Malays J Pathol 2024; 46(1) : 91 – 94

CASE SERIES

Navigating an unexpected diagnosis – experience of a tertiary referral centre with two cases of intraplacental choriocarcinoma

Caleb LIM Chun Wei[1]*, Lavisha S. PUNJABI[2]*, Anju BHATIA[3], Qiu Ju NG[4], Gareth Peter JEVON[5], Ieera Madan AGGARWAL[4]

[1]Department of Obstetrics & Gynaecology, KK Women's & Children's Hospital, Singapore; [2]Department of Pathology & Laboratory Medicine, KK Women's & Children's Hospital, Singapore; [3]Department of Maternal-Fetal Medicine, KK Women's & Children's Hospital, Singapore; [4]Department of Gynaecological Oncology, KK Women's & Children's Hospital, Singapore; [5]Department of Pathology & Laboratory Medicine, KK Women's & Children's Hospital, Singapore.

Abstract

Intraplacental choriocarcinoma is a rare tumour, with approximately 62 reported cases. It may manifest as a spectrum of disease ranging from an incidental lesion diagnosed on routine placental examination to disseminated maternal and/or neonatal disease. In this case series, we presented two rare cases of intraplacental choriocarcinoma with extremely varied clinical presentations. The extremely varied clinical presentations of both patients described in the case series complicated the process of arriving at the diagnosis. In both cases, subsequent investigations showed no maternal or neonatal metastasis, and maternal serum beta-hCG levels downtrended with conservative management. We aim to highlight the importance of performing a detailed physical examination and evaluation of the patient and multidisciplinary management with oncology opinion. A detailed examination of the placenta should also be considered when faced with obstetric complications so that early diagnosis and the required management can be executed in a prompt fashion.

Keywords: choriocarcinoma, gestational trophoblastic disease, gynaecological oncology, placenta histology, hydatidiform mole

INTRODUCTION

Intraplacental choriocarcinoma (IC) is a rare malignant gestational trophoblastic neoplasm (GTN) arising from the placental chorionic villous trophoblast with only 62 cases reported in literature.[1] IC is a rare form of GTN which is confined to the placenta. Documented foetal and obstetric complications include foeto-maternal haemorrhage, placental abruption, foetal hydrops, anaemia, intrauterine growth restriction and foetal death.[2] This letter highlights two such cases.

Case 1

A 29-year-old woman with two previous full-term vaginal deliveries and a first-trimester miscarriage had an uneventful pregnancy with normal antenatal tests. She went into spontaneous labour at 37 weeks of pregnancy. Intrapartum cardiotocography (CTG) showed reduced variability with late decelerations necessitating an emergency caesarean section. The baby girl weighing 2900 g with APGAR scores of 2, 5, 6 had to be intubated at birth due to profound respiratory distress and severe anaemia (haemoglobin 3.0 g/dL). On placental inspection, some lobes appeared boggy and yellowish, prompting the obstetrician to send it for pathologic evaluation. Kleihauer-Betke testing revealed evidence of foeto-maternal haemorrhage.

The placenta weighed 468 g (50th to 75th percentile) with a marginal insertion of a hypercoiled three-vessel umbi lical cord. Cut sections showed a 1 cm pale-yellow nodule (Figure 1A), a 0.8 cm infarct at the periphery of the disc and scattered ill-defined pale areas.

**Address for correspondence:* Caleb LIM Chun Wei, Resident, Department of Obstetrics & Gynaecology, KK Women's & Children's Hospital, Singapore, 100 Bukit Timah Rd, Singapore 229899. Email: *caleblim@gmail.com*

* These authors contributed equally to this work (co-first authors).

Microscopic examination revealed multi-focal villous infarcts with IC, best seen at the margins of the infarcts surmounting the chorionic villi and filling the intervillous spaces (Figures 1B, 1C 1D) There was no vascular invasion.

