

Received: 2024.08.31
Accepted: 2024.11.27
Available online: 2024.12.08
Published: 2025.01.15

Invasive Hydatidiform Mole Mimicking Ectopic Pregnancy: A Case Report and Literature Analysis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF **Amany A. Fathaddin**

Department of Pathology, College of Medicine, King Saud University,
Riyadh, Saudi Arabia

Corresponding Author: Amany Fathaddin, e-mail: afathaddin@ksu.edu.sa
Financial support: None declared
Conflict of interest: None declared

Patient: Female, 41-year-old
Final Diagnosis: Ectopic invasive mole
Symptoms: Abdominal pain • amenorrhea • vaginal bleeding
Clinical Procedure: —
Specialty: Obstetrics and Gynecology • Pathology

Objective: Rare disease
Background: Gestational trophoblastic diseases (GTDs) are a group of benign and malignant tumors that arise from placental tissue. Ectopic pregnancies most commonly occur within the fallopian tubes. The estimated incidence of ectopic gestational trophoblastic diseases (GTDs) is approximated at 1.5 per 1 000 000 pregnancies, which makes it a very rare condition. The diagnosis is challenging since the clinical presentation often mimics conventional ectopic pregnancy, but management approaches are significantly different.
Case Report: A 41-year-old woman (G7 T4 P0 A2 L4) presented to the Emergency Department with a period of amenorrhea followed by vaginal bleeding and abdominal pain. Right-side abdominal tenderness was noted upon physical examination. Laboratory investigations showed elevated serum β -hCG level. Ultrasound examination showed a normal-size uterus. No intrauterine gestational sac was identified. An echogenic mass with central lucency was noted in the right adnexa, measuring 2.1×1.8 cm, with minimal free fluid present in the pouch of Douglas. The findings were suggestive of a ruptured right-side ectopic pregnancy. The patient underwent laparoscopic salpingectomy. Histopathological examination of the specimen revealed a complete hydatidiform mole with vascular invasion. The patient was treated conservatively and was followed up by a serial β -hCG level until she achieved 3 consecutive negative β -hCG titers.
Conclusions: Invasive moles located in the fallopian tube are very rare in the literature, and further research is needed to ascertain the proper management of such cases. Histopathological examination of the salpingectomy specimen has an essential role in confirming the diagnosis of ectopic GTDs and guiding the management.

Keywords: Pregnancy • Fallopian Tubes

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/946388>

 1833  2  4  12



Publisher's note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher

Introduction

Gestational trophoblastic diseases (GTD) are a group of proliferative disorders of the placental trophoblasts, including complete and partial hydatidiform moles, invasive moles, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and choriocarcinomas. The last 4 are malignant and are termed gestational trophoblastic neoplasia (GTN) [1]. Ectopic pregnancies constitute a significant clinical concern, most commonly occurring within the fallopian tubes. With an estimated incidence of 20 per 1000 pregnancies, ectopic pregnancies pose serious risks to maternal health due to the potential for tubal rupture and hemorrhage [2]. However, ectopic GTDs are exceedingly rare, with an estimated incidence of only 1.5 per 1 000 000 pregnancies [3]. Partial moles were the most common form of GTD diagnosed in ectopic sites [4,5]. Reported cases of ectopic invasive mole, however, are scarce, with only 7 cases reported in the literature [1,2,4,6-8]. The clinical presentation of ectopic GTDs often mimics that of conventional ectopic pregnancies, making accurate diagnosis challenging. However, the distinction between the 2 entities is crucial, as their management strategies differ significantly. The diagnosis of GTD and GTN is achieved by ultrasound (US), beta-human chorionic gonadotropin hormone (β -hCG) titer, which is an essential biomarker of diagnosis and follow-up, and histopathology examination [9,10]. Management options for GTN depend on stage and classification according to the FIGO 2000 staging and classification [11,12].

Histopathological examination plays a pivotal role in confirming the diagnosis of ectopic GTDs and guiding appropriate therapeutic interventions.

In this report, we present a rare and challenging case of an ectopic invasive mole in a 41-year-old woman who presented with vaginal bleeding. Ultrasound examination initially suggested an ectopic tubal pregnancy, but histopathological examination revealed a complete hydatidiform mole with evidence of vascular invasion. After surgery, the β -hCG titer was monitored until it reached zero without chemotherapy. Such cases are rare in the literature and further research is needed to ascertain their proper management.

