Case Reports in Oncology

Case Rep Oncol 2023;16:157–162
DOI: 10.1159/000529736
Received: January 18, 2023
Accepted: February 10, 2023
Published online: March 15, 2023

Case Report

Intraplacental Choriocarcinoma in Twin Pregnancy Causing Fetomaternal Haemorrhage and Single Twin Demise: Case Report

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Keywords
Choriocarcinoma · Fetomaternal haemorrhage · Twins · Gestational trophoblastic neoplasia

Abstract
Gestational choriocarcinoma is a rare aggressive form of gestational trophoblastic neoplasia. In cases of intraplacental choriocarcinoma, the tumour is confined to the placenta. Intraplacental choriocarcinoma in twin pregnancies is a very rare occurrence with less than 5 previously reported cases in the literature. In this case, a 34-year-old primiparous woman, pregnant with dichorionic diamniotic twins, underwent an emergency caesarean section for fetal distress at 35 weeks gestation after presenting in preterm labour. Twin A was delivered with no signs of life. The demise was attributed to fetomaternal haemorrhage (FMH) secondary to intraplacental choriocarcinoma. The mother's HCG normalised quickly postpartum with no radiological signs of metastatic disease. She has been managed conservatively with monthly HCG surveillance with no signs of recurrence. Twin B remains well with negative HCG surveillance. Although gestational choriocarcinoma can be aggressive and associated with poor obstetric outcomes, it has a good prognosis when diagnosed and treated early. The importance of detailed histopathological placental examination and clinical suspicion for choriocarcinoma following FMH is highlighted by this case.

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Introduction

Gestational choriocarcinoma is a rare form of gestational trophoblastic neoplasia (GTN). Global incidence is relatively unknown, with minimal data available [1]. In Europe and UK, the incidence is estimated to be 1:40,000–50,000 [2, 3]. Incidence is thought to increase with maternal age [1, 3]. Up to 50% of gestational choriocarcinomas follow complete hydatidiform molar pregnancies but 25–50% are associated with term pregnancies [3]. This highly aggressive tumour can present as persistent human chorionic gonadotrophin (HCG) levels postpartum, vaginal bleeding, or haemoptysis [1, 4]. Common sites of metastases are the lungs, liver, and brain [1, 2]. Although uncommon, dissemination to the fetus can occur [1]. Intraplacental choriocarcinoma (IC) is a rare type of gestational choriocarcinoma where the neoplasm is confined to the placenta. Diagnosis may be incidental or delayed as cases are often asymptomatic.

Case

Antenatally, a 34-year-old primiparous woman with spontaneously conceived dichorionic diamniotic twins was medically well with no comorbidities, a normal BMI, and a non-smoker. Her routine antenatal bloods and screening investigations were normal. She was commenced on progesterone pessaries at 24 weeks for a short cervix. Regular ultrasounds were performed as part of dichorionic diamniotic twin pregnancy monitoring. Growth of Twin A was normal throughout the pregnancy, however, Twin B was found to be small for gestational age at 28 weeks (8th percentile). All Doppler studies and amniotic fluid levels remained normal throughout, including at an ultrasound performed early during the 35th week. The patient presented a few days later in preterm labour and underwent an emergency caesarean section for fetal distress of Twin A. Twin A was born with no signs of life, profound anaemia (haemoglobin 21) and was unable to be resuscitated. Twin B was delivered with no complications. IC was incidentally found in Twin A's placenta on histopathological examination. Post-delivery and autopsy investigations identified fetomaternal haemorrhage (FMH) as the cause of this twin's demise. The choriocarcinoma appeared confined to the placenta with no dissemination to twin A. Staging cytotrophoblast (CT) of the brain, chest, abdomen, and pelvis of the mother showed no metastatic disease. The mother's HCG was 18 IU/L 1 month postpartum, measured due to the diagnosis of IC. This quickly normalised within 2 weeks and remains negative 11 months later. She did not require chemotherapy and is currently being managed conservatively with monthly HCG surveillance only. Twin B has had negative HCG monitoring throughout, with no choriocarcinoma found within the placenta. To date, both mother and infant remain well.

