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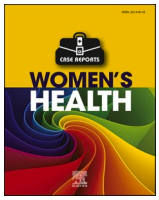

Uterine perforation associated with gestational trophoblastic disease and arteriovenous malformation: A case report

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ABSTRACT

This case report outlines the clinical course of a young woman who presented as haemodynamically unstable due to uterine perforation. She had undergone suction dilation and curettage three weeks prior and received a diagnosis of complete molar pregnancy. During her most recent acute presentation, an emergency laparotomy revealed a full-thickness fundal uterine rupture in a region of newly identified arteriovenous malformation. Haemostasis was achieved with the primary repair of the perforation. She was subsequently diagnosed with gestational trophoblastic neoplasm (GTN), a condition characterised by abnormal proliferation of trophoblastic tissue. She received three courses of methotrexate followed by a two-month course of dactinomycin. At one-year surveillance, she had made a complete recovery.

1. Introduction

Gestational trophoblastic disease (GTD) describes a spectrum of pregnancy-associated conditions arising from the abnormal proliferation of trophoblastic tissue [1,2]. In the literature, the incidence ranges from 1:500 to 1:1000 pregnancies [1,2]. The disease spectrum spans from benign conditions, such as partial and complete molar pregnancies, to malignant conditions labelled gestational trophoblastic neoplasm (GTN), including invasive mole, choriocarcinoma, placental site trophoblastic tumour (PSTT), and epithelioid trophoblastic tumour [1–4].

Patients with GTD often present with elevated levels of beta-human chorionic gonadotropin (BHCG) for their gestational age. Other associated findings include vaginal bleeding, hyperemesis gravidarum, hyperthyroidism, and hypertension [1–4]. An examination may reveal a uterus that is enlarged for its gestational age and vaginal bleeding often described as having a 'prune juice'-like colour due to the liquefaction of old blood. In the context of a complete molar pregnancy, ultrasound imaging might show clusters of cystic spaces, pseudo-anembryonic pregnancy, or a mass with variable echogenicity. The 'snowstorm' pattern observed with older imaging technology represents the proliferation of hydropic villi [1–5]. In such cases, histopathology from tissue samples, taken either at the time of examination or during dilation and curettage, confirms the diagnosis [1–4].

GTN is a progression from GTD. A diagnosis necessitates one of the following: a plateau of BHCG levels over three weeks; an increase of 10% across three values over two weeks; persistent BHCG at six months post-evacuation; histopathologic confirmation; or the presence of metastatic disease [4]. GTN is further categorised as either a low-risk or high-risk disease in line with FIGO and WHO scoring systems [4]. For those diagnosed with low-risk disease, the prognosis is excellent, with remission achieved in nearly 90% of patients through single-agent chemotherapy [4]. In contrast, high-risk disease treated with multi-agent regimens has remission rates of 70% and long-term survival rates as high as 95% [4].

The need for fertility preservation becomes a topic of discussion when invasive and metastatic disease is evident [6]. The following case elaborates on fertility preservation in such contexts, along with prognosis and follow-up.

2. Case Presentation

A 30-year-old nulliparous woman was referred to the gynaecology service with a suspected molar pregnancy. She had a rapidly rising BHCG, which increased from 5000 to 300,000 within 48 h. An index referral ultrasound revealed multiple cystic spaces within the endometrial cavity. Following uncomplicated suction dilation and curettage, histopathology confirmed a complete molar pregnancy (Fig. 1). Routine follow-up was arranged with a plan of weekly BHCG tracking as per RANZCOG guidelines [7]. At review three weeks post-surgery, the