Case Report

A 41-year-old woman (G7 T4 P0 A2 L4) presented to the Emergency Department with a period of amenorrhea followed by a 1-day history of vaginal bleeding and abdominal pain. Her obstetric history included 4 uncomplicated vaginal deliveries and 2 spontaneous abortions, with 1 necessitating dilatation and curettage. Based on the date of her last menstrual period

(LMP), the estimated gestational age was 5 weeks 3 days. She had no other significant surgical or medical history.

Upon examination, she was hemodynamically stable, with normal vital signs. Abdominal tenderness, predominantly on the right side, was noted upon palpation. Speculum examination revealed a closed cervical os without active bleeding. Bimanual pelvic examination elicited mild tenderness in the right adnexal region without palpable masses or cervical motion tenderness.

US examination showed a normal-size uterus. No intrauterine gestational sac was identified. The left ovary was normal; however, the right ovary showed an anechoic cyst measuring 3.0×2.8 cm. An echogenic mass with central lucency was noted in the right adnexa, measuring 2.1×1.8 cm. An adjacent heterogeneous mass was present, measuring 3.7×3.0 cm. Minimal free fluid was present in the pouch of Douglas. These findings suggested a ruptured right-side ectopic pregnancy (2.1×1.8 cm gestational sac with an adjacent blood/blood clot) and an additional finding of a right ovarian cyst.

Laboratory results showed an elevated serum β -hCG level at 21 143 IU/L (normal range at 5-6 weeks of normal pregnancy in our lab is 861-88 769 IU/L), while hematological and routine chemistry workup results were within normal limits. Given the presence of an echogenic mass with central lucency in the right adnexa, elevated β -hCG levels, and the absence of an intrauterine gestational sac, a ruptured right-sided ectopic pregnancy was suspected. The patient was taken to the operating room and the intra-operative findings confirmed the presence of a ruptured right fallopian tube with a gestational sac and a right ovarian cyst; therefore, a laparoscopic right salpingectomy and ovarian cystectomy were performed. The patient tolerated the surgery well and was vitally stable. She was discharged the next day.

Microscopic examination of formalin-fixed, paraffin-embedded and hematoxylin, and eosin-stained tissue sections revealed abnormal chorionic villi within the fallopian tube wall (**Figure 1**). The villi were diffusely hydropic with karyorrhectic debris, were avascular, and showed marked circumferential trophoblastic proliferation. Vascular invasion was noted in paratubal blood vessels (**Figure 2**) and was confirmed by Desmin, Smooth-muscle actin, CD34, and CD31 (**Figure 3**) immunohistochemical stains. Based on these findings, a diagnosis of an ectopic tubal invasive complete hydatidiform mole was rendered with an additional finding of a benign ovarian serous cyst. The histopathology report was available 7 days after the surgery.

The patient underwent a computed tomography (CT) scan for chest, abdomen, pelvis, and brain and there were no signs of

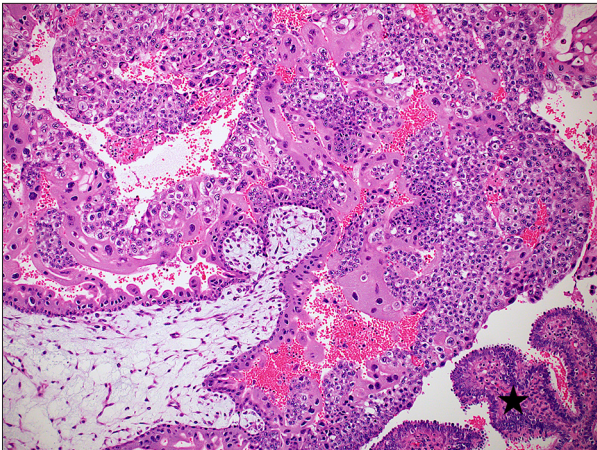


Figure 1. A photomicrograph showing an abnormal avascular chorionic villous with diffuse cytotrophoblastic and syncytiotrophoblastic proliferation. Part of the fallopian tube is shown in the right lower corner (star) (hematoxylin and eosin, ×100 magnification).

