CASE SERIES

Atypical Presentation of Gestational Trophoblastic Neoplasia Imparting Lesson: A Case Series and Review of Literature

Upasana Verma[1], Rachna Agarwal[2], Bhanu Priya[3], Sandhya Jain[4], Anshuja Singla[5], Seema Prakash[6], Richa Pawar[7]

Received on: 26 February 2024; *Accepted on:* 24 May 2024; *Published on:* 09 July 2024

Abstract

Introduction: Gestational trophoblastic neoplasia (GTN) is a malignant form of gestational trophoblastic diseases originating from abnormal proliferation of placental trophoblasts. Owing to unusual and variable presentations, the diagnosis is sometimes delayed and become catastrophic. Though, survival outcomes are good following chemotherapy, but still surgery becomes first choice in hemodynamically unstable patient which is to be followed by chemotherapy depending upon the World Health Organization (WHO) prognostic score. The reproductive outcomes following chemotherapy is variable. Here, we are reporting a case series of GTN with varied presentation giving different lessons which were managed to best of our possible efforts.

Case discussion: The first case highlights the management of women who had ruptured choriocarcinoma post manual vaginal examination for which hysterectomy was performed as a life-saving procedure followed by chemotherapy. The other case surprised the clinician with metastatic perforating invasive mole along with unusual finding of ovarian and iliac vein thrombosis. Although, planned for chemotherapy, hysterectomy with debulking was done for hemoperitoneum. The last case perplexed us with the normal twin conception just following the completion of chemotherapy for post-molar high-risk GTN and is continuing her viable pregnancy.

Conclusion and clinical implication: Our case series imparted few lessons to obstetricians. Pelvic examination in GTN needs to be guarded so as to prevent untoward life-threatening complications. Invasive mole may present lately with devastating rupture uterus with exuberant pelvic vein thrombosis (PVT). Spontaneous conception with good reproductive outcome may still occur immediately following completion of multi-agent chemotherapy in high-risk GTN.

Keywords: Choriocarcinoma, Gestational trophoblastic neoplasia, Invasive mole, Pelvic vein thrombosis, Reproductive outcome, Rupture uterus.

Journal of South Asian Federation of Obstetrics and Gynaecology (2024): 10.5005/jp-journals-10006-2453

Introduction

Gestational trophoblastic diseases are pregnancy disorders which develop from abnormal trophoblastic proliferation of placenta. It encompasses the spectrum of conditions ranging from benign (potentially malignant) to malignant diseases. Malignant group of gestational trophoblastic disorders is termed as gestational trophoblastic neoplasia (GTN) which comprises of invasive mole, gestational choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and atypical placental site nodule. Gestational trophoblastic neoplasia are chemo-sensitive tumors having high cure rates with chemotherapeutic regimens. The extent of presentation of advanced disease is from perforating choriocarcinoma to metastatic GTN. We present two cases of atypical presentations of that GTN which presented at verge of uterine perforation and managed surgically to best of our efforts. Our first case was an eyeopener where she had sudden hemoperitoneum following pelvic examination probably because of uterine rupture. Devastating metastatic invasive mole with extensive pelvic vein thrombosis (PVT) was evidenced by our second case. Our third case epitomized the reproductive outcome of post-molar GTN who conceived with twin gestation just after 2 month following last chemotherapy cycle.

Case 1

A 20-year-old parous female (Parity 1 Live 1 Abortion 1) presented to gynecology emergency with complaints of irregular vaginal bleeding for 6 months and lower pain abdomen for 2 months. She gave history of 2 months amenorrhea followed by spontaneous abortion 6 months back which was followed by dilatation and evacuation. She carried a prior ultrasound report (Fig. 1) suggestive of infiltrative heterogeneous lesion of 5.6 × 5.4 cm invading the myometrium along with raised vascularity over the lesion, with normal bilateral adnexa. She was hemodynamically stable at presentation with an unremarkable chest and cardiovascular examination. On per abdomen examination, there was no guarding, rigidity, and organomegaly. On per speculum examination, cervix and vagina were normal with no active bleeding. Uterus was 8–10 weeks size palpable on bimanual examination. Her urine