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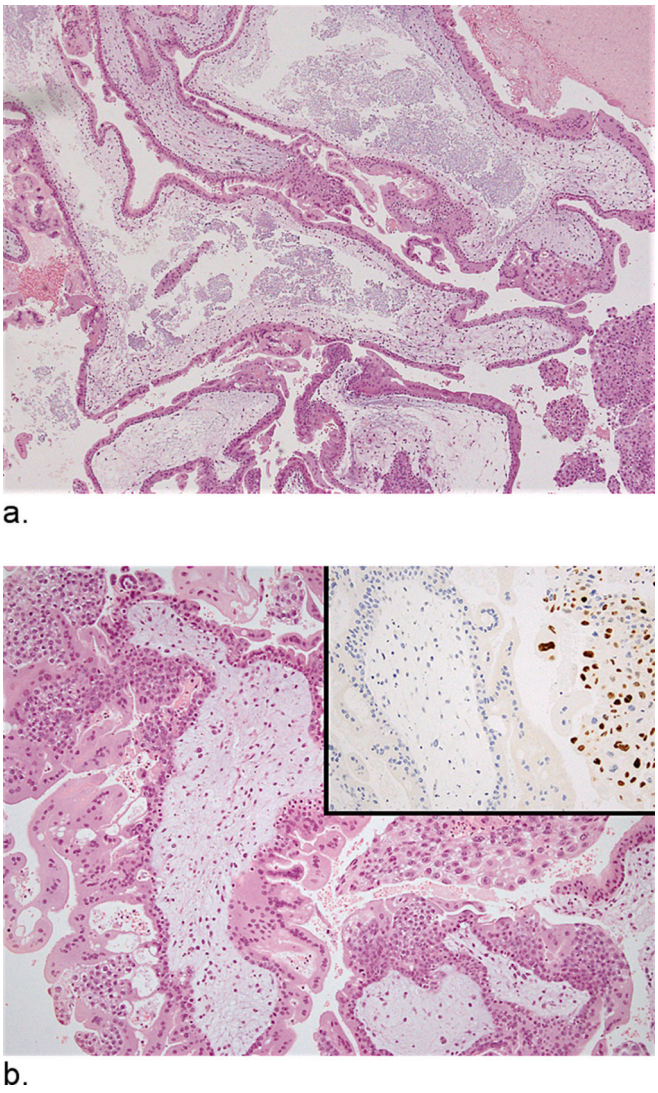

Fig. 1. a. Low-magnification image showing markedly enlarged chorionic villi with central cisterns; b. Chorionic villi displaying circumferential trophoblast proliferation. The cytotrophoblast and villous stromal cells are negative for p57 (inset, left), whereas the extra villous trophoblast demonstrates retained p57 expression (inset, right).

patient reported a single episode of painless per vaginal bleeding despite an appropriately down-trending BHCG (Table 1).

Tertiary-level ultrasound was arranged. Within the uterine fundal myometrium was a new region of high-grade turbulent flow and overlapping arterial and venous waveforms, consistent with an AVM (Fig. 2). However, due to the lack of classically dilated and tortuous vessels, the final impression was of an atypical AVM due to uterine instrumentation. The absence of a focal or metastatic uterine mass made GTN unlikely. Given the appropriately down-trending BHCG and radiological impression, close outpatient monitoring was planned.

Twelve hours later, the patient presented to the emergency department (ED) with new non-pleuritic epigastric pain and haemodynamic instability. The pain was precipitated by eating and was not associated with nausea, vomiting, or bowel changes. On arrival at the ED, her observations were: BP 85/36, HR 72, RR 27, SPO2 100% RA, and a temperature of 36.0 °C. Clinically, she appeared pale and had a distended abdomen with guarding and peritonism. Blood tests taken upon arrival are documented in Table 1. Notably, her haemoglobin level was 104. After fluid resuscitation and liaison with general surgery, a CT scan was done (Fig. 3). It revealed significant free fluid, suspected to be a

Table 1
Comparison of blood tests taken upon diagnosis, arrival at the Emergency Department, at discharge, at weekly follow-up, and upon commencement of methotrexate and daptomycin. Urea, Electrolytes and Liver function tests were completed prior to commencement of methotrexate and daptomycin, both found to be within normal ranges and remained within normal range throughout treatment.

