International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2022; 6(3): 55-58
Received: 02-03-2022
Accepted: 10-04-2022

Dr. Lynette Fernandes
Senior Resident, Department of OBG, Goa Medical College, Goa, India

Dr. Manjusha Jindal
Associate Professor, Department of OBG, Goa Medical College, Goa, India

Dr. Rupa Padwalkar
Lecturer, Department of OBG, Goa Medical College, Goa, India

Corresponding Author:
Dr. Manjusha Jindal
Associate Professor, Department of OBG, Goa Medical College, Goa, India

A case series of gestational trophoblastic disease, it's variants, management and outcomes in a tertiary health care centre: A report of three cases

Dr. Lynette Fernandes, Dr. Manjusha Jindal and Dr. Rupa Padwalkar

DOI: https://doi.org/10.33545/gynae.2022.v6.i3a.1184

Abstract
Gestational trophoblastic disease (GTD) forms a group of disorders spanning the conditions of complete and partial molar pregnancies through to the malignant conditions of invasive mole, choriocarcinoma and the very rare placental site trophoblastic tumor (PSTT).
Presented here are three cases, which included all of the three above mentioned forms of GTD. Each case had a different line of management and outcome and presented to our hospital within a span of one year.
The rarity of these cases, in incidence and presentation is of especial importance and thus deserve a mention in modern day obstetrics.

Keywords: Gestational trophoblastic neoplasia, molar pregnancy, Placental site trophoblastic tumor chorio carcinoma, EMACO regimen

Introduction
Gestational trophoblastic disease is divided into molar and non molar tumors. Non molar tumors are grouped as gestational trophoblastic neoplasia (GTN) [2].
GTN are classified histologically into three distinct subgroups, invasive mole, choriocarcinoma and placental site trophoblastic tumor (PSTT) [3].
Choriocarcinoma is a highly malignant tumor of trophoblastic origin. It is composed of two types of cells, syncytiotrophoblasts and cytotrophoblasts. The syncytiotrophoblast is the differentiated hormone secreting component [4].
Most cases of choriocarcinoma are intra-uterine and of gestational origin, however, extrauterine gestational choriocarcinomas may also arise at a site of ectopic pregnancy. The non-gestational choriocarcinomas are believed to develop from pluripotent germ cells, most commonly arising in the gonads. Most cases present within one year of the antecedent pregnancy (molar or non-molar). However, very rarely, choriocarcinoma can develop from germ cells or from dedifferentiation of endometrial carcinoma into choriocarcinoma [5].
Choriocarcinoma in postmenopausal women is very rare, however a few cases of choriocarcinoma developing after a long latent period from last pregnancy have been reported [6-9]. We have presented here, a case of choriocarcinoma in a 54 year old postmenopausal lady.
PSTT is a rare and special type of GTD. First described in 1976 by Kurman [10], its malignant potential earned attention in 1981 when Twiggs reported a death secondary to it [11]. In 1983, WHO formally acknowledged PSTT as a neoplastic lesion and christened it as we know it. The incidence of PSTT is approximately 1/1,00,000 of all pregnancies and approximately 1-2% of all GTD's. its mortality is 25% [12]. To date, almost 300 cases of PSTT have been reported around the world [13]. We have encountered a case of PSTT in our hospital in April 2017, and is the first such case seen at this hospital.
Invasive mole is characterized by the presence of whole chorionic vili that accompany excessive trophoblastic overgrowth and invasion. These tissues penetrate deep into the myometrium, sometimes involving the peritoneum and vaginal vault. Such moles are locally invasive, but lack the tendency to develop widespread metastases. It follows approximately 10-15% of complete hydadtiform mole [14]. Our case was a confirmed case of invasive mole, however, due to her poor compliance, rather than chemotherapy alone, we used a combination therapy of surgical and medical management.

Cases

Case 1

Our patient was a 54 year old Para3, ligated, who presented with one episode of bleeding PV, 1 year after cessation of her menses, to a peripheral heath centre. She underwent a Dilatation and Currettage at said PHC. Her D and C histopathological report showed ?trophoblastic cells with pleomorphism. She was referred to our hospital in view of the same.