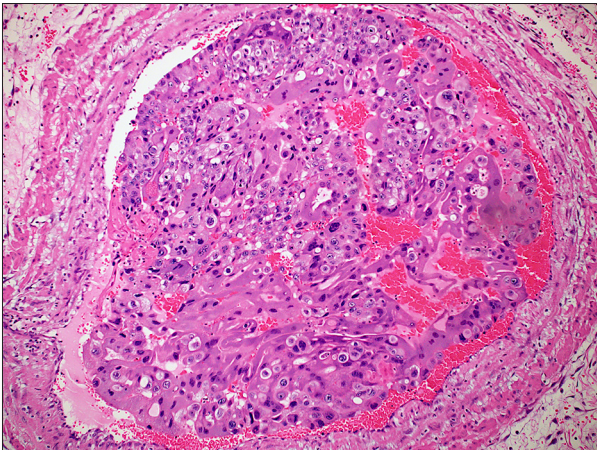


Figure 2. A photomicrograph depicting vascular invasion by sheets of proliferating cytotrophoblasts and syncytiotrophoblasts (hematoxylin and eosin, ×100 magnification).

abdominopelvic, intrathoracic, or intracranial involvement. Her serum β -hCG level dropped to 33.7 IU/L within 3 weeks after the surgery.

According to FIGO staging and classification and the Modified WHO Prognostic Scoring System as Adapted by FIGO [11,12], the patient was classified as stage II, score 2, low-risk group (age: >40 (score 1), antecedent pregnancy: mole (score 0), interval from index pregnancy: <4 months (score 0), pretreatment hCG mIU/ml: 10^3 to 10^4 (score 1), largest tumor size including uterus, cm <3 (score 0), site of metastases: (score 0), number of metastases (score 0), previous failed chemotherapy (score 0)).

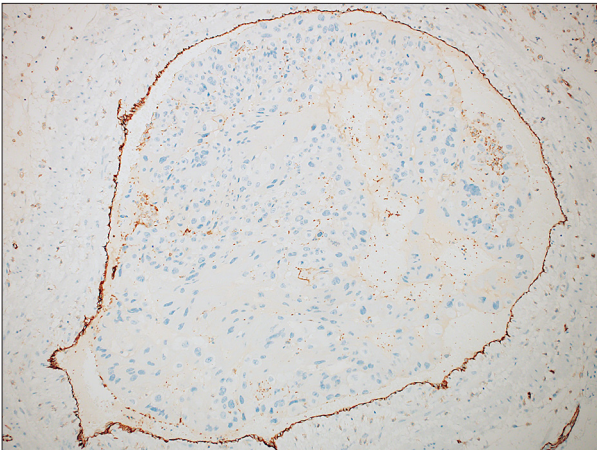


Figure 3. CD31 immunohistochemical stain highlighting the endothelial cells in an invaded blood vessel (CD31 immunohistochemical stain, ×100 magnification).

Table 1. Serial β -hCG blood levels monitoring from the time of diagnosis until reaching 3 consecutive negative results.

Date	Beta hCG level (mIU/mL)
One day before surgery (gestational age of 5 weeks 3 days)	21 143.8
Day of surgery	21 691.2
Postoperative day 22	33.7
Postoperative day 29	24.2
Postoperative day 36	40.1
Postoperative day 43	56.3
Postoperative day 50	41.1
Postoperative day 80	38.4
Postoperative day 87	13.2
Postoperative day 93	12.5
Postoperative day 100	5.7
Postoperative day 107	4.1
Postoperative day 114	3.6
Postoperative day 125	<2.00
Postoperative day 160	<2.00
Postoperative day 183	0

As this was an unusual case of ectopic invasive mole, the case was presented in a multidisciplinary tumor board and 3 options were discussed: 1) definitive surgical treatment with a total hysterectomy, bilateral oophorectomy, and left salpingectomy, 2) single-agent chemotherapy, and 3) close follow-up. The board voted against the first option since the involved organ (the right fallopian tube) was completely excised with no evidence of other organs involvement, in addition to the

