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Full length article

Vaginal metastasis in gestational trophoblastic neoplasia: Experience from Sheffield trophoblastic disease Centre and recommendations for management

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ABSTRACT

Introduction: Gestational trophoblastic neoplasia (GTN) is rare in the UK, with an estimated incidence of one in 50,000 live births. Cases of vaginal metastasis are even rarer, with only eight case series reporting 187 cases over the past 40 years. Management recommendations in the literature are scarce despite the potential risk of massive, potentially life-threatening vaginal haemorrhage.

Methods: This retrospective cohort study with interval analysis was performed at Sheffield Trophoblastic Disease Centre. It included all patients diagnosed with GTN with documented evidence of vaginal metastases between 1 January 1974 and 31 December 2023.

Results: Twenty-five patients with GTN and vaginal metastases were identified during the study period, accounting for < 1 % of all GTN registrations during this period. All patients had chemotherapy representative of chemotherapeutic regimens employed at the time of diagnosis. Vaginal metastases were treated to resolution by chemotherapy alone in 76 % of cases. In addition to chemotherapy, 12 % of patients were managed with vaginal packing, 4 % underwent localized excision, 4 % underwent internal iliac embolization, and 12 % received targeted radiotherapy. Forty-four percent of patients had repeated blood transfusions due to persistent haemorrhage associated with the vaginal metastasis. One patient died from disease, 80 % achieved complete remission (cured), and 16 % (recently diagnosed) are in remission.

Conclusion: The presence of vaginal metastases in patients with GTN has little prognostic significance, and their presence should not alter management plans. Tailored treatment should be determined by patient factors, with chemotherapeutic regimens based upon World Health Organization prognostic scores. A conservative management approach should be considered, as most cases will resolve with chemotherapy alone.

Introduction

Gestational trophoblastic disease (GTD) embodies a spectrum of cellular proliferative diseases derived from placental trophoblasts, encompassing both benign diagnoses (complete and partial hydatidiform mole) and malignant conditions (invasive mole, choriocarcinoma, placental site trophoblastic tumour and epithelioid trophoblastic tumour), collectively known as 'gestational trophoblastic neoplasia' (GTN).

GTD remains relatively rare in the UK, with a calculated incidence of one in 714 live births. GTN presents even less frequently, with an estimated incidence of one in 50,000 live births [1]. Despite its infrequency, the cure rate for post-molar GTN approaches 100 % in the UK [2], achieved through tailored management protocols determined by various patient factors, culminating in an International Federation of Gynecology and Obstetrics (FIGO) stage [3] and a World Health Organization (WHO) prognostic score [2].

The most common site of metastasis in patients with GTN is the lung, followed by the vagina [4]. However, cases of vaginal metastasis are rare, reported to occur in 4.5–27 % of cases of GTN. At the time of writing, five case reports have been published in the literature over the previous 5 years [5–9], and eight case series reporting 187 cases have

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been published over the previous 40 years [10–17]. Whilst vaginal metastases are thought to be of little prognostic significance [11,18,19] due to the remarkable response of these tumours to chemotherapeutic regimens, patients may present with life-threatening haemorrhage. As such, an understanding of the management of vaginal metastases is essential for anyone dealing with such an event.

This study aimed to review the local experience of Sheffield Trophoblastic Disease Centre (STDC) in the management of vaginal metastases in patients with GTN; to compare this with international literature; and to formulate guidance for clinicians encountering such patients, especially those working predominantly within the field of GTN.

Methods

A retrospective cohort study with interval analysis was performed at STDC, Sheffield, UK. The clinical database at STDC was searched for all patients diagnosed with GTD or GTN, with documented evidence of vaginal metastases, between 1 January 1974 and 31 December 2023. All patients with vaginal metastases identified at primary diagnosis were included in the study. No cases of recurrent disease were included. As patients are rarely examined vaginally at quaternary referral centres, all cases of vaginal metastasis were diagnosed by higher imaging, including computed tomography or magnetic resonance imaging (MRI).