Computed Tomography (CT) scan of the patient's thorax, abdomen and pelvis did not detect any lymphadenopathy or distant metastasis. The patient declined chemotherapy, opting for surveillance with beta-hCG monitoring. The maternal serum beta-hCG decreased from 2446.6 IU/L on post-operative day three to normal levels six weeks postnatally. Radiological investigations in the neonate did not reveal any evidence of metastasis. The infant's serum beta-hCG levels on Day 1 were 132 IU/L and normalised by Day 25 of life. The patient and infant are currently well.

Case 2

In the second case, a 29-year-old primigravida had routine antenatal course with a normal fetal anomaly scan at 20 weeks. Growth scan at 33 weeks revealed foetal abdominal ascites with no evidence of cardiomegaly, hydrops or foetal anaemia. Amniotic fluid index was normal. Maternal blood pressure was normal with no proteinuria. Serological tests for toxoplasma, cytomegalovirus and parvovirus B19 infections were negative. Repeat ultrasound one week later showed fetal hydrops, persistent abdominal ascites and skin oedema with normal foetal dopplers. CTG showed unprovoked shallow decelerations with poor variability necessitating an emergency caesarean section. The baby boy weighing 2900 g with APGAR 5,7 was cyanosed at birth with gross abdominal distention and required immediate intubation. In view of foetal hydrops, the placenta was sent for histological evaluation.

The placenta weighed 690g (> 97th percentile) with an unremarkable three-vessel umbilical cord. Cut sections revealed a 5 x 3 x 1.5 cm friable, necrotic lesion (Figure 2A) near the cord insertion. Microscopic examination showed a tumour with extensive central necrosis (Figure 2B), rimmed by markedly pleomorphic trophoblastic cells surmounting the chorionic