[1,4–6]Department of Obstetrics and Gynaecology, Guru Teg Bahadur Hospital and University College of Medical Sciences, New Delhi, India

[2]Department of Obstetrics and Gynaecology, University College of Medical Sciences and Guru Teg Bahadur Hospital, New Delhi, India

[3]Department of Obstetrics and Gynaecology, University College of Medical Sciences, New Delhi, India

[7]Department of Pathology, Pandit Bhagwat Dayal Sharma University of Health Sciences, Rohtak, Haryana, India

Corresponding Author: Bhanu Priya, Department of Obstetrics and Gynaecology, University College of Medical Sciences, New Delhi, India, Phone: +91 9650514269, e-mail: drpriyabhanu@gmail.com

How to cite this article: Verma U, Agarwal R, Priya B, *et al*. Atypical Presentation of Gestational Trophoblastic Neoplasia Imparting Lesson: A Case Series and Review of Literature. J South Asian Feder Obst Gynae 2024;16(4):437–442.

Source of support: Nil

Conflict of interest: None

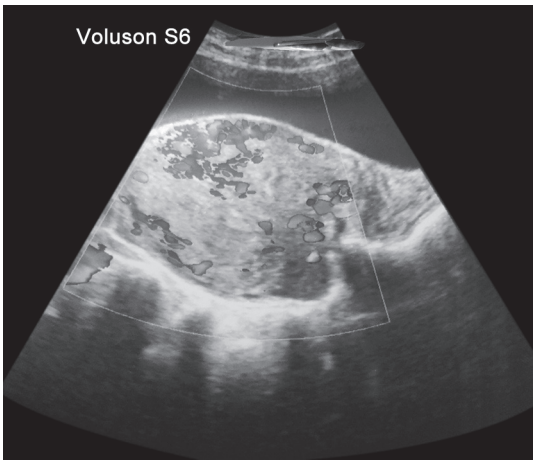
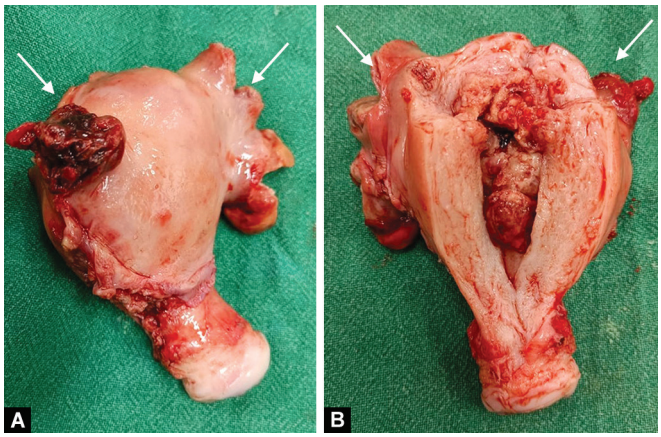


Fig. 1: Transvaginal Doppler showing hypervascular infiltrative lesion mainly in anterior myometrium