The database was cross-referenced with, where appropriate, patient notes and the trust-based integrated clinical environment system (established web-based requesting and reporting service) to confirm histopathological findings and imaging results, where necessary.

Data were collated regarding year of registration, age at registration, ethnicity, histological diagnosis, FIGO stage at presentation, WHO risk score, risk category (low risk, high risk, ultra-high risk), pre-treatment human chorionic gonadotrophin (HCG) level, MRI results, treatment received (including additional treatments for vaginal metastasis), location and size of vaginal metastasis (where available), and overall

Table 1
Vaginal metastases in gestational trophoblastic neoplasia at the Sheffield Trophoblastic Disease Centre: Demographic Data.

Patient no.	Year of diagnosis	Age at diagnosis (years)	Ethnicity	Histological diagnosis	Pre-treatment HCG	FIGO stage at presentation	WHO risk core	Risk category	Treatment
1	1974	39	White British	Choriocarcinoma	10,400,000	III	7	HR	IMMTX
2	1974	21	White British	Choriocarcinoma	75,000	IV	10	HR	IMMTX, IVA, CP
3	1974	27	White British	Complete hydatidiform mole	3945	I	2	LR	IMMTX
4	1975	45	White British	Partial hydatidiform mole	12,000	IV	7	HR	IMMTX, AVC
5	1976	38	White British	Complete hydatidiform mole	4122	I	4	LR	IMMTX
6	1977	26	White British	Choriocarcinoma	26,100	III	7	HR	IMMTX, AVC, ITMA, VP
7	1977	53	White British	Choriocarcinoma	169,918	III	8	HR	IMMTX, AVC
8	1978	23	White British	Choriocarcinoma	663,300	IV	8	HR	IMMTX, AVC
9	1978	30	Black Caribbean	Choriocarcinoma	960,000	III	9	HR	IMMTX
10	1981	31	White British	Choriocarcinoma	32,440	III	7	HR	IMMTX
11	1997	32	Black Caribbean	Choriocarcinoma	183,630	III	12	HR	MAE, IVA
12	1998	26	Pakistani	Choriocarcinoma	88,298	I	9	HR	MAE
13	1998	31	White British	Choriocarcinoma	88,398	III	7	HR	MAE
14	2000	31	White British	Complete hydatidiform mole	20,664	III	5	LR	IMMTX, EA
15	2002	40	White British	Choriocarcinoma	58,348	III	15	UHR	MAE
16	2008	30	White British	Partial hydatidiform mole	39,205	I	3	LR	IMMTX
17	2009	21	White British	Complete hydatidiform mole	13,105	I	3	LR	IMMTX
18	2011	39	Unknown	Choriocarcinoma	18,801	III	6	LR	MAE
19	2016	15	White British	Complete hydatidiform mole	49,628	II	5	LR	IMMTX
20	2017	27	White British	Complete hydatidiform mole	6652	II	2	LR	IMMTX
21	2018	34	White British	Twin pregnancy with mole	242,504	IV	16	UHR	EP, EMA, IMMTX
22	2023	34	White British	Complete hydatidiform mole	47,167	II	5	LR	IMMTX, IVA
23	2023	55	Asian	Choriocarcinoma	73,555	III	15	UHR	EP, EMA
24	2023	22	White British	Choriocarcinoma	10,908	III	7	HR	EMA
25	2023	41	White British	Post-partum choriocarcinoma	1367	IV	8	HR	EP/EMA

HCG, human chorionic gonadotrophin; FIGO, International Federations of Gynecology and Obstetrics; WHO, World Health Organization; LR, low risk; HR, high risk; UHR, ultra-high risk; AVC, actinomycin, vincristine, cyclophosphamide; CP, cyclophosphamide; EA, etoposide, cytarabine; EMA, etoposide, methotrexate, actinomycin; EP, etoposide, cisplatin; ITMA, hydroxyurea, vincristine, methotrexate, leucovorin, cyclophosphamide, actinomycin D, adriamycin, melphalan; IVA, intravenous actinomycin D; MAE, methotrexate, dactinomycin, etoposide; MTX, methotrexate; IMMTX, low-dose methotrexate; VP, etoposide.

outcome of treatment.