		Results prior to dilation and curettage	Results at follow-up 3 weeks post dilation and curettage	Results on arrival to ED	After 30 min in the ED	Results day 1 post laparotomy	Results 1 week post laparotomy	Results 2 weeks post laparotomy	Results at time of Gynae Oncology takeover of care	Results at first Methotrexate administration	Results at the time of Daptomycin administration	Units of measurement	Normal range
Full Blood Picture	HB	120		104	84	117				119	129	g/L	115–160
	WCC	10.28		12	14	6.3				4.6	4.86	g/L	5–15
	Platelets	302		356	321	445				279	326	g/L	150–400
	HCT	0.36		0.31	0.25	0.35				0.36	0.39	g/L	0.33–0.43
	Neutrophils	7.9		7	11	15				2.3	2.9	g/L	
Urea and Electrolytes	Na	135		139	138	138						mmol/L	135–145
	K	4.2		2.9	3.5	4.1						mmol/L	3.5–4.5
	Bicarb	18		21	21	21						mmol/L	22–25
	Urea	4.2		4.9	4.9	4.9						mmol/L	3–8
	Creatinine	42		55	55	42						mmol/L	<70
	EGFR	>90		>90		>90							>60
Liver function tests	Bilirubin			3								g/L	<20
	ALT			17								g/L	<35
	ALP			36								g/L	<35
	Lipase			20								u/L	<40
	CRP			<1									<15
	BHCG	382,000	46,400	34,500		3830	10,400	11,900	15,100	7720	811	IU/L	<5

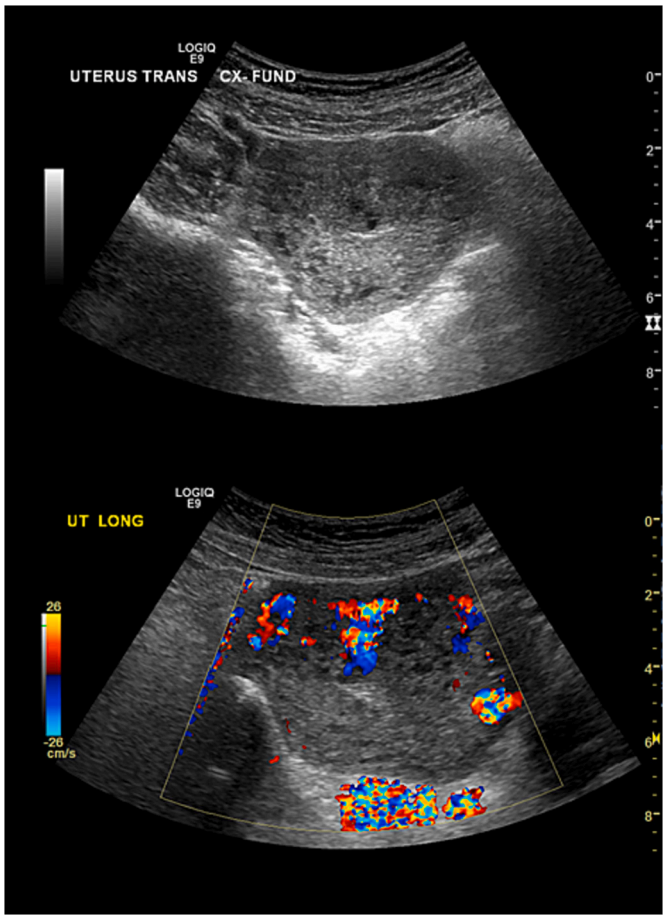

Fig. 2. Tertiary-level ultrasound performed 3 weeks post-dilation and curettage. Images of the fundal myometrium show highly vascular areas and overlapping arterial and venous waveforms consistent with a diagnosis of atypical AVM.

haemoperitoneum, with an area of active bleeding from the uterine fundus. This corresponded to the region of the atypical AVM identified during ultrasound earlier that day. After stabilisation with three units of PRBC, she underwent an emergency exploratory laparotomy. Here, the haemoperitoneum was confirmed, and a full-thickness perforation was identified in the region approximating the AVM. No uterine mass or suspicious tissue growth was found intraoperatively. This localised perforation was attributed to rupture of the AVM given the clinical course of events, absence of free fluid on ultrasound earlier in the day and three-week delay between dilation and curettage and clinical presentation. The perforation was repaired in two layers using 3.0 Monocryl, and haemostasis was achieved using a fibrillar. The estimated total blood loss from the perforation was 3.5 L.