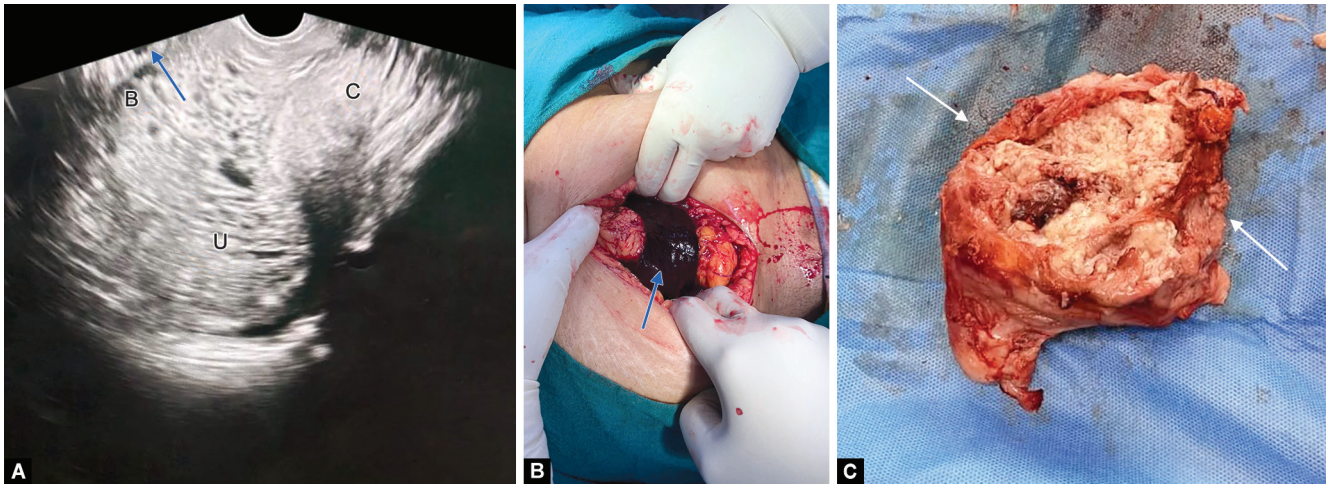


Figs 2A and B: (A) Hysterectomy specimen showing perforating tumor; (B) Cut section from posterior surface showing tumor in the cavity

pregnancy test was positive with absolute beta hCG value of 973,776 IU/mL. A provisional diagnosis of GTN was made. Following per vaginum examination, she complained of severe pain in abdomen and collapsed. Her pulse rate was 130/minute with low volume with BP of 90/60 mm Hg with significant pallor. Her abdomen was distended. Rigidity and guarding were present on palpation. She was immediately taken for exploratory laparotomy in view of suspected uterine perforation of a case of GTN with hemoperitoneum. Peroperatively, two liters of hemoperitoneum were present. There was 5 × 5 cm growth near the right cornua of the uterus perforating through the serosa. There was other two growths of 3 cm size extending up to serosa near the left cornu of the uterus (Fig. 2). Bilateral tubes and ovaries were normal. Rest of the whole abdomen was normal on palpation. Total abdominal hysterectomy was done. Postoperatively, she received four packed red blood cells, four fresh frozen plasma, and four platelet concentrates. The cut section of specimen was suggestive of perforating GTN (Fig. 2). Her post-surgery beta hCG was 182,535 IU/mL documenting a fall of approximately 80% in comparison to the baseline values. Her metastatic work up revealed multiple pulmonary metastasis, bilateral pleural effusion, and mediastinal lymphadenopathy on computerized tomography (CT) of chest. Computerized tomography abdomen, pelvis, and brain were unremarkable. Histopathological report revealed features of gestational choriocarcinoma. In view of FIGO scoring more than 7, she was started on multi-agent chemotherapy. Patient received six cycles of EMA-CO and got lost to our follow-up.