Major haemorrhage was defined as loss of more than one circulating blood volume within 24 h (approximately 70 ml/kg or approximately 5 l in a 70-kg adult), loss of 50 % of total blood volume in < 3 h, or bleeding > 150 ml/min.

Ethnicity was determined using the list of ethnic groups from the Office for National Statistics 2021 census [20]. Stage and risk score were calculated according to the FIGO staging system [3] and the WHO scoring system [2].

Baseline statistical analysis was performed following cleaning and coding of data. Where appropriate, the results were analysed using Chi-squared test (GraphPad Prism Version 9.3.1). As the study was performed in the context of a service review, ethical approval was not required.

Results

In total, 25 patients with GTN and vaginal metastases were treated between 1 January 1974 and 31 December 2023 at STDC. This accounted for < 1 % of all GTN registrations during this period. Median age was 31 years (range 15–55 years). Most patients were White British (n = 21, 84 %) two (8 %) were Black Caribbean, and two (8 %) were Asian or Asian British.

The primary diagnosis was choriocarcinoma in 14 (56 %) patients, complete mole in seven (28 %) patients, partial mole in two (8 %) patients, post-partum choriocarcinoma in one (4 %) patient, and a molar twin pregnancy in one (4 %) patient (Table 1).

The majority of patients presented with FIGO stage III (n = 12, 48 %) or IV (n = 5, 20 %) disease, three had stage II disease (12 %), and five were initially considered to have stage I disease (20 %) but were ultimately considered to have stage II disease because of the presence of a vaginal metastasis. WHO risk scores ranged between 2 and 16; nine (36 %) patients were regarded as low risk (score ≤ 6), 13 (52 %) patients were regarding as high risk (score ≥ 7), and three (12 %) patients were regarded as ultra-high risk (score ≥ 13).

The location of the vaginal metastasis was recorded in 15 (60 %) patients. Of these, the vaginal metastasis was located on the anterior vaginal wall in 13 (87 %) patients, on the right lateral vaginal wall in one (6.5 %) patient, and one (6.5 %) patient had multiple metastases located on the posterior and lateral vaginal walls (Table 2).

All patients were treated with chemotherapy representative of chemotherapeutic regimens employed at the time of diagnosis, and dependent upon WHO risk score categorization (Table 1).

Vaginal metastases were treated to resolution by chemotherapy alone in 19 (76 %) patients. Three (12 %) patients were also managed with vaginal packing, one of whom (4 %) also underwent local excision of the vaginal metastasis, and one (4 %) underwent internal iliac embolization. Three (12 %) patients underwent targeted radiotherapy as well as chemotherapy. In total, 11 (44 %) patients had repeated blood transfusions due to persistent haemorrhage associated with vaginal metastases.

The overall outcomes for patients in this study were as follows: one (4 %) patient died, 20 (80 %) patients achieved complete remission (cured), and four (16 %) patients, diagnosed in 2023, are currently in remission.

Discussion

GTN classically disseminates via a haematogenous route. The vagina is supplied by the vaginal and uterine arteries, which are branches of the internal iliac artery. The vaginal arteries anastomose with a branch of the uterine artery to form azygos arteries of the vagina, which run longitudinally on the anterior and posterior walls of the vagina. The vaginal wall is highly vascularized with both a venous and arterial plexus [21]. Vaginal metastases have been shown to communicate with the markedly dilated arteriovenous channels created in the pelvis by

Table 2
Location and management of vaginal metastases in gestational trophoblastic neoplasia at Sheffield Trophoblastic Disease Centre.

