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Case Study

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Acute Onset Non-Immune Hydrops in a Term Pregnancy Affected by Choriocarcinoma

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Précis: Choriocarcinoma can develop during a term pregnancy and can present with acute onset non-immune hydrops fetalis secondary to fetomaternal hemorrhage.

Abstract

Background: Intraplacental choriocarcinoma (IC) is a rare version of Gestational Trophoblastic Neoplasia (GTN) that can present during a term pregnancy.

Case: A 24-year-old multigravida presented at term with decreased fetal movement over several days and found to have non-reassuring fetal heart tracing and new onset fetal hydrops on ultrasound. At birth, the neonate was encephalopathic and severely anemic. Macroscopic and histologic evaluation of the placenta did not reveal any abnormalities. She was ultimately diagnosed with choriocarcinoma on postoperative day 20 when she had a dilation and curettage for heavy vaginal bleeding.

Conclusion: Non-immune hydrops fetalis is a rare presentation of IC and likely caused by fetomaternal hemorrhage from tumor invasion. IC should be suspected in new onset NIHF and suspected fetomaternal hemorrhage.

- Teaching Points:
- Choriocarcinoma can develop during a term pregnancy and can present with acute onset non-immune hydrops fetalis.
- Fetomaternal Hemorrhage is a cause of non-immune hydrops and the likely mechanism by which choriocarcinoma causes hydrops.
- Intraplacental Choriocarcinoma can easily be missed on gross and even microscopic evaluation of the placenta. Clinicopathologic correlation and communication with pathology is key to achieving a diagnosis.

Keywords: Antenatal complications; Fetomaternal Hemorrhage; Intraplacental; Pregnancy

Introduction

Gestational neoplastic disease (GTD) refers to a group of tumors marked by abnormal trophoblastic proliferation. These tumors can be divided into premalignant varieties such as partial and complete molar pregnancies, and malignant forms, such as invasive moles, choriocarcinoma, placental site and epithelioid trophoblastic tumors. Choriocarcinoma is a rare, aggressive form of GTD with an incidence of 1 in 40,000 pregnancies in Europe and North America [1]. While over 50% of choriocarcinoma occurs after a molar pregnancy, 25% of cases occur after a term or preterm gestation [2]. Even rarer are cases of intraplacental

choriocarcinoma (IC), which account for approximately 0.04% cases of GTD [3]. The presentation of IC is variable [4]. While some are clinically silent, [5-8] others are associated with antenatal complications, such as fetal demise, or with metastatic maternal or infantile disease [9]. Massive fetomaternal hemorrhage (FMH) with associated fetal hydrops [10-12] and severe anemia at birth has been reported [3,10,13-17]. We present a case of new onset fetal hydrops secondary to FMH due to unrecognized choriocarcinoma.

Case

A healthy 24 year-old Gravida 2 Para 1001 presented at 37 weeks and 5 days gestation to the obstetric triage unit for non-reassuring antenatal testing performed at her outpatient obstetric office. She had no significant past medical history. The fetus had urinary tract dilation of the left kidney at 20 weeks, seen on a routine anatomy ultrasound; however it had resolved on repeat ultrasound at 35 weeks gestation. Her blood type was O positive, and her type and screen was without antibodies. The patient reported decreased fetal movement for 2-3 days at her routine 37-week prenatal visit. At that time, a non-stress test (NST) was performed in the office and the fetal heart rate (FHR) notable for minimal variability and late decelerations. The patient was directed to OB triage at the local tertiary care hospital for further evaluation. In triage, the fetal heart tracing was nonreactive, again with minimal variability and occasional late decelerations. A biophysical profile (BPP) was ordered and performed immediately. The BPP noted a score of 2/10 (+2 points for fluid), however the ultrasound also showed a new diagnosis of fetal hydrops based on findings of fetal ascites, pleural effusions, and thickened skin measuring 14 mm. Due to these findings, primary cesarean section was recommended to expedite delivery. Cesarean section was uncomplicated. Ovaries were visualized at the time of surgery and looked normal. The placenta was sent to pathology for evaluation. Grossly, the placenta was large but without signs of infarcts or abnormalities. The pathologist reviewed representative sections, which showed normal placenta.

The infant was resuscitated and intubated by the neonatal intensive care team in the delivery room and transferred to the Neonatal Intensive Care Unit. The infant weighed 3.3kg and had APGARs of 1 and 5 at 1 minute and 5 minutes respectively. Cord gas was pH 6.96, base excess -17 and the infant was encephalopathic on exam, so passive cooling initiated. Poor perfusion and pallor were noted immediately at birth. The neonate subsequently had hypotension that improved with fluid resuscitation. Lactate was 18.4, but blood cultures were negative. Fetal hemoglobin was 2.1g/dL. The neonate was transfused 1 unit of packed red blood cells and 1 unit of fresh frozen plasma. The plan was for further blood transfusion and then partial exchange transfusion, however the patient expressed desire to switch to compassionate care. The infant died on the first day of life. The microarray was collected, however, not sent per parental request and the patient also declined fetal autopsy.