Case 2

A 40-year-old female para 3 presented to the gynecological emergency with chief complaints of mild to moderate intensity lower abdominal pain since 2–3 weeks, low grade fever for 1 week. She had three normal vaginal deliveries and one spontaneous abortion 5 months back at 2 months of gestation, which was followed by surgical evacuation. Following abortion, she gave history of irregular bleeding for which she never consulted any doctor. There was neither history of any syncopal attack nor bladder and bowel complaints. She was moderately built. Urine pregnancy test was positive. She was febrile (100°F), had tachycardia, hypertension, and tachypnea (PR = 110 beats/minute, BP = 144/94 mm Hg, RR = 20/minute). Her oxygen saturation was normal. Mild pallor was present. Thyroid and breast were normal. Breath sounds were reduced bilaterally on auscultation. Per abdominal examination revealed a firm slightly tender mass corresponding to 20 weeks gravid uterus arising from pelvis with restricted mobility. Upper abdomen showed soft distension with no hepatosplenomegaly. Local genitalia was normal. Cervix was smeared with foul smelling brownish discharge with normal vaginal mucosa on per speculum examination. On per vaginal examination, cervix was bulky, uterus was tender and enlarged to 20 weeks size of gravid uterus with restricted mobility. Bilateral fornixes were tender and foreshortened. On transabdominal and transvaginal ultrasonography, uterus was enlarged with honeycomb appearance and myometrium appeared to be thinned out anteriorly suggestive of invasive molar pregnancy (Fig. 3A). Her blood investigations revealed moderate anemia, leukocytosis, normal coagulation profile with deranged liver and renal function tests (Hb = 8 gm%, TLC = 20000/µL, platelet = 1 lakh, blood urea = 38 mg/dL, Serum creatinine = 2.2 mg/dL, S. bilirubin = 1.0 mg/dL, SGOT = 106 Units/L, SGPT = 115 Units/L, ALP = 210 Units/L, TSH = 2.87, INR = 0.9) with beta hCG value of 905 IU. Her tests for malarial antigen, typhoid, dengue, and blood culture were negative. Chest X-ray showed bilateral pleural effusion. Computerized tomography abdomen and pelvis reported bulky heterogeneously enhancing uterus with large heterogenous enhancing mass measuring 17.6 × 11.6 × 16.1 cm, arising from the fundus of uterus extending into endometrial cavity, anterior and posterior myometrium with raised vascularity. Loss of fat planes found from all sides abutting the adjacent structures suggestive of GTN. Bilateral ovaries were not visualized. Note was made of thrombosed and tortuous bilateral ovarian veins till the level of L4 and L5 vertebrae with multiple bilateral collaterals in broad ligament. Right internal iliac vein and its tributaries were also thrombosed till the level of common iliac vein. However, there was no thrombosis in left internal iliac vein. Rest of the abdominal organ did not reveal any evidence of metastasis. There were multiple confluent nodal opacities with ground glass opacities in bilateral lung parenchyma with bilateral pleural effusion in CT chest. The GTN score was >8. Patient was started on intravenous antibiotics, low molecular heparin and consultation was taken for chemotherapy from medical oncologist. In the meanwhile, patient developed signs and symptoms of acute abdomen suggestive of uterine rupture and hemoperitoneum at 36 hours of admission. Emergency exploratory laparotomy was performed. Intraoperatively, there was 2 liters of hemoperitoneum and uterine rupture along



Figs 3A to C: (A) Transvaginal sonography showing heterogeneous infiltrative lesion in the uterus, B, bladder; C, cervix; U, uterus; (B) Intraoperative finding showing large clot beneath the anterior abdominal wall; (C) Invasive mole with rupture uterus along the right lateral wall

the right lateral wall (Figs 3B and C) was seen through which tumor vesicles were coming out filling the whole of the peritoneal cavity and invading the right broad ligament and pelvic wall. Extremely vascular adhesions were present all around the uterus. Subtotal hysterectomy with debulking performed. She was given transfusion of multiple products intraoperatively and shifted to intensive care unit on ventilatory support. Unfortunately, she expired 24 hours after the surgery. Histopathology revealed invasive mole.

Case 3

A 24-year-old woman, Gravida2 Para1 at 10 weeks of gestation was diagnosed to be molar pregnancy. She underwent suction and evacuation at peripheral hospital. Her histopathological report confirmed molar pregnancy. Then, she was referred to our tertiary center 15 days later with post-evacuation raised beta hCG value of 2.5 lakhs. She had one normal delivery 3 years back. On admission to our hospital, patient was stable. Uterine height corresponded to 14 weeks gestation with no tenderness on per abdominal examination. On per vaginum examination, cervical os was closed and uterus was soft and enlarged to 14 weeks. There was a heteroechoic content of 7.6 × 7.2 cm in the uterus with raised vascularity on transabdominal ultrasound. Her metastatic work up including hemogram, liver and kidney function tests, thyroid profile, basic coagulation profile and chest X-ray revealed no abnormality. Her diagnosis of post-molar GTN was made. Owing to her GTN score of 7, she was started on multiagent chemotherapy Etoposide Methotrexate Actinomycin D Cyclophosphamide Vincristine (EMACO) regimen after discussion with medical oncologist. She was also provided with contraceptive counseling. She received 7 cycles of chemotherapy with last three beta hCG values were normal. Following 2 months of last cycle she came to us with positive urine pregnancy test. Ultrasound revealed live dichorionic diamniotic twin pregnancy corresponding to 7 weeks. Her subsequent early anomaly and level II ultrasonography showed appropriate growth of both fetuses and no congenital anomaly. At present, she has crossed 28 weeks of gestation and is on regular follow-up with us to know the pregnancy outcome (Fig. 4).