Except for hypertension, she had no other significant history. Her last childbirth was 21 years ago. She belonged to the lower middle class of the socio economic strata.

On examination

On general examination, no significant abnormality was found. Her gynaecological examination revealed an erosion on her cervix on speculum examination, well as an irregular friable area between 4'o clock and 6'o clock on the cervix, which bled on touch. Uterine size of 14 to 16 weeks, regularly enlarged. No other significant findings were noted. Her UPT was positive.

A baseline beta HCG was sent and an USG and MRI performed. Her slides were also reviewed, which confirmed trophoblastic cells. Her HCG value was 52,133 and USG showed a 5.6X4.8X4.8 cm mass distending the uterine cavity.

MRI showed an echogenic lesion distending the endometrial cavity and stranding of the fat in the right parametrium was noted. There was no evidence of metastasis to the lungs. A staging of stage II and a prognostic score of 11 was assigned.

Decision for starting EMACO regimen of chemotherapy was taken and initiated.

Patient received 4 cycles with an interval of 15 days between each cycle uneventfully. All investigations were done before and after cycle and each chemo dose monitored.

Patients response to chemotherapy was very reassuring. Clinically, the size of the uterus reduced to 8 weeks size. Radiologically also, the mass showed a reduction in size to 3X3X2cm. Her beta HCG levels fell to 21.4 mIU/ml after the fourth cycle.

During the fifth cycle, however, patient developed acute Myelosuppresion. Her Absolute Neutrophil Count prior to starting the cycle was 6536, however, during the course of the cycle, she developed GI symptoms and fever, as well as cutaneous side effects. GCSF was started for her and the cycle was interrupted. Despite that, her total count continued to fall and she developed sepsis with MODS. She eventually succumbed to septic shock.

Discussion

Choriocarcinoma is considered as one of the most curable cancer, even in the presence of metastases [15]. Although rare, the possibility should be considered in postmenopausal women, and if occurred, the management should be initiated at the earliest [15]. GTN, especially choriocarcinoma is very rare after menopause [16]. When choriocarcinoma occurs in postmenopausal women, it is difficult to rule out trophoblastic differentiation within an endometrial cancer [5]. Khuu *et al* reported a case of uterine carcinsarcoma with choriocarcinomatous dedifferentiation in a 71 year old [17]. In that case, histology results suggested choriocarcinoma intermixed with adenocarcinoma and stromal sarcoma. In our patient however, only isolated trophoblastic cells were found. In literature review, there are very few cases of gestational disease in postmenopausal women. Garcia *et al* reported that 109 cases of GTD in women older than 50 years were evaluated in the larger historical series and found malignant disease in 28.4% and benign moles in 47.7% [18]. The occurrence of pregnancy may be possible, but without symptoms [15]. Desai *et al* reported a case of choricarcinoma in a 73 year old, developing 38 years after last pregnancy and 23 years after menopause [5]. In fact, there are reports of a very long latent period between last pregnancy and occurrence of choriocarcinoma with no known mechanism [5, 19]. Evsen *et al* reported a case of post menopausal bleeding with a history of molar pregnancy, three years after menopause at 52 years, and subsequently developing choriocarcinoma at 58 years [20]. In the present case, the duration between pregnancy and diagnosis was 21 years while that between menopause and diagnosis was one year.

Choriocarcinoma is very chemo-sensitive [15]. Nearly 90% remits, with available chemo regimens [20]. In our study however, our patient unfortunately succumbed, which is also not unheard of, as reported by Bazinet *et al*. [21]. They could not rescue their patient due to poor conditions [21].

Case 2

Our patient was a 46 year old Para1Abortion2L1 with previous LSCS. Her LMP was 16/01/17. She underwent an evacuation and curettage on the 22/03/17, in a private hospital, in view of her USG showing anembryonic demise with spotting PV.

