Case Reports in Women's Health 31 (2021) e00341

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Late diagnosis of intraplacental choriocarcinoma co-existing with fetomaternal haemorrhage causing fetal demise: A case report

S. Monteiro *, M. Burling, H. Doyle

Westmead Hospital, Western Sydney Local Health District, Sydney, Australia

ARTICLE INFO

Keywords:
Choriocarcinoma
Intraplacental
Fetomaternal haemorrhage
Trophoblastic disease

ABSTRACT

Intraplacental choriocarcinoma (IC) is a rare disease, occurring in approximately 1 in 50,000 pregnancies. A 33-year-old woman, gravida 2 para 0, sustained an intrauterine fetal death due to fetomaternal haemorrhage (FMH) at 36 weeks of gestation after presenting with decreased fetal movements in the days prior. The placenta macroscopically appeared normal. However, histological examination revealed an intraplacental choriocarcinoma. Assessment of this woman's quantitative beta human chorionic gonadotropin (bHCG) level was negative and a computerized tomography scan of her chest, abdomen and pelvis revealed no metastatic disease yet a bulky uterus. After discussion at a multidisciplinary tumour board meeting, the patient had endometrial curettings to rule out any uterine pathology and serial bHCG tests until one year post-partum. Following this, the patient successfully carried and delivered a live female term infant. Although FMH is a rare clinical manifestation of IC it should always alert clinicians to investigate the cause further, through urgent and careful histopathological examination of the placenta. This will allow for appropriate management with chemotherapy if indicated and a reduction in maternal morbidity and mortality.

1. Background

Intraplacental choriocarcinoma (IC) is a rare and highly malignant form of gestational trophoblastic disease (GTD) [1]. It is a focal neoplastic proliferation of the chorionic villous trophoblast [2]. It occurs in approximately 1 in 50,000 pregnancies and diagnosis is unfortunately late, after identification of maternal metastatic disease [3]. Due to its rareness, information available is still limited, as it accounts for no more than 0.04% of all GTD [2]. As placental histopathological examination is not routinely performed and as lesions have an inconspicuous appearance, the incidence is possibly underestimated [4].

Most choriocarcinomas arise as primary uterine tumours in women at the extremes of age, with the majority of trophoblastic tumours commonly metastasizing to the lungs. IC, however, may co-exist with or following abortion, ectopic pregnancy, hydatidiform mole or term gestation [5]. IC co-existing with an intrauterine gestation is exceedingly rare and carries a very high mortality rate of the mother and fetus, 62% and 65% respectively [5]. Due to the rarity of IC, the aetiology, pathogenesis, natural history and adequate therapy of IC are still unknown, and it is not surprising that the cases reported in the literature describe different outcomes. Some authors describe fatal outcomes associated with maternal or fetal/infant metastatic disease, while others report no implications [2]. Complications such as intrauterine growth restriction, premature birth, fetal anaemia and transplacental haemorrhage have also been reported [2,4,6,7].

FMH occurring in combination with IC is even rarer, with only 25 cases confirmed in the literature to date [3]. The clinical manifestation of FMH was reported in 9.91% of case reports published between 1998 and 2015 in English [8]. Massive FMH should alert clinicians to the possibility of choriocarcinoma arising from the placenta [9].

2. Case Presentation

A 33-year-old Caucasian woman, gravida 2 para 0, presented to an obstetric assessment unit with decreased fetal movements at 35 weeks and 6 days of gestation. On review, fetal movements had resumed and cardiotocography revealed a possible isolated deceleration. The patient was referred for an ultrasound scan, which was done 5 days later and which confirmed a fetal death in-utero. Her labour was induced at 36 weeks and 6 days of gestation and she proceeded to a normal vaginal birth of an extremely pale stillborn male infant weighing 2580 g. Her post-natal course was significant with a 1.7 L post-partum haemorrhage

* Corresponding author.
E-mail address: samantha.monteiro@health.nsw.gov.au (S. Monteiro).

https://doi.org/10.1016/j.crwh.2021.e00341
Received 11 May 2021; Received in revised form 6 July 2021; Accepted 7 July 2021
Available online 10 July 2021