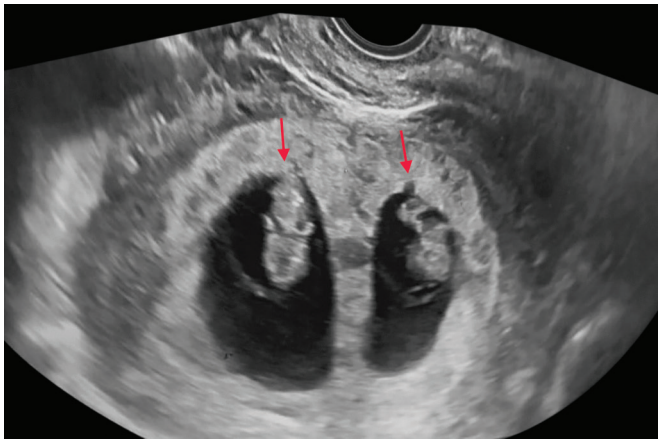


Fig. 4: Transvaginal sonography showing intrauterine dichorionic diamniotic twin pregnancy

Discussion

Gestational trophoblastic disease is a spectrum of benign and malignant pathologies originating from placenta. Complete and partial hydatidiform moles are benign trophoblastic placental pathologies, whereas invasive mole, post-molar GTN, gestational choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor, and atypical placental site nodule are malignant forms of gestational trophoblastic diseases, also termed as GTN.[1] Benign group is treatable but needs stringent clinical and biochemical follow-up with beta hCG levels to detect any malignant transformation. About 50% of GTN arise from hydatidiform mole, 25% following the term or preterm pregnancies and another 25% from abortions or tubal pregnancies.[2] In our study, all the three cases had prior history of gestational event followed by surgical evacuation.

The clinical presentation of GTNs is highly variable ranging from asymptomatic to acute hemoperitoneum with shock as supported by various studies.[3,4] In our study, third case of post-molar GTN was stable on presentation and reported to us with raised beta hCG (2.5 Lakh IU/mL) post-molar evacuation whereas first two cases (perforating choriocarcinoma and invasive mole with thrombosis) presented with emergency of acute pain abdomen for which lifesaving exploratory laparotomy was done. Usually, GTNs present with high beta hCG values which has also been seen in our first and third case. But, interestingly, our case of advanced metastatic

invasive mole had a beta hCG value of just 905 IU/mL inspite of life-threatening uterine rupture with extensive PVT and no case of invasive mole in literature has been reported to have beta hCG value less than 50,000 IU/mL.

Commonly, invasive mole is known for its progressively infiltrating nature, as trophoblastic tissue may invade the vascular wall and can lead to grave complications like massive hemorrhage, shock and in few cases sepsis with peritonitis.[5] However, in our case of invasive mole, apart from uterine perforation, widespread PVT was also present which is very unusual. Pelvic vein thrombosis is rare condition and has been seen in postpartum patients especially in the form of ovarian vein thrombosis. It has also been detected in association with malignancies, pelvic inflammatory diseases, inflammatory bowel disease, sepsis, and recent pelvic surgeries.[6] Clinical features include abdominal pain, fever, and leukocytosis which is also present in our case. Pulmonary embolism is a life-threatening complication. In literature, till date, only one case of GTN (post-molar-stage 2 GTN) has been reported to be associated with ovarian vein thrombosis and had successful outcome following single agent chemotherapy and anticoagulant therapy.[7] But, our case reported to us in advanced metastatic stage with thrombosis of bilateral ovarian veins, widespread internal iliac veins, and its tributaries. Unfortunately, she expired within 24 hours of emergency laparotomy and we did not get enough time to further investigate.