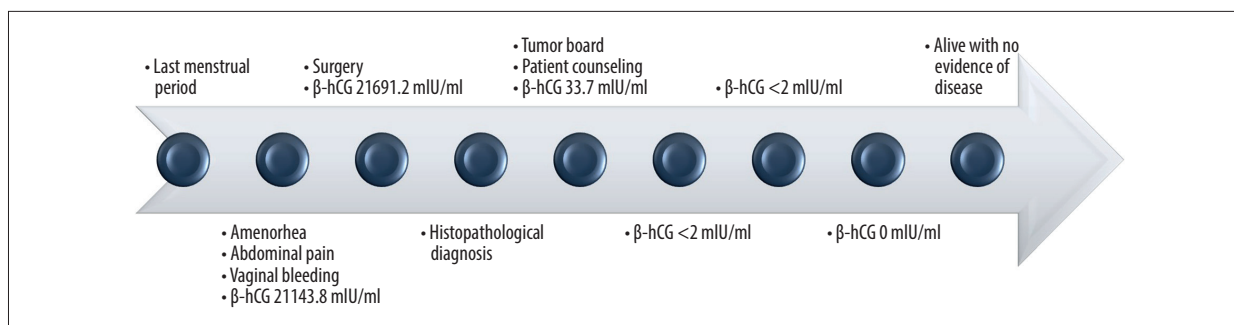


Figure 4. A timeline showing the clinical presentation from the time of presentation until the last follow-up.

known patient's desire to preserve her fertility. The second option was also revoked since the β -hCG level had dropped significantly within 3 weeks of surgery, which suggests the complete removal of the disease.

The patient was counseled regarding her diagnosis and management options. She opted for conservative medical management, which included oral contraceptive pills and serial β -hCG blood level monitoring. After 6 months, the patient had 3 consecutive negative β -hCG titers (Table 1). She then returned to her routine medical visits, with no evidence of disease to date (Figure 4).

Discussion

Gestational trophoblastic diseases (GTD) encompass a spectrum of proliferative disorders originating from abnormal development of placental trophoblasts. This spectrum includes histologically and clinically diverse entities [9]. The World Health Organization classification of GTDs includes: hydatidiform mole (partial, complete), invasive mole, gestational choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor and tumor-like conditions, including exaggerated placental site, placental site nodule, and/or mixed or unclassified trophoblastic lesions [10]. GTDs can arise from any pregnancy event, including term or preterm pregnancy, spontaneous abortion, or ectopic pregnancy. Ectopic GTDs are rare occurrences with few case reports or case series [3-5,9]. The clinical presentation of ectopic GTDs is like that of conventional ectopic pregnancies. A partial mole was the most common form of GTD diagnosed in ectopic sites [4,5].

Invasive moles show aggressive growth characteristics, with invasion to the myometrium, parametrial tissues, or blood vessels by the abnormal hydropic chorionic villi. Overall, invasive moles occur at an estimated rate of 1 in 15 000 pregnancies. About 10-17% of hydatidiform moles resulted in invasive moles, and they are more common in complete molar pregnancies than in partial molar pregnancies [5].

Follow-up with β -hCG titers is the key for early diagnosis of GTN, and treatment is generally by chemotherapy. The revised FIGO 2000 system is used for staging and risk categorization. It keeps the original staging system of FIGO (stages I, II, III, IV) and includes a modification of the WHO prognostic index score for risk assessment (scoring indices of 0, 1, 2, 3, 4) [11,12]. Accordingly, patients are divided into 2 categories: low- and high-risk. The aim of this categorization is to determine the best treatment and the outcome. Low-risk GTN (FIGO Stages I-III: score <7) is treated with single-agent chemotherapy but may require additional agents; although scores 5-6 are associated with more drug resistance, survival approaches 100%. High-risk GTN (FIGO Stages II-III: score $\geq$ 7 and Stage IV) are treated with multi-agent chemotherapy, with or without adjuvant surgery or radiotherapy for brain metastases, with a survival rate of approximately 90% [11,12].

Regarding tubal invasive molar pregnancy, it is confirmed by histopathologic findings of hydropic chorionic villi accompanied by trophoblastic proliferation, destruction of smooth muscle, and vesicle invasion into the tubal wall and vessels. The differential diagnoses include ovarian cyst, tubo-ovarian abscess, endometriosis, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and choriocarcinoma.

Management of ectopic molar pregnancies includes immediate surgical removal of the gestational tissue and, possibly, post-operative chemotherapy. Serial β -hCG titers should be measured until reaching zero [1,4].