Postoperatively, the patient was transferred to the ICU for inotropic support. While in the ICU, she received an additional three units of PRCB, two units of FFP, and one unit of platelets. She showed significant post-surgical improvement and was weaned off inotropes and vasopressors by the second day. Due to the possible invasive nature of the AVM, despite the down-trending BHCG, gynaecology oncology opinion was sought. Invasive disease was not suspected and outpatient follow-up with BHCG tracking was advised, with the plan to continue until consecutive negative BHCG, evidence of plateau or rise in levels sufficient to fulfil criteria for GTN.

Close outpatient monitoring was commenced. By the second week of monitoring (after the laparotomy) BHCG levels had risen by over 10%, triggering a diagnosis of GTN (see Table 1). Oncology services assumed patient care. A CT scan of her chest, abdomen, and pelvis, as well as an

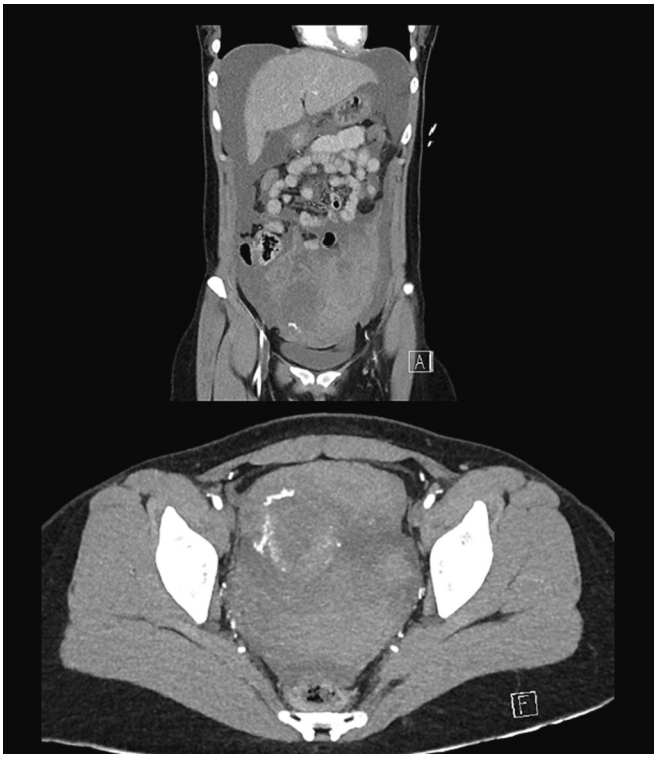

Fig. 3. CT of the abdomen performed shortly after arrival at the emergency department revealed significant haemoperitoneum. During both arterial phase and venous phases, the images demonstrate contrast extravasation at the uterine fundus, indicating an area of high-velocity active haemorrhage. This region is close to the abnormal vascularity observed on ultrasound, suggestive of bleeding from an AVM.

MRI scan of her brain, excluded either local or distant metastasis. She underwent three courses of methotrexate without a favourable response, prior to commencing dactinomycin. Negative BHCG levels were achieved within two months of dactinomycin commencement. At her 12-month follow-up, BHCG levels remained negative.

3. Discussion

GTD presenting as uterine perforation with bleeding from an AVM is a rare confluence of two uncommon gynaecological conditions [8–12]. Uterine rupture due to GTD, on its own, is infrequently reported in the literature [8–12]. Among the few case reports available, most presentations were noted in pregnancies that were initially believed to be normal [8–12]. Lobo et al. and David-West et al., in their respective case reports, described patients who presented with pain and haemoperitoneum, and in whom invasive mole was identified only during laparotomy [8,9]. In these instances, the breach of the uterine myometrium and protrusion of malignant tissue led to substantial intrabdominal bleeding. Both institutions opted for uterine artery embolisation as an initial step to aid haemostasis prior to laparotomy [9].