She had presented on 19/04/17 with history of continuous spotting PV since the procedure. At admission, there was pallor and tachycardia. No significant findings were noted on per abdomen examination. Gynaecological examination revealed a uterine size of 8 weeks with an open os and few clots within the uterine cavity. UPT was strongly positive. An USG was done which was s/o retained products.

A baseline beta HCG was sent and in view of suspicion of retained products, E and C was done. Her HPE was inconclusive.

However, patient had another bout of bleeding 24 hours post evacuation. Her baseline beta HCG was 20,000 mIU/ml and an USG was done which showed a 3.5X3.5 cm echogenic lesion filling the endometrial cavity and invading into the myometrium. A suspicion of molar pregnancy was there and an MRI was done which showed the same lesion but no invasion.

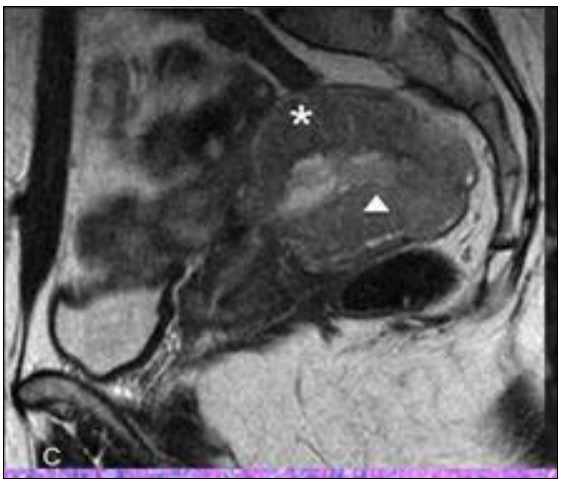

Fig 1: MRI imaging of PSTT

Patient was given single agent chemotherapy with methotrexate and a beta HCG repeated on day 7. This value was 19,400 mIU/ml.

Since patient had completed her family, and was perimenopausal as well as not responding to chemotherapy, a TAH without BSO was performed, however, due to bleeding from the right

infundibulopelvic ligament, a RSO also to later be performed during hemostasis confirmation. Both her ovaries were normal on ot table. Other findings on table included a few adhesions and a 1X1 cm nodular lesion over the cervix.

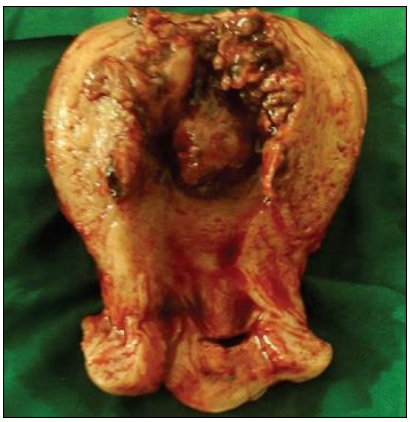

Fig 2: Surgical specimen of radiological image

Her histopathological report was suggestive of PSTT, with a mitotic figure rate of less than 5. A prognostic score of 4 was assigned.
On the 7th post op day, her beta HCG fell to 2603 mIU/ml.
Patient was discharged after above and was routinely following up at our opd, her last beta HCG value was less than 5 mIU/ml, done six months after she presented to us.

Discussion
PSTT frequently develops in women of reproductive age group. The interval from prior pregnancy to tumor development is usually less than 2 years [22]. PSTT is typically secondary to varieties of pregnancies and often follows a term labor for a female infant or an abortion, molar pregnancy or ectopic pregnancy [23]. Unlike other GTN's, the level of serum beta hcg is usually under the measurable limit or slightly elevated [22]. Our patient's levels, contradictory to this, were around 20,000. The beta hcg levels, however, are not associated with malignant behaviour [24]. Therefore, the level of serum beta hcg cannot accurately reflect the tumor burden and has limited value as a prognostic tool. Histologically, PSTT findings are specific, however, they are unable to differentiate between benign and malignant. A high mitotic rate of more than 5/10 HPF (and especially more than 10/10 HPF), and substantial haemorrhaging and necrosis are suggestive of malignancy [22].
Tumor cells cannot be effectively removed by curettage because they invade uterine muscle fibres [22]. In addition, they tend to spread via lymphatics, resulting in relative resistance to chemotherapy [25]. Therefore, TAH is recommended provided the disease is localised to the uterus [22]. Additionally, ovarian metastasis are rare and an oophorectomy cannot prevent postoperative extrauterine metastasis or improve prognosis. Our patient's ovaries were normal on OT table, and thus preserved, except the right ovary, which had to be removed to secure hemostasis. She has not displayed any signs of recurrence till November 2017.

