriocarcinoma during a viable pregnancy.

In contrast, there is a sizable amount of literature indicating that choriocarcinoma may be identified in the placenta of normal postpartum women.3,5,8,10,15,17,19 Because these tumors are usually silent during the gestational period, it is not surprising that the majority of these cases are identified by symptomatic metastases many months after a pregnancy.14,15,17 In one recent report,17 the authors suggested that the incidence of asymptomatic or occult choriocarcinoma evacuated at the time of fetal delivery or dilatation and curettage may be higher than previously assumed. Nonetheless, the presence of a viable pregnancy along with a metastatic choriocarcinoma is clearly an exceptionally rare event and raises a number of interesting issues from both pathological and case management perspectives. The level of β-HCG is a useful marker for both pregnancy and choriocarcinoma. Levels of β-HCG rise steadily during the first 30 to 45 days of normal pregnancy and begin to diminish during the remainder of the gestational period.21 Typical levels of β-HCG are variable, but only rarely will exceed 10^10 to 2 x 10^10. In contrast, β-HCG levels observed with choriocarcinoma are directly related to the number of tumor cells, with an estimated 10^10 cells producing a β-HCG level of 1 ng/ml.2 Thus, serum levels can range from less than 100 ng/ml to greater than 10^7 ng/ml, as seen in this case. When cerebral metastases are suspected, a cerebrospinal fluid/serum β-HCG ratio greater than 1:60 can be expected.3 Despite these general rules, β-HCG levels attributable to either pregnancy or choriocarcinoma can vary widely, and this marker should not be used as an independent measure of the presence of tumor. Nevertheless, it does provide an excellent marker for the measurement of response to chemotherapy when treating cases of gestational trophoblastic tumor.

Choriocarcinoma grows rapidly and is exquisitely sensitive to chemotherapy and/or radiotherapy; thus, initiation of therapy immediately after diagnosis is critical to successful management. Untreated patients or those with progressive disease despite chemotherapy face a median survival of less than 4 months.5,14,17,18,22 Choriocarcinoma is very chemosensitive, and carries a greater than 90% chance of cure in response to multiple drug regimens such as etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine or methotrexate with citrovorum factor rescue.17,18,20,25 Cure rates in excess of 75% have been reported in many series,17,18 even in patients with widespread metastases to the lung and liver. Although the presence of brain metastases is reported to be a negative prognostic factor,3 even in those cases a cure rate of up to 80% may be expected in response to aggressive therapy.16,19,22,26

In the absence of a life-threatening mass effect, brain metastases are usually treated with whole-brain radiotherapy in conjunction with chemotherapy, because most of these tumors completely regress in response to irradiation. Surgical removal has been advocated when significant progressive mass effect is present.22 Our report is the only one that we have identified in which surgical removal of a brain metastasis was performed in conjunction with fetal delivery to facilitate the reduction of mass effect and the prompt initiation of chemotherapy for the remaining systemic disease.
Usually the ability to initiate aggressive therapy is not affected by the pregnancy because the overwhelming majority of cases come to light after the pregnancy. In our particular case, medical decision making was predicated on the wellbeing of the fetus, the mass effect of the tumor, and the need to treat the tumor rapidly. The decision to delay surgical removal of the brain tumor was made when the patient exhibited an excellent reversal of neurological deterioration following administration of mannitol. Once the patient appeared more stable, it was believed that administration of high-dose steroid medications for at least 24 to 48 hours would facilitate fetal lung development and that premature delivery of the fetus be necessary. Because the serum β-HCG was so high, our suspicion of choriocarcinoma was very strong, and we realized that chemotherapy needed to be started quickly. Our treatment rationale was based on the assumption that the best possible outcome would include the healthy survival of both fetus and mother, with no neurological deficit. Coordination of care among the members of neurosurgery, obstetrics, medical oncology, and neonatology services and the slight delay in surgical intervention in a patient who appeared to be temporarily stable permitted the best possible outcome. When the patient suffered repeated episodes of neurosurgical compromise, members of all services were available to facilitate delivery of the fetus and removal of the tumor. Although we cannot be conclusive, the high Apgar scores and excellent respiratory efforts of the infant may have been facilitated by the 36 hours of steroid therapy administered prior to delivery. Delivery of the fetus at the time of brain tumor removal permitted rapid administration of chemotherapy a few days after surgery, and avoided any potential ethical conflicts should the mother become comatose or die.

When pregnant patients harbor intracranial tumors that exhibit significant mass effect, the decision to deliver the fetus prematurely must balance the survivability of the fetus against the medical need of the mother. Following premature delivery at 30 weeks of gestation, an infant has a chance of survival in excess of 90%, whereas at 25 weeks there is less than a 50% chance of survival, and at 22 weeks there is less than a 5% chance of survival. Although administration of corticosteroid medication may improve these statistics, ultimately the age of the fetus is the primary determinant in the decision to deliver the child or to continue the pregnancy. In a patient with metastatic choriocarcinoma, delayed administration of chemotherapy markedly worsens the prognosis for cure. Therefore, barring any moral, ethical, or religious issues, delivery of the fetus and therapeutic abortion would be considered reasonable treatment options and largely depend on the age of the fetus. If choriocarcinoma is not suspected, however, focused treatment of the intracranial lesion and subsequent delay of additional therapy until the fetus has matured to an age that would likely ensure survival may be a very reasonable treatment plan.

**Conclusions**

Metastatic spread of choriocarcinoma during a viable pregnancy is an extremely rare occurrence, but must be considered when an intracranial mass is identified in a pregnant woman. The serum level of β-HCG may be a useful marker to differentiate metastatic choriocarcinoma from other diagnostic possibilities. Prompt surgical intervention to relieve mass effect and/or confirm a tissue diagnosis may be necessary in these cases. The decision to deliver the fetus in these situations should be based on fetal age, opportunity to administer steroid medications before delivery, and the potential need for aggressive chemotherapy or radiotherapy that cannot be delayed until after the pregnancy. Multidisciplinary planning of treatment can greatly facilitate this process.

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