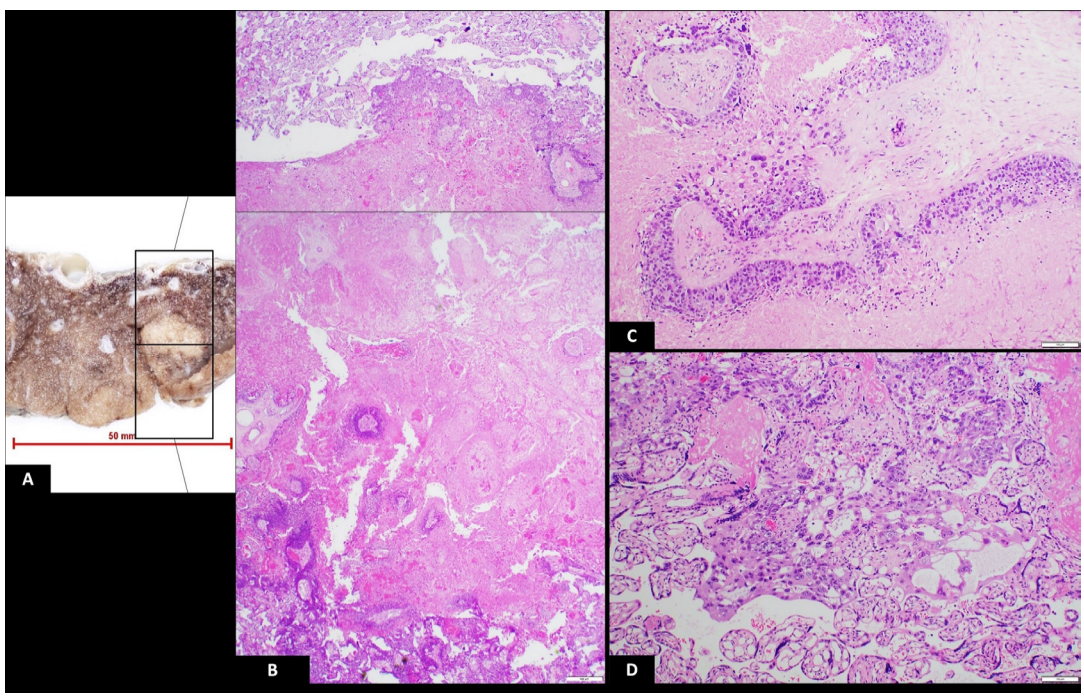

FIG. 1: (A) After formalin fixation, a 1cm nodule in the placental disc displayed a firm, pale yellow appearance. (B) This corresponded to an infarct with a haemorrhagic and cellular rim at low power microscopic examination (H&E stain, 20x magnification, scale at the bottom right of the image). (C) At high power examination, the cellular rim of the infarct was composed of aggregates of malignant cytotrophoblasts and synctiotrophoblasts surmounting the stem villi (H&E stain, 100x magnification, scale at the bottom right of the image) and (D) chorionic villi (H&E stain, 100x magnification, scale at the bottom right of the image).

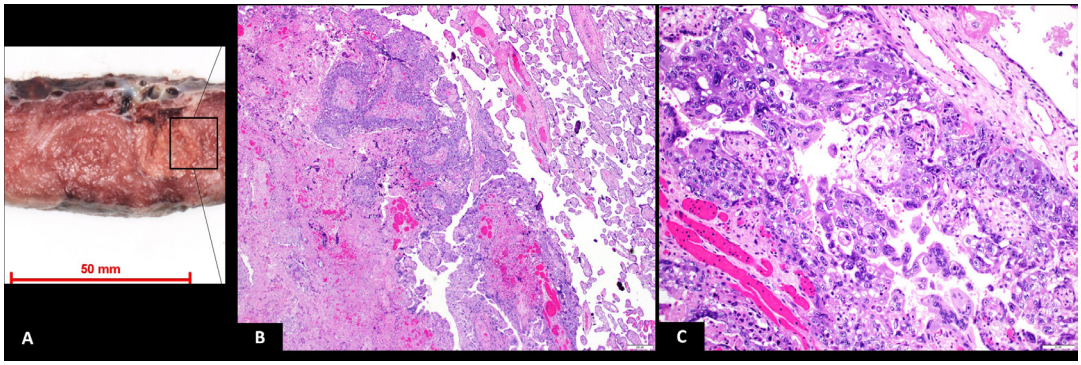

FIG. 2: (A) The friable and necrotic lesion on macroscopic examination of the placenta. (B) Tumour with extensive central necrosis and haemorrhage (H&E stain, 40x magnification, scale at the bottom right of the image). (C) At high power examination, the viable component of the tumour at the periphery was represented by malignant cytotrophoblasts as well as syncytiotrophoblasts arising from the chorionic villi and expanding the intervillous space (H&E stain, 200x magnification, scale at the bottom right of the image).

villi and expanding the intervillous spaces with no vascular invasion (Figure 2C).

Radiological investigations in both the mother and the neonate did not reveal any lymphadenopathy or distant metastasis. Initial maternal serum beta-hCG levels of 19635.5 IU/L on postoperative day two, normalised three months postnatally. Neonatal ascitic fluid cytology was negative for malignancy and his beta-hCG levels normalised by day 18 of life. The patient and child are currently well.

DISCUSSION

We presented two cases of IC diagnosed on placental histopathological examination. GTN is rare, with incidence ranging from 1 in 40000-50000 pregnancies.[3-5] IC comprises 2% of gestational choriocarcinomas diagnosed.[6] Risk factors include extremes of childbearing ages (<20 and > 45 years old) and prior history of gestational trophoblastic disease or miscarriage.

Clinical presentations of intraplacental choriocarcinoma can be varied. In a systematic review by Jiao *et al*[1], more than half of the cases were asymptomatic and diagnosed on placental histological examination triggered by antenatal or intrapartum complications e.g., foeto-maternal haemorrhage, unexplained stillbirth, or foetal distress. The other patients presented with disease-related symptoms, predominantly vaginal bleeding or distant metastasis causing respiratory or neurological symptoms.