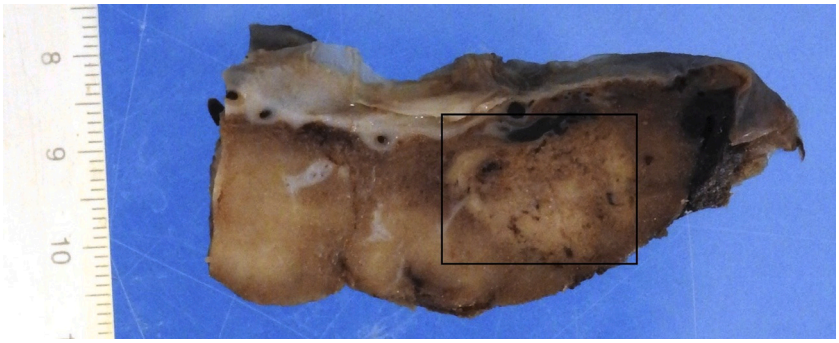

Fig. 1. Macroscopic tumour.

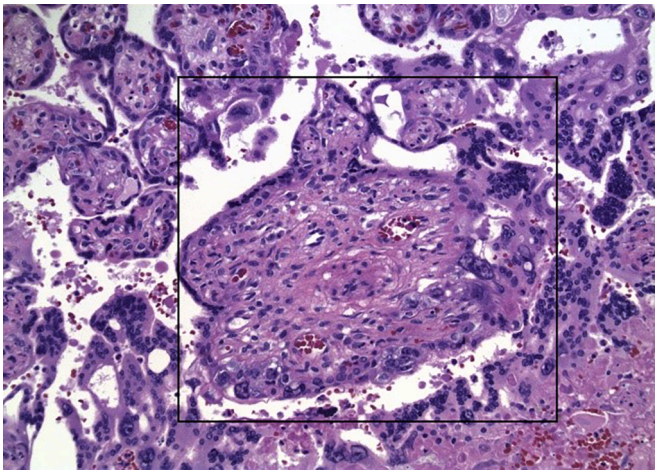

Fig. 2. Haematoxylin & eosin stain, magnification x200.

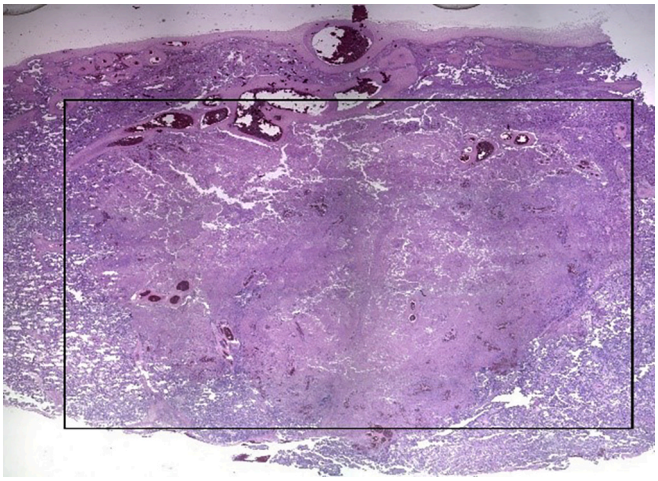

Fig. 3. Haematoxylin & eosin stain, magnification x40.

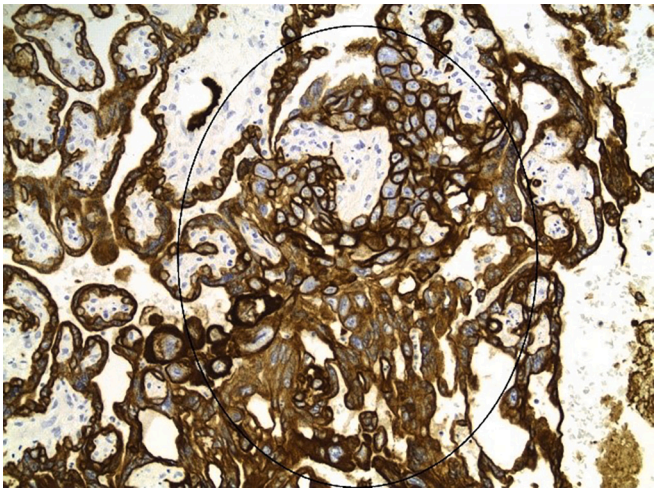

Fig. 4. Cytokeratin stain, magnification x200.

