

Infantile and Maternal Choriocarcinoma: A Case Report and Review of Literature

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ABSTRACT

Choriocarcinoma is a rare and highly malignant trophoblastic neoplasm. It can be preceded by any form of gestation including a complete or a partial mole, miscarriage, and normal pregnancy. Simultaneous intraplacental choriocarcinoma involving both mother and infant is extremely rare. The diagnostic triad of choriocarcinoma includes hepatomegaly, anemia, and elevated β HCG. Herein, we report the case of a 6-week-old Afghan girl infant with intraplacental choriocarcinoma presented by severe anemia and widespread multiple metastatic lesions in the liver, lungs, and brain with an elevated level of β HCG. Given the rarity, rapid progression, and the high mortality rate of the disease with delay in diagnosis and intervention, choriocarcinoma should be one of the differential diagnoses in case of severe infantile and maternal anemia without any antecedent reason. Considering the highly vascular and friable nature of the tumor, biopsy can be dangerous for diagnosis. As choriocarcinoma secretes β HCG, measurement of serum β HCG is the most common method used for the diagnosis of choriocarcinoma.

Keywords: Choriocarcinoma, Infantile, Metastasis, Neonate

Introduction

Choriocarcinoma is a rare, high-grade cytotrophoblastic and syncytiotrophoblastic tumor. It can be found in association with any form of gestation (1, 2). Simultaneous intraplacental choriocarcinoma as a variant of gestational choriocarcinoma involving both mother and infant is extremely rare (1 in 50,000 live births) (3).

The complications of intraplacental choriocarcinoma are severe fetomaternal hemorrhage, retroplacental hemorrhage, placental abruption, and fetal hydrops, which may often lead to fetal distress, fetal anemia, intrauterine growth restriction, intrauterine fetal death, and stillbirth (1, 4-6).

Infantile choriocarcinoma was first described by Witzleben and Bruninga in 1968 with a triad of anemia, pallor, and hepatomegaly (7). It usually becomes symptomatic in infants aged 0-6 months (with a median age of one month). Anemia, hepatomegaly, hemorrhagic syndromes, and failure to thrive are its most common symptoms (1). Usual sites of metastasis are the liver, lungs, brain, and

skin (8).

The natural course of the disease is progressive, and early diagnosis and treatment can significantly improve its prognosis. As choriocarcinoma secretes β HCG, measuring its serum level provides a useful diagnostic tool for prompt diagnosis and appropriate treatment of this condition (1, 9).

To the best of our knowledge, since 1968, around 30 cases of infantile choriocarcinoma have been reported in the literature (1, 2, 10). In the present study, we reported a new case with severe anemia and widespread metastatic lesions.

Case Presentation

A 6-week-old Afghan girl infant presented with recurrent vomiting for four days and poor-feeding. There was no fever or abdominal distention. The infant had a birth weight of 1,000 g and a history of neonatal intensive care unit (NICU) admission due to prematurity during the first days of life. Her mother

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was a 22-year-old (gravida: 1, para: 0) woman with 31 weeks of gestational age. The pregnancy was terminated by cesarean section because of maternal illness and severe anemia; the mother died 30 days after delivery. The family had no evidence of the mother's disease.

In the first examination, the infant was ill, pale, with decreased neonatal reflexes. She had stable vital signs. Except for a systolic murmur, chest examination was normal. She had no abdominal distention or organomegalies. Megalocornea and leukocoria were detected in both eyes, which was more severe in the right side.

Sepsis, metabolic disorders, and TORCH were considered as differential diagnosis. Severe anemia (Hb=5.1 g/dl, Mean corpuscular volume (MCV) =91 fL, reticulocyte count=9.05, white blood cell=10510 [neutrophils=39.4%, lymph= 49.6%], C-reactive protein=1) were detected in the laboratorial data. There was no acidosis, and the levels of ammonia and lactate were normal. The patient also had normal high-performance liquid chromatography (HPLC) of serum amino acids and no evidence of TORCH. We found a mass lesion in the right hemithorax in chest X-ray that looked like a round pneumonia or bronchial cyst (Figure1). The patient was treated by packed cells and antibiotics. Ophthalmologic consult reported huge vascular lesions in the right vitreous and left retinal vascularization. Chest CT scan revealed two vascular lesions in the right lung and liver that suggested hemangiomatosis. Measurement of alpha-fetoprotein and β HCG was requested.

Brain and orbital magnetic resonance imaging (MRI) showed a large heterogeneous signal in the left occipital lobe with severe peripheral vasogenic edema and mass effect and midline shift, which was relatively hypersignal in T1-weighted images. At least four similar appearances of hemorrhage and hemosiderin deposits were detected in the left frontal lobe, left thalamus, right parietal, and left cerebellar hemisphere. Furthermore, abnormal signal in the vitreous cavity in the right globe and dysplastic changes of the anterior chamber were noted, without any obvious post-contrast enhancements (Figure 2).

At the same time, we received a document about our patient's mother in which she was diagnosed with choriocarcinoma. She suffered from severe anemia and fatigue during the pregnancy.

Considering normal alpha-fetoprotein and elevated β HCG level (>1000 with normal range <50) the most probable diagnosis was choriocarcinoma.

Unfortunately, before chemotherapy the infant passed away because of severe intracranial hemorrhage and cerebral herniation.