Patient no.	Year of diagnosis	Location	Size of lesion on MRI (mm)	Management	Patient outcome
1	1974	Not recorded	45	Chemotherapy alone	Complete remission
2	1974	Not recorded	Not recorded	Chemotherapy, radiotherapy, multiple blood transfusions	Died from disease
3	1974	Not recorded	Not recorded	Chemotherapy alone	Complete remission
4	1975	Not recorded	40	Chemotherapy, radiotherapy	Complete remission
5	1976	Not recorded	7	Chemotherapy alone	Complete remission
6	1977	Not recorded	45	Chemotherapy alone	Complete remission
7	1977	Not recorded	Not recorded	Chemotherapy, radiotherapy, multiple blood transfusions	Complete remission
8	1978	Not recorded	10	Chemotherapy alone	Complete remission
9	1978	Not recorded	40x30	Chemotherapy alone	Complete remission
10	1981	Not recorded	15	Chemotherapy alone	Complete remission
11	1997	Anterior vaginal wall	50	Chemotherapy, multiple blood transfusions	Complete remission
12	1998	Anterior vaginal wall	50x30	Chemotherapy, multiple blood transfusions	Complete remission
13	1998	Anterior vaginal wall	15	Chemotherapy, multiple blood transfusions, vaginal packing	Complete remission
14	2000	Anterior vaginal wall	Not recorded	Chemotherapy alone	Complete remission
15	2002	Right lateral wall	Not recorded	Chemotherapy, multiple blood transfusions, vaginal packing, internal iliac artery embolization	Complete remission
16	2008	2 posterior vaginal wall, 1 left lateral vaginal wall	20	Chemotherapy alone	Complete remission
17	2009	Anterior vagina fornix	37x38x26	Chemotherapy alone	Complete remission
18	2011	Anterior vaginal wall	Not recorded	Chemotherapy, multiple blood transfusions, vaginal packing, excision of vaginal lesion	Complete remission
19	2016	Anterior vaginal wall	50	Chemotherapy alone	Complete remission
20	2017	Anterior vaginal wall	12	Chemotherapy, multiple blood transfusions	Complete remission
21	2018	Anterior vaginal wall	65	Chemotherapy, multiple blood transfusions	Complete remission

(continued on next page)

Table 2 (*continued*)

Patient no.	Year of diagnosis	Location	Size of lesion on MRI (mm)	Management	Patient outcome
22	2023	Anterior vaginal wall	50	Chemotherapy, multiple blood transfusions	In remission
23	2023	Anterior vaginal wall	50	Chemotherapy alone	In remission
24	2023	Anterior vaginal wall	Not recorded	Chemotherapy, multiple blood transfusions	In remission
25	2023	Anterior vaginal wall	20–30	Chemotherapy alone	In remission

MRI, magnetic resonance imaging.

GTN [19]. It is therefore not surprising, regarding the vascular supply of the vagina, that the majority (87 %) of vaginal metastases (with a documented location) in this study, and in other case series, (76 %) [10–13,15,16], were in the lower third of the anterior vaginal wall.

As a result of an abundant vascular supply, patients with vaginal metastases are at risk of life-threatening bleeding events requiring implementation of a major haemorrhage protocol; early liaison with haematology is therefore essential. The findings of this study, where 44 % of patients required repeated blood transfusions due to persistent haemorrhage from vaginal metastases, are in line with data published in prior case series [10,11,13–17], where 67 of 156 (43 %) patients were recorded as having major haemorrhage.

The potential benefit of a highly vascularized vaginal wall in patients with vaginal metastases is that it makes the lesions receptive to chemotherapy [17]. The present study supports this concept, as vaginal metastases were treated to resolution by chemotherapy alone in 76 % of patients; this finding is mirrored by previous case series [10–17]. The main difference between the present study and the literature concerns the incidence of vaginal metastases in the GTN population, with an incidence rate < 1 % in the present study compared with 4–36 % in the literature [22,23]. However, case series reveal that the incidence of vaginal metastases worldwide is more likely to range between 4.5 % and 16 % [12–15,17], as, although Ghaemmaghami et al. [16] reported rates of 27 %, these data are skewed as they only included GTN cases with lung metastases, which is not representative of a GTN population (Table 3).