In contrast to previously available literature regarding rare potential for perforation of uterus in cases of choriocarcinoma, our first case had invading choriocarcinoma at three sites in uterus which perforated after routine pelvic examination.[8] Till 2014, 11 cases reported with spontaneous choriocarcinoma perforation has been quoted by Incebiyik et al. and further review of literature till date added 10 more cases to the list as detailed in Table 1.[9]

This table summarizes cases of perforated choriocarcinoma in literature similar to ours along with their varied clinical presentation and treatment modality. Typically, these cases had presented as acute abdomen in shock with most common diagnosis of ruptured ectopic pregnancy made preoperatively in view of positive urine pregnancy test.[4,10–13] Another unusual presentation of perforated choriocarcinoma was cesarean scar pregnancy reported by Sherer et al.[14] COVID pandemic too led to delay in acquiring treatment in two cases of GTN which finally needed life-saving surgeries.[15,16]

Table 1: Article review for cases of ruptured choriocarcinoma after 2014

S. No	*Author and year of publication*	*Study location*	*Age (years)*	*Condition mimicking*	*Beta hCG (IU/mL)*	*Metastasis*	*Management*	*Final diagnosis*
1	Sherer et al., 2015[14]	New York	34	Cesarean scar pregnancy	76,038	Lung	Laparoscopic guided excision of protruding mass from uterine scar	Choriocarcinoma
2	Agarwal et al., 2015[15]	India	28	Acute abdomen with uterine rupture and shock	7,00,000	Nil	TAH with partial cystectomy and omental biopsy with post-operative chemotherapy	Choriocarcinoma
3	Hashemi et al., 2016[11]	Iran	32	Rupture ectopic	14,000	Thoracic	Postoperative chemotherapy	Choriocarcinoma diagnosed after histopathology report
4	Chavan et al., 2016[10]	India	19	Ruptured ectopic during lactational amenorrhea	2.8 lakhs	Lungs and peritoneum	Subtotal hysterectomy with left salpingo-oophorectomy and right ovarian tissue reconstruction with post-operative chemotherapy	Choriocarcinoma
5	Gueye et al., 2017[3]	Senegal	24	Uterine rupture	NA	No metastasis	TAH, Chemotherapy scheduled Pt died, lack of follow-up	Choriocarcinoma
6	Pinkee et al., 2017[4]	India (Delhi)	30	Ruptured ectopic	2,11,000	No metastasis	TAH	Choriocarcinoma
7	Mehr et al., 2020[13]	Iran	34	Uterine rupture in patient confirmed Covid-19:	1,975,255	Lung	TAH followed by EMACO	Choriocarcinoma
8	Yeoh et al., 2021[12]	Malaysia	41	Ruptured ectopic pregnancy	NA	NIL	Wedge resection f/b TAH 3 months later after confirming choriocarcinoma on HPE	Choriocarcinoma
9	Bas et al., 2021[16]	Turkey	19	AUB, uterine rupture with shock	21,005	NIL	TAH	Choriocarcinoma
10	Case 1 (in our study)	India	20	AUB with acute abdomen	9,73,776	Lung	TAH	Choriocarcinoma f/b chemotherapy

Two cases reported to have managed as abnormal uterine bleeding and one even received GnRH analogue.[4,15] Eventually, both women underwent laparotomy for hemoperitoneum. Similarly, our first case also had irregular uterine bleeding for 6 months which later on developed abdominal hemorrhage after per vaginum examination which was an eye-opener.