Placental Pathology

A 15 × 10 mm placental lesion with central necrosis was identified. Nests, irregular sheets, and tongues of atypical cells, including syncytiotrophoblast (ST), intermediate trophoblast (IT), and CT were present with disrupted villi seen focally in keeping with stromal invasion (shown in Fig. 1). Intravascular tumour was not identified. Immunohistochemistry confirmed trophoblastic lineage with positivity for GATA-3 (CT and IT), HCG (ST), and HPL (IT), supporting the diagnosis of choriocarcinoma (shown in Fig. 2, 3). The tumour appeared confined to the placenta, clear of the decidual surface. The CARE checklist has been completely by authors for this case report, attached as supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529736).

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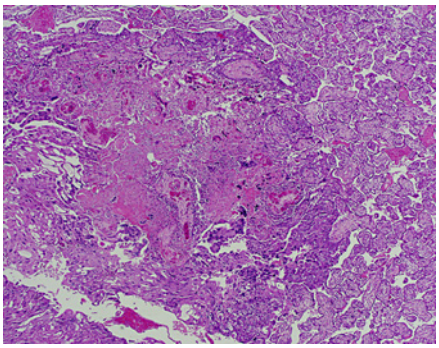

Fig. 1. Low power view of the tumour showing necrosis centrally, with sheets of atypical trophoblasts to the left and normal background placental villi to the right.

Discussion

Though rare, the diagnosis of IC is often made incidentally during placental analysis. True incidence of IC is therefore difficult to estimate as pathological analysis of the placenta is not routine following an uncomplicated pregnancy and delivery. One systematic review found IC accounted for 0.3% of all GTN identified [4]. Choriocarcinoma in twin pregnancies is a rare occurrence with very few cases published in the literature [5, 6]. Twin pregnancies with the presence of a complete hydatidiform mole and co-existent normal fetus are more common, although still rare [7]. In this case, diagnosis of IC was not suspected and only made when the placentas were sent for formal histopathological examination [5, 6]. Reports describe the incidental diagnosis of IC following poor obstetric outcomes such as FMH or fetal complications (fetal growth restriction, fetal death in utero) after which it is standard to formally review the placenta [2, 4, 8, 9]. No previous cases described twin demise.

Grossly, on slicing the placenta, the IC appears as a variably sized heterogeneous area with haemorrhage and necrosis. The histological appearance is of abnormal, triphasic trophoblastic cells including IT, CT, and ST that line the villous surface (and may invade), with solid areas of growth and areas of necrosis and haemorrhage [9, 10].

Choriocarcinoma has an excellent response to chemotherapy and is therefore associated with a good prognosis in the majority of cases. Literature estimates a cure rate of more than 99% for FIGO low-risk disease and 85–95% for those with metastatic high-risk disease [1, 10]. In cases where the tumour appears confined to the placenta with no dissemination or metastases, conservative management may be appropriate [2, 4, 11]. A systemic review from the Charing Cross Gestational Trophoblastic Disease Centre found that from 25 out of 62 women with IC that had been managed conservatively only one experienced choriocarcinoma relapse [4]. All patients, regardless of the management strategy, require close follow-up to ensure that they remain asymptomatic with a negative HCG [11]. Optimal duration of follow-up is unknown but is recommended for at least 12 months [10].

Poor fetal and neonatal outcomes can occur in cases of IC such as fetal growth restriction, fetal death in utero, prematurity, and anaemia [4, 12]. Poor outcomes are usually secondary to IC associated FMH. Metastatic disease within liveborn infants is rare and the prognosis for affected infants is usually good [4].

Prenatal diagnosis of IC remains difficult with no specific identifying biomarker, radiological features, or clinical signs. Whilst ultrasound plays a role in diagnosis of molar pregnancies, in IC, radiological imaging is used to determine extent of local disease or metastatic disease following histopathological confirmation or clinical suspicion [7, 13]. Clinical suspicion should be raised with high βhCG levels or unexplained FMH, in which case formal placental histopathology examination should be performed [14]. Routine general macroscopic inspection of the placenta occurs following all deliveries, however, as IC tumours