It is likely that the incidence of vaginal metastases in the study population is low as small asymptomatic lesions may not be detected on imaging, and patients do not undergo routine speculum or vaginal examinations on presentation at STDC. Patients in the UK are usually diagnosed relatively early. Home pregnancy tests have been available since the 1970 s [24], with tests being inexpensive, readily available, and able to detect trace levels of HCG from as early as 8 days post-ovulation. Also, since the establishment of early pregnancy assessment units in the early 1990 s [25], ultrasound is readily available to women presenting with complications in early pregnancy. Intervention occurs relatively quickly, with products of conception reviewed histologically in a timely manner, potentially resulting in a diagnosis of GTD or GTN. Whilst ultrasound detection of molar pregnancy remains a diagnostic challenge (sensitivity 52.2 %, specificity 92.6 %) [26], there has been progress since the first description of the classical snowstorm appearance of hydatidiform mole on ultrasound by Donald et al. in 1963 [27].

Data from previous studies [10–17] (excluding 12 patients lost to follow-up [14,17] and 12 patients with unreported outcomes [17]) in patients presenting with GTN complicated by vaginal metastases revealed that 151 of 166 (91 %) patients achieved complete remission and 15 (9 %) died from disease (Table 4). The present study revealed a 96 % survival rate, with one death (patient diagnosed with choriocarcinoma in 1974 at 21 years of age). This overall outcome is not surprising as the UK boasts a remarkable near-100 % cure rate for post-molar GTN; patients have been referred to and managed at specialist centres for over 50 years [2].

However, the literature suggests that the detection of vaginal metastases following molar pregnancy should not be the sole indication for starting chemotherapy, as spontaneous resolution occurred in four

Table 3
Vaginal metastases in patients with gestational trophoblastic neoplasia (GTN): comparative data from reported case series.

Reference	Year of diagnosis	Total no. of patients with GTN	No. of patients with vaginal metastases	Histological diagnosis and antecedent pregnancy	FIGO stage				WHO risk score		Location of vaginal metastasis
					I	II	III	IV	Low	High	
Bloch et al. [10]	NR	NR	6	Choriocarcinoma = 4 Invasive mole = 2	Not recorded				2	4	Anterior = 6
Goldberg et al. [11]	NR	NR	5	Abortion = 2 Term pregnancy = 3	0	1	4	0	1	4	Anterior = 4 Posterior = 1
Wong et al. [12]	1976–1988	320	18 (5.6 %)	Abortion = 2 Invasive mole = 16	Not recorded				7	8	Anterior = 12 Lateral = 3 Posterior = 3 Vaginal vault = 2 (NB: some with multiple sites)
Varder et al. [13]	1990–1997	75	12 (16 %)	Choriocarcinoma = 8 Invasive mole = 4	Not recorded				6	6	Anterior = 9 Anterior and posterior = 3
Yingya et al. [14]	1985–2000	820	51 (6.1 %)	Choriocarcinoma = 33 Invasive mole = 18	Not recorded				9	42	Anterior = 22 Unknown = 29
Berry et al. [15]	1962–2006	804	36 (4.5 %)	Choriocarcinoma = 25 (69 %) Invasive mole = 8 (22 %) Unknown = 3 (8 %)	0	13	22	1	25	11	Anterior = 28 Lateral = 15 Posterior = 11 Unknown = 3 (NB: some with multiple sites)
Ghaemmaghemi et al. [16]	1996–2006	48 (all also had lung metastases)	13 (27.1 %)	Abortion = 3 Invasive mole = 5 Term pregnancy = 5	0	0	48	0	9	4	Anterior = 9 Fornix = 4
Cagayan [17]	1998–2008	424	46 (11 %)	Chorocarcinoma = 12 Invasive mole = 3 Unknown = 31	0	9	32	5	10	36	Not recorded

FIGO, International Federation of Gynecology and Obstetrics; WHO, World Health Organization.