Significantly in this case, the patient also presented with AVM, a recognised but infrequent complication of uterine instrumentation in the management of GTD [14,15]. This aligns with the solitary case report by Lamrissi et al., in which an AVM was observed post-uterine instrumentation during management of molar pregnancy [15]. Contrary to the current case, this patient presented with significant per-vaginal bleeding, rather than intra-abdominal bleeding, as a precursor to neovascularisation [15]. There are no documented instances of intrabdominal bleeding associated with an AVM in the context of GTD, emphasising the distinctiveness of this case presentation. Although such presentations are rare, the consequences of a new diagnosis of AVM in

cases of GTD should prompt more extensive investigations and heightened vigilance during management planning.

The treatment of unstable patients with GTD, beyond immediate stabilisation, is contingent on the resources at hand and the patient's specific circumstances [8–15]. Lobo et al. and David-West et al. detailed successful fertility-conserving procedures using wedge resection, repeat dilation and curettage, and uterine artery embolization. Unfortunately, patients presenting with late-stage invasive disease presentation and haemodynamic instability may require a life-saving hysterectomy, and fertility preservation is rarely an option [8–15]. For those considering fertility-preserving strategies, the potential risk of recurrence and disease progression must be factored into management plans [4,6].

While the progression of GTD to GTN is uncommon, the incidence is not negligible. Approximately 15–25% of complete moles and 0.5–4% of partial moles progress to malignant disease [4]. Treatment of invasive mole and choriocarcinoma (FIGO stages up to 3) yields high cure rates—around 90%—with single-agent chemotherapy [4]. Higher-grade diseases, those at stage 4 and above, as well as PSTT and epithelioid trophoblastic tumour, require at least multi-agent regimens to achieve remission [4]. Response rates can be as high as 70% [4].

In cases managed with fertility-sparing modalities, the recurrence rates reported in the literature range from 1% to 4% following one molar pregnancy, and this increases to 20% after two molar pregnancies [4,6]. After treating a molar pregnancy, the rates of successful conception and delivery stand at 67%, with a spontaneous pregnancy loss rate of 18% [4,6]. From individual cases noted in the literature, both Lobo et al. and David et al. reported successful pregnancies. The potential for subsequent successful pregnancies in such patients is encouraging [6,8,9]. Collectively, these cases underscore the significance of tailoring patient management, swiftly identifying 'at risk' patients, and allowing time to develop patient-specific management strategies.

4. Conclusion

This case report describes the rare coalescence of GTD with uterine perforation and AVM, and the management of the resulting surgical emergency. By consistently maintaining a heightened vigilance for rare and serious complications, the management of GTD can be tailored to offer the most favourable outcomes, including fertility preservation. This case accentuates the value of multidisciplinary collaboration and customised management strategies in provision of patient care.

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Contributors

Lauren Fisher was involved in patient care, conception of the case, acquisition and interpretation case information, undertaking the literature review, and drafting and revision of the article.

Amin Bahabri was involved in patient care, conception of the case, and drafting and revision of the article for critical appraisal and important intellectual content.

Anna Clare was involved in editing and review of the original article for important intellectual content.

Babak Shakeri was involved in patient care, and review of the original article for important intellectual content.

All authors approved the final submitted manuscript.

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Patient consent

Obtained.

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Conflict of interest statement

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

References

[1] C. Maheut, I. Rollin, P. Baissas, P. Panel, J. Niro, Management of uterine rupture during molar pregnancy, J. Gynecol. Obstet. Hum. Reprod. 50 (7) (2021) 102058, https://doi.org/10.1016/j.jogoh.2020.102058. ISSN 2468–7847.

[2] D.I. Bruner, A.M. Pritchard, J. Clarke, Uterine rupture due to invasive metastatic gestational trophoblastic neoplasm, West. J. Emerg. Med. 14 (5) (2013) 444–447, https://doi.org/10.5811/westjem.2013.4.15868. PMID: 24106538; PMCID: PMC3789904.