The GTNs are extremely chemosensitive tumors with high survival and cure rate even in advanced and metastatic condition. But, in rare circumstances of acute tumor hemorrhage, bladder and bowel obstruction and infection, in which surgical intervention becomes mandatory like in our first two cases. On the contrary, epithelioid trophoblastic tumor and placental site trophoblastic tumor are the chemoresistant tumors, requiring primary surgery in the form of hysterectomy.

Through our third case, we also want to emphasize on the reproductive outcome of patients after treatment of high-risk GTN. In literature, though the overall pregnancy outcome after chemotherapy is reassuring in low risk GTN as compared with high-risk (70–85% vs 50–55%, respectively).[17] Gupta et al. reported successful pregnancy outcome in high-risk GTN.[18] Additionally, higher abortion rates had been reported in patients who conceived within 6 months of chemotherapy (35–71%) compared with those who conceived later.[19] Few studies also demonstrated the increased occurrence of congenital malformation.[20] Therefore, contraception till 1 year is recommended after disease remission.[21] Though, our case being high-risk GTN conceived in 2 months after last cycle of multiagent chemotherapy inspite of contraceptive counseling. Fortunately, her pregnancy has progressed to the period of viability with normal fetus, placenta and no detectable congenital anomaly on ultrasonography and now, she is kept on regular maternal surveillance and fetal monitoring.

To summarize, we wish to highlight the rarity of presentation in varied spectrum of GTN such as perforated choriocarcinoma following pelvic examination, invasive mole with extensive PVT, conception following chemotherapy in post-molar GTN.

Conclusion

This case series imparts message of careful vigilant approach to GTD cases in the form of guarded pelvic examination which might lead to life-threatening condition. We want to make aware the obstetricians regarding PVT following GTN, a rare complication of invasive mole. The GTN is tricky disease which can be risky sometimes or it can be well managed by the obstetrician. Thereby, we wish to give hope to high-risk GTN for fair reproductive outcome inspite of multiagent chemotherapy immediately following GTN remission.

Orcid

Upasana Verma https://orcid.org/0009-0002-3366-2003
Rachna Agarwal https://orcid.org/0000-0002-2358-7778
Bhanu Priya https://orcid.org/0000-0002-3536-6171
Sandhya Jain https://orcid.org/0000-0001-6945-9790