Table 4
Management of vaginal metastases in patients with gestational trophoblastic neoplasia: comparative study data.

Reference	Publication year	Publication country	*n*	Additional management for vaginal metastases								Patient outcomes
				Chemotherapy	Vaginal packing	Vaginal suturing/ ligation	Local excision	Internal iliac ligation	Selective embolization	Radiotherapy	Other	Major haemorrhage	
Bloch et al. [10]	1983	South Africa	6	5 (1 spontaneous regression)	1	1	2	0	0	0	0	0	Complete remission = 6
Goldberg et al. [11]	1986	South Africa	5	5	4	4	0	0	1	0	0	5	Complete remission = 5
Wong et al. [12]	1990	Hong Kong	18	15 (3 spontaneous regression)	0	2	0	0	0	0	2 Incision and drainage of haematoma	NR	Complete remission = 18
Varder et al. [13]	2000	Turkey	12	12	Not discussed							10	Complete remission = 11 Death = 1 (1 month after chemotherapy)
Yingya et al. [14]	2002	Beijing	51	49	16	0	2	1	3	0	14 Local injection of 5-FU every 3 days	18	Complete remission = 44 Death = 2 (before chemotherapy) Abandoned treatment = 5 (economic reasons)
Berry et al. [15]	2008	USA	36	36	0	7	3	1	1	1	0	13	Complete remission = 29 Death = 7
Ghaemmaghemi et al. [16]	2008	Iran	13	12	Not discussed							10	Complete remission = 12 Death = 1 (before chemotherapy)
Cagayan [17]	2010	Philippines	46	37	11 (5 packed with MTX solution)	5	0	4	0	1	1 MTX infiltration of vaginal mass	11	Complete remission = 26 Death = 4 (during treatment) Self-discharged = 7 (financial constraint after remission)

MTX, methotrexate; 5-FU, 5-fluorouracil.

reported cases [10,12]. Prior studies have also suggested that response to treatment may be dependent on the size of the vaginal metastasis [13,15,16]; however, the present authors and others [17] disagree with this. In the present study, the response of patients with vaginal metastases to chemotherapy was no different from other patients with GTN, and the presence of vaginal metastases in GTN does not confer a worse prognosis, in keeping with other series [12,15]. Other authors have considered the presence of vaginal metastases as an indication for high-risk classification, and an indication for initial treatment with multi-agent chemotherapy [10,11,13,14,16]. The present authors consider that most vaginal lesions respond quickly and completely to systemic chemotherapy (76 % in this study), and that patients with vaginal metastases and a WHO prognostic score < 7 can be treated successfully with single-agent chemotherapy in most cases [15].

This study aimed to formulate guidance for clinicians encountering GTN patients with vaginal metastases (Fig. 1), especially for those working predominantly within the field of GTN. Haemorrhage from such vaginal metastases can be life-threatening and terrifying for the patient, and challenging and traumatic for the clinician to manage. The present authors agree with the authors of previous studies [16,17] that biopsy of the vaginal lesion should be avoided, unless the vaginal metastasis is the only source of diagnostic pathology if required, in view of the risk of massive haemorrhage. If vaginal metastases are asymptomatic, local excision of the lesion is not recommended, and further intervention may not be warranted at all, as some lesions may regress spontaneously [10–12]. However, early implementation of chemotherapeutic regimens based on the WHO prognostic score should be instituted. Even if asymptomatic, all patients should be advised regarding the potential risk for massive haemorrhage, and provided with instructions regarding rapid access to their nearest, most appropriate medical service. In addition, advice should be provided on whether sexual intercourse is appropriate, which will be case dependent.