The patient was discharged from the hospital and returned on postoperative day 4 with a fever of 38.4 C and concerns for postpartum endometritis. She had significant fundal tenderness with no other localizing symptoms and a white blood cell count of 10.6. Transvaginal ultrasound showed a 10.3 mm endometrial stripe, without concerns for retained products. She received IV clindamycin and gentamicin until she was afebrile for 24 hours. She was discharged home with Bactrim.

On postoperative day 20, the patient again presented to the hospital, now with heavy vaginal bleeding. Transvaginal ultrasound showed a 17 mm endometrial strip with increased vascularity, concerning for retained products of conception. She underwent an exam under anesthesia and dilation and evacuation under ultrasound guidance. The pathology showed abnormal proliferation of malignant-appearing syncytiotrophoblasts and cytotrophoblasts with areas of hemorrhage and necrosis consistent with choriocarcinoma. No normal villi were seen.

Upon receipt of these results, the patient had a chest x-ray that was negative for disease and an hCG of 5388 IU/L. She was referred to gynecologic oncology who suggested she get a CT abdomen and pelvis as well as a head MRI to rule out metastasis. If the metastatic workup was negative, she would be classified as having low risk disease with a World Health Organization score of 3, secondary to development of choriocarcinoma following a term pregnancy and her elevated hCG [18]. The tentative treatment plan pending normal imaging was methotrexate and leucovorin until her hCG is negative, followed by consolidation therapy for 3 cycles thereafter. The patient however decided to get treatment in her home country, Italy, and did not follow up with our practice.

Discussion

Choriocarcinoma confined to the placenta is exceedingly rare and thought to account for approximately 2.3% of gestational choriocarcinoma cases.4 A systematic review of IC cases found that 50% of women were asymptomatic and a diagnosis of IC was made only after placental examination was performed secondary to other reasons, largely fetal distress at birth or cases of intrauterine fetal demise (IUFD) [4,10,13-16,19]. The true incidence of the disease is, therefore, unknown and likely underreported because histopathologic evaluation of placental tissue is not routinely performed following most deliveries.

Of the cases presenting with fetal distress, however, fetomaternal hemorrhage appears to be the most common, seen in over a quarter of live births [4] reported one of the first cases of FMH from choriocarcinoma [20]. While the mechanism is not fully understood, it is believed that malignant trophoblastic tissue invades the intervillous space and disrupts the placental barrier between fetal and maternal circulation [9,16,20]. Of the case reports describing FMH in relation to IC, similar patterns of presentation were noted, including maternal complaints of decreased fetal movements [10,11,13-16], new onset of fetal hydrops [10-12] abnormalities on fetal heart tracing including sinusoidal wave form or minimal variability with late decelerations [10,13-16]. At birth, severe neonatal pallor, low Apgar score, and severe anemia have been noted [11,13-16]. In our case, similar findings were noted, with the mother complaining of decreased fetal movement for several days, a fetal heart tracing with minimal variability and late decelerations, as well as neonatal pallor with severe anemia and a hemoglobin of 2.1 g/dL at birth. In this case, new onset fetal hydrops was also seen on BPP. To the authors' knowledge, this is the fourth case report of fetal hydrops associated with choriocarcinoma (search terms: choriocarcinoma, fetal hydrops, gestational trophoblastic disease, pregnancy). While a Kleihauer-

Betke test was not performed to assess for FMH, this is likely the cause of fetal anemia and subsequent non-immune fetal hydrops (NIFH) seen on presentation.

Conditions associated with FMH include abdominal trauma, placental abruption, manual removal of the placenta, and amniocentesis [21]. In over 80% of cases, however, the cause is unknown [22]. Some of these unknown cases may be from IC and it is imperative that it remain on the differential diagnosis as a cause for severe FMH diagnosed in the setting of an otherwise previously normal and uncomplicated pregnancy. In addition to gross, macroscopic examination of the placenta, microscopic, histopathologic examination of the placenta should also be performed in such cases.

Macroscopic evaluation of placentas found to have choriocarcinoma is for the most part unremarkable [5-7,9,11,16]. When lesions are present, they can be very small and easily missed, with sizes as small as 3-4 mm reported [23] and often grossly resemble an infarct [3,10]. In some cases, a diagnosis of IC was only made after a second re-evaluation of the placenta [5,14]. In one specific case, initial gross and histologic examination of the placenta did not show IC, however, after the presence of severe FMH was communicated to the pathologist, closer reinspection led to a diagnosis of IC [14]. In our case, histopathologic evaluation of the placenta was performed following delivery and found to be negative. It was not until dilation and curettage was performed, 20 days after delivery, for suspected retained products of conception in the setting of heavy vaginal bleeding, that the diagnosis of choriocarcinoma was made. Our case supports the theory that cases of choriocarcinoma following a term pregnancy likely start within the placenta and are frequently not detected because it is often a small focus, or because the placenta was not examined.