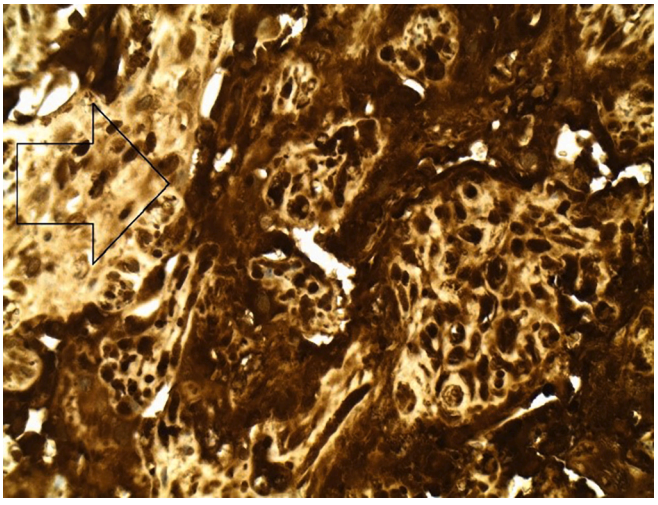

Fig. 5. bHCG stain, magnification x400.

from uterine atony and a Kleihauer test positive for 74 mL of fetal blood within maternal circulation (equivalent to 29.7 mL/kg of fetal blood loss). The placenta appeared normal.

Prior to this, the pregnancy had been uneventful, with a first trimester ultrasound scan indicating low risk and non-invasive testing was negative for aneuploidy. A morphology scan showed a low-lying placenta and normal fetal morphology, and further ultrasound scans at 32 and 35 weeks were normal. The patient's obstetric history included a previous surgical termination of pregnancy at 6 weeks of gestation and a past medical history of herpes simplex virus. The patient was otherwise fit and healthy and a non-smoker.

Histological examination of the placenta was delayed due to clinical backlog and completed when the fetal autopsy was conducted. Histology of the placenta revealed a 21x19mm haemorrhagic IC invading the full thickness of the placenta, 7 months post-delivery (Fig. 1). Macroscopically the placenta appeared normal. Microscopically there was evidence of extensive loss of functional placental tissue due to high-grade fetal

vascular malperfusion, maternal vascular malperfusion including early infarct formation, secondary compensatory changes including increasing vascularity of villi and circulating fetal haematopoietic percursors, and low-grade chronic villitis (likely villitis of unknown aetiology) (Figs. 2–5). The autopsy showed mild to moderate maceration with no internal or external malformations and no convincing evidence of asymmetrical growth restriction with global growth parameters on the 50th percentile. There was evidence of acute and chronic intrauterine stress most likely due to fetal anaemia and placental insufficiency as well as bilateral pleural effusions, chronic involutional changes in the thymus, adrenal glands and growth plate, and acute hypoxic changes in the central nervous system. No evidence of fetal metastasis was seen.

The patient was reviewed by the gynaecology oncology team following the IC diagnosis and had reportedly been well and asymptomatic since delivery. A computerized tomography scan of her chest, abdomen and pelvis was conducted and was normal aside from a bulky uterus and the patient's bHCG at time of review was <2 mIU/mL. A curettage was completed for the findings of the bulky uterus and revealed proliferative endometrium with evidence of breakdown. The patient was managed conservatively with serial monitoring of bHCG levels for 12 months, which remained <2 mIU/mL. At the time of this report, the patient has proceeded to have a subsequent successful term delivery of a live female infant.

3. Discussion

IC is a well described but rare form of GTD, and is most commonly reported as an incidental finding in the third trimester placenta examined for an unrelated indication. The incidence is likely to be higher than reported, due to underdiagnosis as the majority of cases are asymptomatic with no indication for placental pathological examination [10].

FMH is a common associated event and was reported in up to 30% of cases in one series [10]. Benson et al. described the first case of massive fetal haemorrhage into maternal circulation as a complication of choriocarcinoma, in 1962 [9]. Large fetal haemorrhages into the maternal circulation are probably caused by invasion of trophoblastic tissue into the intervillous space. Massive FMH should therefore alert obstetricians and pathologists to the possibility of choriocarcinoma arising from the placenta, especially in the absence of obvious antecedent causes such as traumatic diagnostic amniocentesis or external cephalic version [11].