When major haemorrhage ensues, there should be immediate implementation of major haemorrhage protocols, early liaison with haematology, and consideration for infusion with intravenous tranexamic acid. Tranexamic acid is associated with a reduction in mortality, a reduction in transfusion requirements, and fewer bleeding episodes. Tranexamic acid should be given as soon as possible after the injury and no later than 3 h (a common prescription is 1 g intravenous bolus over 10 min followed by 1 g infusion over 8 h), including in patients with mild-to-moderate total blood loss [28]. As a first-line measure, vaginal packing with an indwelling catheter should be considered, depending upon the location of the vaginal metastases, with pressure packs applied to metastases lying low in the vagina, towards the introitus, or encroaching on the vulva. Whilst vaginal packing is inexpensive, readily available, simple to perform, relatively low risk, and has the potential for repeated application, it may be uncomfortable, can run the risk of infection and necrosis in longer-term use, and can be associated with the

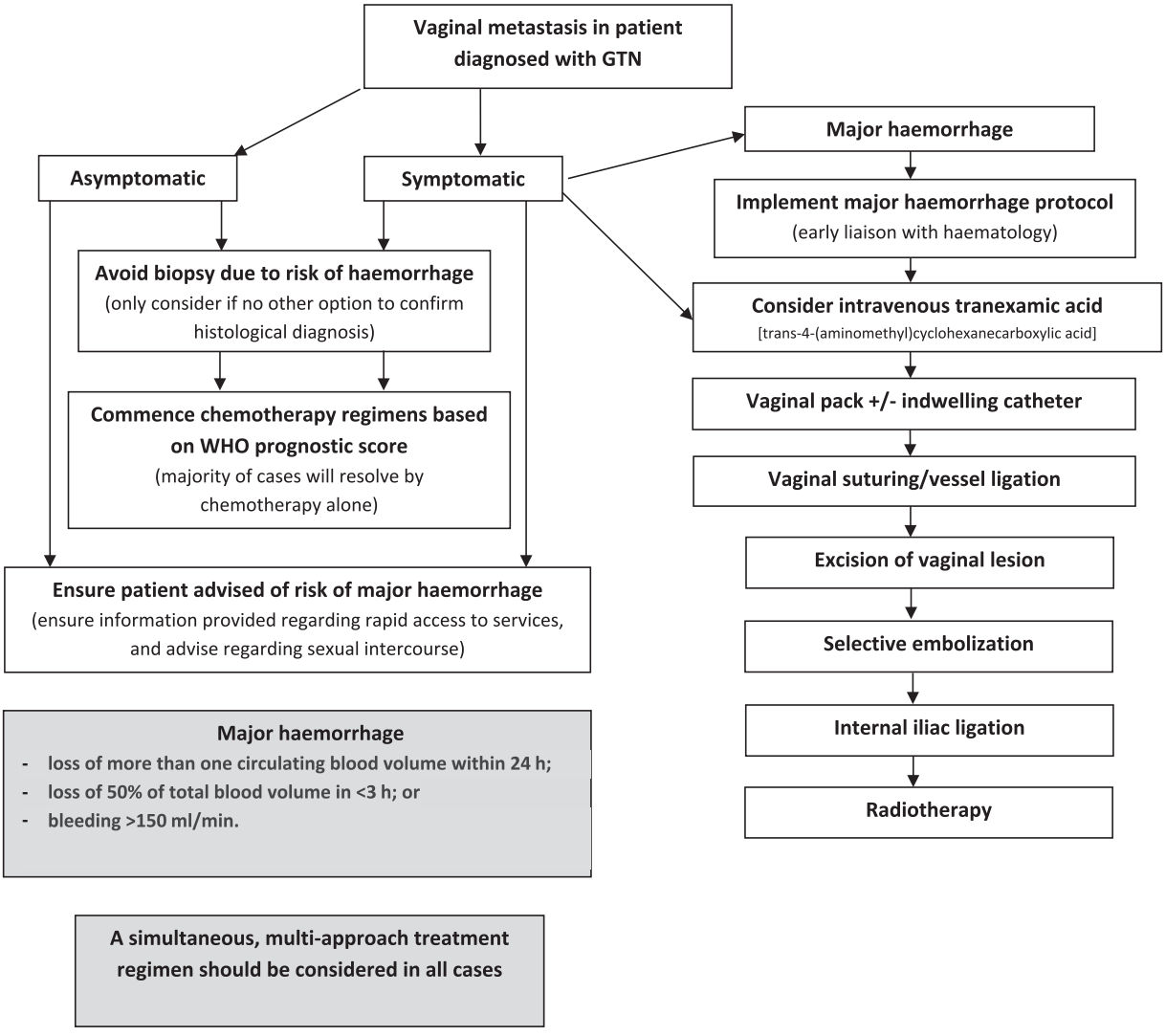

Fig. 1. Guidelines for the management of vaginal metastases in gestational trophoblastic neoplasia (GTN).

formation of haematoma. Vaginal suturing or vessel ligation has also been reported in the literature [10–12,15,17], and is a further consideration which is, again, inexpensive, readily available, simple to perform, and has the potential for repeated application. However, there is a risk of prolonged haemorrhage, anaesthesia, post-procedure pain, scarring and altered anatomy. Local excision of the vaginal metastasis has been reported [10,14,15], and is a consideration in smaller superficial lesions. However, this is a risky strategy in larger highly vascular lesions, primarily due to the risk of uncontrollable haemorrhage. The majority of patients are young, so the risk of scarring with significantly altered anatomy, causing altered appearance and altered sexual function, must be considered. If resources permit, selective embolization should be considered if simple treatment options have failed (tranexamic acid, vaginal packing/suturing/vessel ligation). Alternatively, embolization can be explored/arranged whilst simultaneously deploying the above first-line measures. This option was reportedly successful in controlling haemorrhage in approximately six cases in the literature [11,14,15], although as this technique has not been implemented systemically in all patients, accurate success rates cannot be provided. Early liaison with vascular radiology in patients with repeated bleeding from vaginal metastases, and