Conclusion

In summary, while IC is thought to be rare, it is likely underdiagnosed as many patients are asymptomatic, placentas are often macroscopically normal and not routinely sent for histologic evaluation, and even when they are, small foci of disease can easily be missed. In the setting of suspected FMH following an otherwise unremarkable pregnancy course, choriocarcinoma, while rare, should remain on the differential diagnosis. Additionally, relevant clinical information should be communicated to the pathologist as this can guide the evaluation of the placenta.

References

1. Lurain JR (2010) Gestational trophoblastic disease I: Epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol 203: 531-539.
2. Lurain JR (1990) Gestational trophoblastic tumors. Semin Surg Oncology 6: 347-353.
3. Sebire NJ, Lindsay I, Fisher RA, Seckl MJ (2005) Intraplacental choriocarcinoma: Experience from a tertiary referral center and relationship with infantile choriocarcinoma. Fetal Pediatr Pathol 24: 21-29.
4. Jiao L, Ghorani E, Sebire NJ, Seckl MJ (2016) Intraplacental choriocarcinoma: Systematic review and management guidance. Gynecol Oncol 141: 624-631.
5. Ganapathi KA, Paczos T, George MD, Goodloe S, Balos LL, et al. (2010) Incidental finding of placental choriocarcinoma after an uncomplicated term pregnancy: A case report with review of the literature. Int J Gynecol Pathol 29: 476-478.
6. Chung C, Kao MS, Gersell D (2008) Incidental placental choriocarcinoma in a term pregnancy: A case report. J Med Case Rep 2:1-4.
7. Barghorn A, Bannwart F, Stallmach T (1998) Incidental choriocarcinoma confined to a near-term placenta. Virchows Arch 433: 89-91.
8. Takai N, Miyazaki T, Yoshimatsu J, Moriuchi A, Miyakawa I (2000) Intraplacental choriocarcinoma with fetomaternal transfusion. Pathol Int 50: 258-261.
9. Liu J and Guo L (2006) Intraplacental choriocarcinoma in a term placenta with both maternal and infantile metastases: A case report and review of the literature. Gynecol Oncol 103: 1147-1151.
10. Jeong JE, Moon SH, Park KH, Shin N, Lee CH, et al. (2012) Fetomaternal hemorrhage caused by an intraplacental choriocarcinoma. Korean J Obstet Gynecol 55: 33.
11. Lee E and Cho H (2019) A Case of Intraplacental Choriocarcinoma with Pulmonary Metastasis. Case Rep Oncol 12: 802-806.
12. Zarafu IW, Tseng PI, Chuachingco J (1978) 1041 HYDROPS FETALIS, FETAL MATERNAL TRANSFUSION AND CHORIOCARCINOMA OF THE PLACENTA. Pediatr Res 12: 537.
13. She Q, Cheng Z, El-Chaar D, Luo F, Guo X, et al. (2018). Intraplacental choriocarcinoma coexisting with fetomaternal hemorrhage: Case report, chemotherapy management, and literature review. Medicine (Baltimore). 97: e9977.
14. Henningsen AKA, Maroun LL, Havsteen H, Svare J (2010) Massive fetomaternal hemorrhage caused by an intraplacental choriocarcinoma: A case report. Case Rep Med 2010: 3-5.
15. Peng HH, Ng ZP, Tang YH, Chua AAA, Huang KG (2016) Term pregnancy with choriocarcinoma presenting as severe fetal anemia and postpartum hemorrhage. Taiwan J Obstet Gynecol 55: 430-433.
16. Aso K, Tsukimori K, Yumoto Y, Hojo S, Fukushima K, et al. (2009) Prenatal findings in a case of massive fetomaternal hemorrhage associated with intraplacental choriocarcinoma. Fetal Diagn Ther 25: 158-162.
17. Blackburn GK (1976) Massive fetomaternal hemorrhage due to choriocarcinoma of the uterus. J Pediatr 89: 680-681.
18. World Health Organization (2014) Gestational trophoblastic neoplasia. 20th Expert Comm Sel Use Essent Med 2014:1-9.
19. Benirschke K, Lele SM, Crowder SE, Grafe MR (1999) Placental pathology casebook: Asymptomatic intraplacental choriocarcinoma diagnosed on routine placental examination. J Perinatol 19: 244-247.
20. Benson PF, Goldsmith KLG, Rankin GLS (1962) Massive foetal haemorrhage into maternal circulation as a complication of choriocarcinoma. Br Med J 1: 841-842.
21. Wylie BJ and D'Alton ME (2010) Fetomaternal hemorrhage. Obstet Gynecol 115: 1039-1051.
22. Rubod C, Deruelle P, Le Goueff F, Tunez V, Fournier M, et al. (2007) Long-term prognosis for infants after massive fetomaternal hemorrhage. Obstet Gynecol 110: 256-260.
23. Brewer JI and Mazur MT (1982) Gestational Choriocarcinoma: It's Origin in the Placenta during Seemingly Normal Nregnancy. Obstet Gynecol Surv 37: 19-21.