References

1. Ngan HYS, Seckl MJ, Berkowitz RS, et al. Update on the diagnosis and management of gestational trophoblastic disease. Int J Gynaecol Obstet 2018;143 Suppl 2:79–85. DOI: 10.1002/ijgo.12615.
2. Brown J, Naumann RW, Seckl MJ, et al. 15 years of progress in gestational trophoblastic disease: Scoring, standardization, and salvage. Gynecol Oncol 2017;144(1):200–207. DOI: 10.1016/j.ygyno.2016.08.330.
3. Gueye M, Gueye MDN, Thiam O, et al. Choriocarcinoma with uterine rupture presenting as acute haemoperitoneum and shock. Int J Reprod Contracept Obstet Gynecol 2017;6(3):1141–1143. DOI: 10.18203/2320-1770.ijrcog20170603.
4. Pinkee S, Godha Z, Poonam L, et al. Perforating uterine choriocarcinoma – A rare case report. Obstet Gynecol Int J 2017;7(4):295–296. DOI: 10.15406/ogij.2017.07.00257.
5. Tamang T, Tshomo U. Gestational choriocarcinoma with varied clinical presentation and treatment outcome: A case series. J South Asian Feder Obst Gynae 2018;10(4):276–280. DOI: 10.5005/jp-journals-10006-1606.
6. Kodali N, Veytsman I, Martyr S, et al. Diagnosis and management of ovarian vein thrombosis in a healthy individual: A case report and a literature review. J Thromb Haemost 2017;15(2):242–245. DOI: 10.1111/jth.13584.
7. Kim IY, Kim SH, Hwang IT, et al. A rare case of ovarian vein thrombosis in a gestational trophoblastic neoplasia patient. Obstet Gynecol Sci 2019;62(3):190–193. DOI: 10.5468/ogs.2019.62.3.190.
8. Mangla M, Singla D, Kaur H, et al. Unusual clinical presentations of choriocarcinoma: A systematic review of case reports. Taiwan J Obstet Gynecol 2017;56(1):1–8. DOI: 10.1016/j.tjog.2015.05.011.
9. Incebiyik A, Hilali NG, Camuzcuoglu A, et al. A rare cause of acute abdomen: Spontaneous uterine rupture due to gestational choriocarcinoma. Research 2014;1(5):719. DOI: 10.13070/rs.en.1.719.
10. Chavan K, Poddar P, Saraogi R, et al. Choriocarcinoma with rupture of uterus during lactational amenorrhea. Indian J Gynecol Oncolog 2016;14(2). p. 29. Available from: https://link.springer.com/article/10.1007/s40944-016-0061-5#:~:text=Cases%20of%20choriocarcinoma%20with%20uterine,cases%20due%20to%20massive%20hemorrhage.
11. Hashemi SM, Derakhshandi H, Fazeli SA, et al. A case of choriocarcinoma with concurrent rare presentations: Spontaneous uterine rupture and extensive thoracic spine metastases. J Obstet Gynaecol 2016;36(5):679–680. DOI: 10.3109/01443615.2015.1127904.
12. Yeoh S, Yong SL, Teoh PI, et al. A positive urine pregnancy test with haemoperitoneum: Misdiagnosed postpartum choriocarcinoma with uterine rupture mimicking ruptured ectopic pregnancy. Horm Mol Biol Clin Investig 2021;43(1):85–88. DOI: 10.1515/hmbci-2021-0048.
13. Mehr SGD, Ayatollahi H, Mohammadi A, et al. Choriocarcinoma with uterine rupture in a patient with confirmed COVID-19 infection: A rare case report. Int J Cancer Manag 2020;13(9):e104080. DOI: 10.5812/ijcm.104080.
14. Sherer DM, Dalloul M, Cho Y, et al. Spontaneous first-trimester perforation of the uterus following Cesarean scar pregnancy choriocarcinoma. Ultrasound Obstet Gynecol 2016;47(4):519–521. DOI: 10.1002/uog.15843.
15. Agarwal M, Kumar R, Pyrbot J, et al. Choriocarcinoma with uterine rupture and shock: A rare case report. J Clin Diagn Res 2015;9(10):ED20-1. DOI: 10.7860/JCDR/2015/15424.6679.
16. Bas S, Seyfettinoglu S, Narin MA, et al. Loss of reproductive ability due to late application of young refugee with choriocarcinoma during the COVID-19 pandemic. J Adolesc Young Adult Oncol 2021;10(3):355–358. DOI: 10.1089/jayao.2020.0177.
17. Madi JM, Paganella MP, Litvin IE, et al. Perinatal outcomes of first pregnancy after chemotherapy for gestational trophoblastic neoplasia: A systematic review of observational studies and meta-analysis. Am J Obstet Gynecol 2021;226(5);633–645;e8. DOI: 10.1016/j.ajog.2021.10.004.
18. Gupta V, Nanda A, Sharma A, et al. Live birth following treatment of metastatic cerebral choriocarcinoma. J South Asian Feder Obs Gynae 2011;3(3):151–152. DOI: 10.5005/jp-journals-10006-1156.
19. Garcia MT, Lin LH, Fushida K, et al. Pregnancy outcomes after chemotherapy for trophoblastic neoplasia. Rev Assoc Med Bras 1992;62(9):837–842. DOI: 10.1590/1806-9282.62.09.837.

20. Goto S, Ino K, Mitsui T, et al. Survival rates of patients with choriocarcinoma treated with chemotherapy without hysterectomy: Effects of anticancer agents on subsequent births. Gynecol Oncol 2004;93(2):529–535. DOI: 10.1016/j.ygyno.2004.02.018.
21. Tidy J, Seckl M, Hancock BW, on behalf of the Royal College of Obstetricians and Gynaecologists. Management of Gestational Trophoblastic Disease. BJOG 2021;128(3):e1–e27. DOI: 10.1111/1471-0528.16266.