Invasive mole in the fallopian tube is extremely rare. An extended review of the literature revealed 7 cases of ectopic tubal invasive molar pregnancy (Table 2) [1,2,4,6-8].

In all 7 cases, patients presented with symptoms of abdominal pain and vaginal bleeding. Laboratory assessments revealed β -hCG values of 6984-103 724 mIU/mL. The diagnosis relied on ultrasound imaging for detecting an ectopic pregnancy, while histopathological examination provided the definitive diagnosis. Management strategies comprised laparoscopic intervention and salpingectomy. Chemotherapy was incorporated in 4

instances: 3 cases with persistently elevated β -hCG levels and 1 involving ovarian metastasis. Our patient presented with symptoms of abdominal pain and vaginal bleeding, with an initial β -hCG level of 21 143 mIU/mL. Subsequent monitoring included serial β -hCG serum titers until achieving 3 consecutive negative results. The clinical significance of differentiating between GTD and other conditions, such as ectopic pregnancies, lies in guiding appropriate management strategies tailored to the individual patient's diagnosis and prognosis. Misdiagnosis or delayed diagnosis can lead to inappropriate treatment and potentially worsen patient outcomes. Additionally, the application of prognostic scoring criteria, such as the WHO/FIGO prognostic score, is essential for predicting the risk of persistent disease or

relapse following initial treatment. Patients with high-risk scores may require more aggressive treatment and closer monitoring to ensure optimal outcomes [12]. Serial monitoring of serum β -hCG levels is essential for assessing treatment response and detecting disease recurrence, with the frequency and intensity of follow-up monitoring guided by the individual's risk profile. It is recommended to start the patient on oral contraceptives during surveillance of β -hCG levels [11]. Our case aligns with this clinical profile, presenting with abdominal pain and vaginal bleeding and an initial serum β -hCG level of 21 143 mIU/mL. Serial monitoring of β -hCG serum titers was conducted until 3 consecutive negative results were achieved, in line with standard management protocols for GTDs.

Table 2. Reported cases of invasive molar pregnancy in the fallopian tube.

Author	Patient's characteristics	β -hcg level at presentation And Prognostic score	Side	Management	Chemotherapy	Outcome
Juan (2013) [1]	A 20-year-old woman (G2, P1) presented at the emergency room with severe low abdominal pain 8 weeks and 4 days after her last menstrual period	6984 mIU/mL Prognostic score was not mentioned	Left fallopian tube	Laparoscopy and salpingectomy for a left ampullary ectopic pregnancy	Not given	Weekly quantitative β -hCG titers were performed until 3 successive β -hCG levels were negative
Toal et al (2021) [2]	A 31-year-old woman (G4P2+1) with an uncertain last menstrual period who presented to the Emergency Department with vaginal bleeding	103,724 mIU/mL Prognostic score: Stage I low-risk with a WHO score of 5	Right fallopian tube	Laparoscopic right cornual wedge resection and right salpingectomy	Methotrexate 0.4 mg/kg IM for 5 days every 14 days	At the time of most recent follow-up 3 months following therapy completion, the patient had no evidence of disease and a negative β -hCG
Obahiagbon et al (2018) [4] (2 cases)	Age range: 20-29 amenorrhea, pelvic pain, and bleeding per vagina	Not mentioned (The cases were among other reported ectopic GTDs with histopathology review only Article title: "Ectopic Gestational Trophoblastic Disease: A 20-Year Histopathological Review in a Tertiary Center")	Right and left fallopian tubes (respectively)	Not mentioned	Not mentioned	Not mentioned

Table 2 continued. Reported cases of invasive molar pregnancy in the fallopian tube.