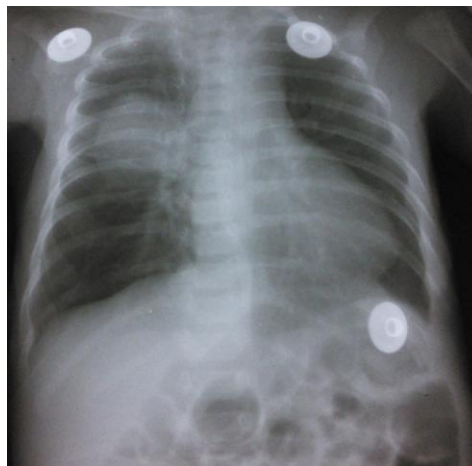


Figure 1. A round mass in the right hemi thorax

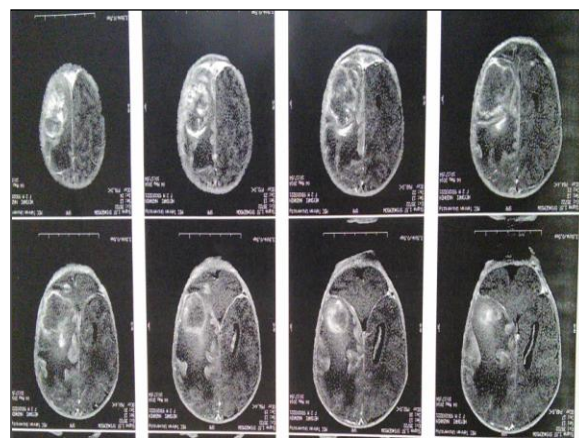


Figure 2. Several appearance of hemorrhage in brain MRI

Discussion

Maternal choriocarcinoma is a rare malignant trophoblastic neoplasm occurring in 1: 50000 pregnancies (3). About half of choriocarcinomas arise from hydatidiform mole, 25% occur following spontaneous abortion or ectopic pregnancy, and the remainder after normal pregnancies (2, 11). Simultaneous malignancy in both mother and infant is even rarer. About 30 cases of infantile choriocarcinoma have been reported in the literature (1, 2, 10).

The characteristic presenting clinical manifestations of infantile choriocarcinoma leading to hospital admission are anemia, hepatomegaly, failure to thrive, respiratory failure, and less frequently, signs of precocious puberty (1, 7, 9, 12).

Infantile choriocarcinoma can clinically manifest at or soon after birth. According to a review by Martin et al., 66% of the patients who were normal at birth became symptomatic up to

the age of 5 months, whereas 33% had prenatal or neonatal symptoms (1). Our case was normal at birth, but was admitted due to severe anemia and poor feeding at 6 weeks of age. Marked anemia is reported in 73% of the affected infants (1, 13, 14). Red cell transfusion, as in our patient, may be required. Anemia could be due to fetomaternal transfusion observed in intraplacental choriocarcinoma or from microangiopathic-induced consumption in the highly vascularised tumors (1, 2, 15). Choriocarcinoma is highly vascular and friable with a high risk of hemorrhage in the tumor or tumor rupture (1).

Precocious puberty may happen due to the effect of β HCG on the hypothalamic-pituitary-gonadal axis and may be observed in infants with prolonged disease (1, 16). Failure to thrive, a nonspecific sign, may be noted in patients, mostly in combination with other symptoms (1).

The placenta is believed to be the source of malignancy, but because of microscopic involvement in the majority of cases, gross examination of the placenta is often normal (1, 17). The placenta is not routinely examined microscopically, and in most cases, is not available for investigation after the diagnosis of infantile choriocarcinoma (18). The microscopic analysis of the placenta in fetomaternal transfusion or severe unknown anemia should be performed (17). DNA study of the placenta can identify the source of malignancy (mother, fetus, or previous pregnancy) (14). The placenta of our case was not available.

Infantile choriocarcinoma is prone to metastasis. In most cases, the tumor affects multiple organs including the liver (77%), lungs (67%), brain (27%), and skin (10%) (1,19). Brain and skin metastasis are rare and may indicate advanced disease (1, 20-22). Involvement of the liver, lungs, and brain were noted in our patient at the same time and indicated a poor prognosis.

Infantile choriocarcinoma can progress rapidly (1, 22). The nonspecific signs of anemia and the rarity of the disease may result in delayed diagnosis. In spite of the combination of anemia and hepatomegaly, because of no access to maternal medical history, we considered sepsis and inborn error of metabolism in our patient.

According to, highly vascular and friable nature of the tumor, biopsy can be dangerous for diagnosis (2). Despite the varied clinical presentations, β HCG is always elevated in the serum and/or urine (9). In severely affected infants, a definitive histology is not necessary for the treatment. The diagnosis is usually confirmed with elevated level of β HCG, and other symptoms and is used to evaluate the response to

treatment (2, 23-25).

Choriocarcinoma is an aggressive tumor. Without appropriate treatment, death happens within an average of three weeks of initial presentation (1); our patient died at 17th day of admission. Fortunately, choriocarcinoma is extremely sensitive to chemotherapeutic agents (1, 2, 26). Its response even in the presence of widespread metastasis is very well. The survival rate of brain metastatic lesion with early diagnosis and treatment is 80% (2).

Early diagnosis and treatment are the most important criteria for good prognosis (23). There are many reports on delayed diagnosis and death due to life threatening bleeding (1, 14). Unfortunately, our patient died before the initiation of chemotherapy after severe intracranial hemorrhage.

Conclusion

Although choriocarcinoma is a very rare malignant tumor, it must be one of the differential diagnoses of severe infantile and maternal anemia without any antecedent reason. The key point for diagnosis is the level of β HCG in a patient with hepatomegaly and anemia, which needs high index of suspicion. To sum up, in patients with no medical history, such as our patient, a combination of exact physical examinations and a high suspicion for this rare malignancy is helpful.

Acknowledgments

The authors appreciate the cooperation of the patient and his parents, who gave their consent.

Conflicts of interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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