The two cases highlight varied presentations as well. In case 1, profound foetal anaemia and foeto-maternal haemorrhage prompted the operating obstetrician to examine the placenta. Noting its grossly abnormal appearance, histopathological examination was requested, leading to the diagnosis of intraplacental choriocarcinoma. This illustrates the value of clinical examination of the placenta at the time of delivery. In case 2, foetal hydrops prompted formal histopathological examination of the placenta. In both cases, the attending obstetrician was informed personally of the diagnosis by the pathologist.

Although both the cases displayed the typical morphology of IC choriocarcinoma microscopically, they showed different macroscopic appearances. In Case 1, the tumour presented as multi-focal infarct-like areas with unusual discolouration in the placental disc, while in Case 2, the tumour presented as a solitary friable necrotic lesion.

Acknowledging inconsistencies in the sampling of infarcts and thrombi in routine placental examination, meticulous search for unusual features - such as friable or papillary appearance[7] and unusual colouration [8] is recommended, especially with a previous history of hydatidiform mole.[2]

Following the histopathological diagnosis of IC, a detailed physical and radiological examination with serial beta-hCG monitoring of both the mother and neonate is advisable to exclude distant metastasis and plan management. Published studies suggest a framework for diagnosis, investigations, management, and surveillance of the disease.[1] However, IC is underdiagnosed as it is typically clinically indolent and masquerades as placental infarcts. In cases with metastatic disease, chemotherapy is the mainstay of treatment. In those with

non-metastatic disease, several authors describe successful surveillance with serial beta-hCG monitoring only, while others suggest chemotherapy, surgery or both.[3-5, 9]

CONCLUSION

In conclusion, this case series illustrates the challenges of diagnosing and managing intraplacental choriocarcinoma and adds to the limited literature on conservative management in localised disease.

Acknowledgements: The authors would like to express their sincere thanks to the patients for their consent to have cases presented in this case series.

Patient consent statement: Both patients described in the cases gave their consent for their cases to be discussed in this manuscript.

Authors' contributions: All authors contributed equally.

Conflict of Interests: The authors declare no conflict of interests.

REFERENCES

1. Jiao L, Ghorani E, Sebire NJ, Seckl MJ. Intraplacental choriocarcinoma: systematic review and management guidance. Gynecol. Oncol. 2016 Jun 1;141(3):624-31.
2. Liu J, Guo L. Intraplacental choriocarcinoma in a term placenta with both maternal and infantile metastases: a case report and review of the literature. Gynecol. oncol. 2006 Dec 1;103(3):1147-51.
3. Hamad E, Al Omari W, Anderson L, Househ Z. Intraplacental choriocarcinoma: a case report. Pathology. 2021 Jul 1;53:S26-7.
4. She Q, Cheng Z, El-Chaar D, Luo F, Guo X, Wen SW. Intraplacental choriocarcinoma coexisting with fetomaternal hemorrhage: case report, chemotherapy management, and literature review. Medicine. 2018 Apr;97(14).
5. Savage P, Monk D, Hernandez Mora JR, *et al*. A case of intraplacental gestational choriocarcinoma; characterised by the methylation pattern of the early placenta and an absence of driver mutations. BMC cancer. 2019 Dec;19(1):1-0.
6. Lee E, Cho H. A case of intraplacental choriocarcinoma with pulmonary metastasis. Case Rep. Oncol. 2019;12(3):802-6.
7. Ganapathi KA, Paczos T, George MD, Goodloe S, Balos LL, Chen F. Incidental finding of placental choriocarcinoma after an uncomplicated term pregnancy: a case report with review of the literature. Int J Gynecol. Pathol. 2010 Sep 1;29(5):476-8.
8. Barghorn A, Bannwart F, Stallmach T. Incidental choriocarcinoma confined to a near-term placenta. Virchows Archiv. 1998 Jul;433(1):89-91.
9. Caldas RF, Oliveira P, Rodrigues C *et al*. Intraplacental choriocarcinoma: rare or underdiagnosed? Report of 2 cases diagnosed after an incomplete miscarriage and a preterm spontaneous vaginal delivery. Case rep. med. 2017 Apr 16;2017.