Author	Patient's characteristics	β -hcg level at presentation And Prognostic score	Side	Management	Chemotherapy	Outcome
Zhang et al (2014) [6]	A 30-year-old woman (G 2 P 1) presented with amenorrhea and vaginal bleeding	13411 mIU/ml. Prognostic score: Stage III according to FIGO 2000	Right fallopian tube	Laparoscopy right salpingo-oophorectomy	Five days chemotherapy with methotrexate (MTX) 10 mg/m ² /d plus 5-fluorouracil (5-FU) 800 mg/m ² /d plus etoposide (VP-16) 60 mg/m ² /d	The final diagnosis of the patient was an invasive mole in fallopian tube with ovarian metastasis. The serum β -hCG level decreased to 51.95 mIU/ml after the first cycle of chemotherapy and fell into the normal range after the 2 nd cycle of chemotherapy and still maintained within normal limits for more than 12 months (the 5 th measurement)
Khelif et al (2016) [7]	A 40-year-old woman (G1 P0), presented at 7 weeks of amenorrhea with sudden acute pain located in the left iliac fossa	27 624 mIU/ml. Prognostic score: Not mentioned; however, CT scan showed no locoregional or distant metastases	Left fallopian tube	Laparoscopic left salpingectomy	8 cycles of Methotrexate (dose was not mentioned)	The outcome was favorable with negativity hCG plasma (monitored weekly) after 8 cycles of chemotherapy and the patient was in complete remission up to 48 months post-treatment
Ikuma et al (1992) [8] (Japanese)	A 41-year-old woman (G3 P0 +2) presented at 9 weeks of amenorrhea with abdominal pain and vaginal bleeding	16 000 mIU/mL Prognostic score: Not mentioned	Isthmus of left fallopian tube	Simple total hysterectomy and left salpingo-oophorectomy	One course of MTX (10 mg/day $\times$ 5 days)	Favorable outcome, negative hCG was achieved, complete remission up to 12 months

Conclusions

Ectopic tubal invasive molar pregnancy is very rare. Despite its resemblance in clinical presentation to conventional ectopic tubal pregnancy, the management approaches for these 2 conditions differ significantly. A meticulous histopathological assessment of salpingectomy specimens suspected of ectopic pregnancy is essential for achieving precise diagnosis and selecting suitable management strategies.

References:

1. Juan CW. Fallopian tube invasive molar disease. *Int J Gynaecol Obstet*. 2013;122(2):161-62
2. Toal C, Garrett AA, Kostadinov S, Boisen M. Gestational trophoblastic neoplasia presenting as an interstitial ectopic pregnancy. *Gynecol Oncol Rep*. 2021;37:100813
3. Ayyash M, Kole M, Le Q, et al. Partial molar pregnancy presenting as a tubal ectopic pregnancy. *Case Rep Obstet Gynecol*. 2022;2022:7414190
4. Obahiagbon I, Ekanem VJ. Ectopic gestational trophoblastic disease: A 20-Year histopathological review in a tertiary center. *Ann Trop Pathol*. 2018;9:59-63
5. Hassadia A, Kew FM, Tidy JA, et al. Ectopic gestational trophoblastic disease: A case series review. *J Reprod Med*. 2012;57(7-8):297-300
6. Zhang Q, Wang H, Lu S, Cao S. An invasive mole localized in the fallopian tube with ovarian metastasis. *Clin. Cancer Res*. 2014;2:a7
7. Khlifi A, Mkhini I, Yaacoubi MT, Khairi H. A cornual invasive hydatiform mole: A literature review. *Med J Armed Forces India*. 2016;72(Suppl. 1):S94-S97
8. Ikuma K, Okada I, Shiotani T, et al. [Invasive hydatidiform mole in the fallopian tube: Report of a case.] *Nihon Sanka Fujinka Gakkai Zasshi* 1992; 44(9):1189-92 [in Japanese]
9. Athanasiou A, Féki A, Fruscalzo A, et al. Ruptured ectopic pregnancy as complete hydatidiform mole: Case report and review of the literature. *Front Surg*. 2022;9:1036435
10. Cheung AN, Hui P, Shih I. Gestational trophoblastic disease. In: World Health Organization Classification of Tumours Editorial Board. *Female Genital Tumours*. International Agency for Research on Cancer; 2020;309-33
11. Ngan HYS, Seckl MJ, Berkowitz RS, et al. Diagnosis and management of gestational trophoblastic disease: 2021 update. *Int J Gynaecol Obstet*. 2021;155(Suppl. 1):86-93
12. FIGO Oncology Committee. FIGO staging for gestational trophoblastic neoplasia 2000. FIGO Oncology Committee. *Int J Gynaecol Obstet*. 2002;77(3):285-87

Declaration of Figures' Authenticity

All figures submitted have been created by the author who confirms that the images are original with no duplication and have not been previously published in whole or in part.