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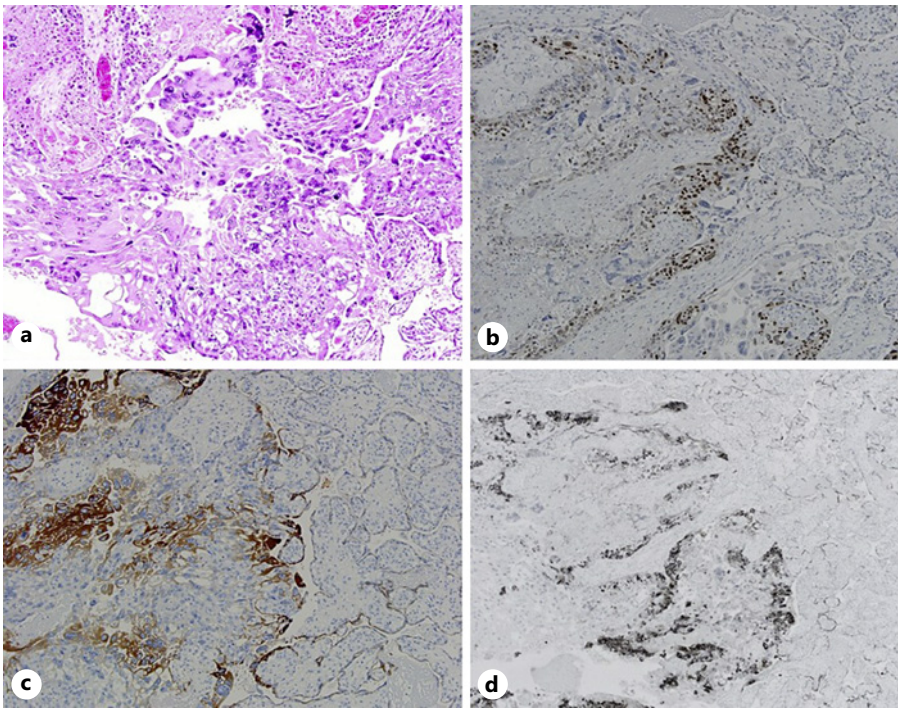

Fig. 2. High power view of the tumour shows a triphasic cell population (**a**), with immunohistochemical stains for GATA-3 highlighting the cytotrophoblasts and intermediate trophoblasts (**b**), human chorionic gonadotrophin staining syncytiotrophoblasts (**c**), and human placental lactogen highlighting intermediate trophoblasts (**d**).

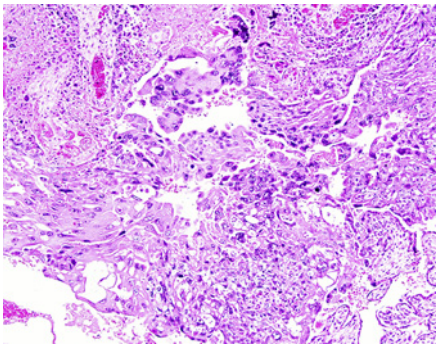

Fig. 3. High power view of tumour illustrating the triphasic population of atypical trophoblasts.

can be small and resemble infarcts they may not be identified without thorough histopathological examination [4, 15]. Some authors have suggested consideration of routine HCG surveillance postpartum in all women with unexplained FMH in order to identify GTN early [8, 16]. Presentation in the postpartum period with symptoms such as per-vaginal bleeding or haemoptysis necessitates quantitative HCG analysis to exclude metastatic GTN [16].

Conclusion

As highlighted by this rare case, perinatal diagnosis of IC can be difficult and can be associated with poor obstetric outcomes. Although aggressive, choriocarcinoma has a good prognosis when diagnosed and treated early [1]. Improved awareness by clinicians of the clinical presentations of IC and performance of HCG levels will promote earlier diagnosis translating to earlier management and better outcomes.

Statement of Ethics

This study was reviewed and approved by the Central Adelaide Local Health Network Human Research Ethics Committee, reference number 17380. Written informed consent has been obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding was received for this study.

Author Contributions

Dr. Catherine Schepisi and Prof. Martin Oehler were responsible for literature review, manuscript preparation, and editing. Dr. Jill Lipsett and Dr. Phoebe Dunsmuir were responsible for pathological examination, provision of histopathology images, description of placental pathology, and manuscript editing.

Data Availability Statement

All data generated or analysed during this study are included in this article and its online supplementary material files. Further enquiries can be directed to the corresponding author.

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