patients with massive haemorrhage, can be critical. Interventional radiology certainly plays a role in the management of GTN, and emergency embolization can be life-saving in cases of malignant erosion, resulting in shorter hospital stays, reduced transfusion rates, and reduced morbidity compared with surgical alternatives. The risks of embolization include infarction, necrosis, nerve injury and infection [29]. Radiotherapy, whilst effective, is perhaps a final solution where other measures have failed, as radiotherapy can cause localized hair loss, skin discoloration, localized pain, scarring and vaginal stenosis, ovarian failure, radiation cystitis or proctitis, and fistula formation. Patients are often young women wishing to preserve their sexual function and future fertility.

This study is clearly limited by its small population size; however, GTN is rare, with the presence of vaginal metastases being rarer still. With only a limited number of dated case series reported in the literature, and a paucity of published case reports, this study contributes significantly to the international literature on this subject, benefits from the fact that the included patients were managed at a quaternary level specialist treatment centre, and provides guidance for future clinicians in the management of this rare and complicated condition.

Conclusion

Vaginal metastasis is a rare complication of GTN that can result in life-threatening haemorrhage. These patients are often young with future fertility considerations. The presence of a vaginal metastasis should not alter management plans, and tailored treatment should be determined by patient factors, with chemotherapeutic regimens based upon WHO prognostic scores. A conservative management approach should be considered, as most cases will resolve with chemotherapy alone, and additional therapeutic interventions may result in adverse short- and longer-term sequelae.

Author contributions.

VLP and JEP were the principal authors and performed the analyses. VLP, EMDH, JEP and KS collected data for the study. VLP, JEP and EMDH performed the interpretation of data and revision of the manuscript. KS and MCW revised the manuscript.

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CRediT authorship contribution statement

V.L. Parker: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **E.M.D. Hodson:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **K. Singh:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **M.C. Winter:** Writing – review & editing, Visualization, Validation. **J.E. Palmer:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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