Histological detection of IC is also known to be difficult because of the frequently small size of the lesion and because of its similar appearance to more common benign lesions of the placenta [9]. This was initially the case for the patient above during preliminary histological reporting as well as the placenta appearing macroscopically normal. It is advisable to hold on to a strict protocol for careful pathological examination of the placenta in any suspected cases of FMH, as proposed by Koike et al., and follow-up of serum bHCG post-partum [9,12].

IC is furthermore assumed to represent de novo neoplastic transformation within the index pregnancy, and a history of previous GTD is rare. Recurrence in subsequent pregnancies is therefore also rarely described [6].

Maternal and fetal metastasis is a known complication [6]. The presence of tumour in the intervillous space and at the maternal surface is of concern for maternal metastasis. Despite the delayed analysis of the placenta in this case, the patient was fortunate and had no evidence of metastasis after appropriate follow-up. Consequentially to this case, the tertiary centre has now changed its practice to conduct histopathological placental analysis immediately after delivery of an IUFD infant, especially when associated with a positive Kleihauer test, instead of concurrently with an autopsy at a later stage.

4. Conclusion

Although FMH is a rare clinical manifestation of IC, it should alert clinicians to suspect IC and prompt urgent histopathological examination of the placenta, especially when associated with IUFD. This will allow early referral to and appropriate management by a gynaecology oncology team to reduce the rate of maternal and fetal morbidity and mortality.

Contributors

S. Monteiro drafted the initial manuscript.

M. Burling was involved in the primary care of the patient and provided guidance and editing of the draft of the case report.

H. Doyle was involved in the primary care of the patient and provided guidance and editing of the draft of the case report.

All authors approved the final manuscript before submission.

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

No funding from an external source supported the publication of this case report.

Patient consent

Obtained.

Provenance and peer review

This case report was peer reviewed.

References

[1] J. Hensley, B. Shviraga, Metastatic Choriocarcinoma in a term pregnancy: a case study, MCN 39 (2014) 8–15.
[2] R. Ferraz Caldas, P. Oliveira, C. Rodrigues, 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 (2017) 1–4.
[3] Q. She, Z. Cheng, D. El-Chaar, et al., Intraplacental choriocarcinoma coexisting with fetomaternal haemorrhage: case report, chemotherapy management, and literature review, Medicine 97 (2018) 14.
[4] J. Jeoung, S. Moon, K. Park, et al., Fetomaternal haemorrhage caused by an intraplacental choriocarcinoma, Korean J. Obstetr. Gynecol. 55 (1) (2012) 33–37.
[5] E.P. Igbodike, C.A. Adepiti, K.O. Ajenifuja, et al., An unusual presentation of choriocarcinoma co-existing with pregnancy, successful delivery, and treatment: a case report and literature review, Niger. J. Clin. Pract. 24 (2021) 445–451.
[6] L. Jiao, E. Ghorani, N.J. Sebire, et al., Intraplacental choriocarcinoma: systemic review and management guidance, Gynaecol. Oncol. 141 (3) (2016) 624–631.
[7] N.J. Sebire, E. Jauniax, Fetal and placental malignancies: prenatal diagnosis and management, Ultrasound Obstet. Gynecol. 33 (2) (2009) 235–244.
[8] M. Mangla, D. Singla, H. Kaur, et al., Unusual clinical presentations of choriocarcinoma: a systemic review of case reports, Taiwan. J. Obstetr. Gynecol. 56 (2015) 1–8.
[9] H. Nagel, F. Vandenbussche, et al., Intraplacental choriocarcinoma as an unexpected cause of intrauterine death at term, Int. J. Gynaecol. Cancer 17 (2007) 1337–1343.
[10] N. Takai, T. Miyazaki, et al., Intra-placental choriocarcinoma with fetomaternal transfusion, Pathol. Int. 50 (2000) 258–261.
[11] P. Benson, K. Goldsmith, et al., Massive foetal haemorrhage into maternal circulation as a complication of choriocarcinoma, Br. Med. J. 1 (1962) 841–842.
[12] Y. Koike, H. Wakamatsu, Y. Kuroki, et al., Fetomaternal haemorrhage caused by intraplacental choriocarcinoma: a case report and review of literature in Japan, Am. J. Perinatol. 23 (2006) 49–52.