[3] H.Y.S. Ngan, M.J. Seckl, R.S. Berkowitz, et al., Diagnosis and management of gestational trophoblastic disease: 2021 update, Int. J. Gynecol. Obstet. 155 (2021) 86–93, https://doi.org/10.1002/ijgo.13877.

[4] H.Y.S. Ngan, M.J. Seckl, R.S. Berkowitz, Y. Xiang, F. Golfier, P.K. Sekharan, J. R. Lurain, L. Massuger, Diagnosis and management of gestational trophoblastic disease: FIGO, 2021, https://doi.org/10.1002/ijgo.13877.

[5] L.L. Lima, R.C. Parente, I. Maestá, J. Amim Junior, J.F. de Rezende Filho, C. A. Montenegro, A. Braga, Clinical and radiological correlations in patients with gestational trophoblastic disease, Radiol. Bras. 49 (4) (2016 Jul–Aug) 241–250, https://doi.org/10.1590/0100-3984.2015.0073 (PMID: 27777478; PMCID: PMC5073391).

[6] U. Joneborg, L. Coopmans, N. van Trommel, M. Seckl, C.A.R. Lok, Fertility and pregnancy outcome in gestational trophoblastic disease, Department of Pelvic Cancer, Karolinska University Hospital, Karolinska Institute Department of Women's and Children's Health, Stockholm 171 76, Sweden, 2023.

[7] Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), Management of Gestational Trophoblastic Disease. [Internet], Available from: https://ranzcog.edu.au/wp-content/uploads/2022/05/Management-of-gestational-trophoblastic-disease.pdf, March 2017.

[8] R.M. Lobo, M. Taha, J.J. Herod, A. Al Ansari, S. Syed, H. Al Malik, H. Farghaly, Management of acute haemorrhage following chemotherapy for invasive molar pregnancy by embolisation and conservative fertility–sparing surgery, Gynecol. Oncol. Rep. 32 (2020) 100556.

[9] G. David-West, S. Jeganathan, N. Cohen, S. Maddineni, B. Friedman, S. Cohen, Conservative management of uterine rupture in gestational trophoblastic neoplasia, Gynecol. Oncol. Rep. (32) (2020 Jan 30) 100539, https://doi.org/10.1016/j.gore.2020.100539. PMID: 32072004; PMCID: PMC7011027.

[10] S. Kittur, Ramlingappa A. Venktesh, A rare case of invasive mole with silent uterine perforation, Int. J. Reprod. Contracept. Obstet. Gynecol. 2 (1) (2013 Mar) 109–110. www.ijrcog.org. pISSN 2320–1770 | eISSN 2320–1789.

[11] M. Gueye, et al., Choriocarcinoma with uterine rupture presenting as acute hemoperitoneum and shock, Int. J. Reprod. Contracept. Obstet. Gynecol. 6 (3) (2017 Mar) 1141–1143. www.ijrcog.org. pISSN 2320–1770 | eISSN 2320–1789.

[12] A. Jha, et al., Invasive mole causing uterine perforation: a case report and literature review, Ijsit 8 (3) (2019) 554–560.

[13] S. Aminimoghaddam, A. Maghsoudnia, Unusual presentation of invasive mole: a case report, J. Reprod. Infertil. 18 (1) (2017 Jan–Mar) 205–209 (PMID: 28377901; PMCID: PMC5359859).

[14] A.S. El-agwany, Uterine intramural persistent mole: a case report following molar pregnancy evacuation with arteriovenous malformation, Egypt. J. Radiol. Nucl. Med. 45 (4) (2014) 1291–1294, https://doi.org/10.1016/j.ejrnm.2014.08.005.

[15] A. Lamrissi, A.F. Mabengui, M. Mourabbih, M. Jalal, K. Fichtali, S. Bouhya, Acquired uterine arterio-venous malformation post molar pregnancy suction–curettage: 2 case reports, 2023.