Case 3
Patient was a 31 year old who presented on 19/01/2017 as a Para3L2 who had undergone a suction evacuation on 04/01/16 in view of a molar pregnancy. Her beta HCG in that pregnancy was 1, 04, 506mIU/ml, pre evacuation. She received single dose methotrexate and thereafter, patient had absconded from the hospital.
When she presented, she gave history of heavy bleeding PV and noticing a mass PA and had severe anemia.
Her uterine size was 24 weeks and gynaecological examination showed the cervix to be replaced by a vascular growth. There was no adnexal mass.
Her baseline beta HCG was 4,37,978 mIU/ml.
Her CT scan was done which showed a 12X10X9 cm central hypodensity within the uterus with invasion into the myometrium as well as metastasis to the lungs. A staging of III and prognostic scoring of 10 was established and EMACO regimen of chemotherapy initiated. Her beta hcg after one cycle of chemotherapy doubled to 8, 14, 000 mIU/ml.
Also, her poor compliance with follow up was another factor. In view of this, decision for hysterectomy was taken. Ot findings were suggestive of impending perforation of the uterine wall and both ovaries normal. A TAH without BSO was performed.
Post-surgery, patient received 5 cycles of EMACO uneventfully. Her beta hcg dropped to 21 mIU/ml after ther 5th cycle.
She comes routinely for follow up and her last beta HCG was less than 5mIU/ml done on 03/09/17. Patient had not followed up thereafter.

Discussion
An invasive mole is a form of GTN that occurs due to abnormal proliferation of placental trophoblast. It most commonly occurs after evacuation of a GTD and is characterised by the presence of edematous chorionic villi with trophoblastic proliferation that invades into the myometrium of the uterus or to adjacent structures such as vagina, vulva, broad ligament and even uterine vessels [14].
Approximately 8% of patient with complete moles will develop a malignant tumor after evacuation [26]. It is therefore imperative to obtain serial beta- hcg levels after evacuation, which if persistently elevated should raise the suspicion of GTN. In our case, since this patient was lost to follow up, this was not possible. With regards to management, the mainstay of treatment involves chemotherapy as these tumors respond well to a wide variety of regimens [27].
Invasive moles are treated with single dose methotrexate, for low risk GTN has shown a success rate of 77.5% [27]. Failure has been reported with methotrexate and various factors like high pre-treatment beta hcg and FIGO scoring have been attributed to it [28, 29], in which case combination chemo regimens have been attempted and succeeded [27].
However, resistance to even this is seen [30], as in our case.
Surgery is done for complications like perforation, haemorrhage, family completed, large mass or PSTT [27], as well as for old age, chemoresistance, poor compliance [24]. Our patient, her completed family, poor compliance, as well chemoresistance prompted us to perform a hysterectomy for her.

Conclusion
The three variants of GTN occurring so close to each other deserved a mention in modern day obstetrics, especially given the rarity of the same. Also, the management for each case should be individualised, with the best interests of the patient at mind.

Conflict of interest: None.
Consent: Duly written and taken.

References
1. RCOG Green-top Guideline no 38, 2010.

2. Williams Obstetrics 23rd edition, 257-65.
3. Moodley M, Tunkyi K. Gestational trophoblastic syndrome, an audit of 112 patients, Int J Gynecol Cancer. 2003;13(2):234-9.
4. Cole LA. New discoveries on the biology and detection of human chorionic gonadotropin. Reprod Biol Endocrinol. 2009;7:8.
5. Desai *et al*. Journal of Medical Case Reports. 2010;4:379.
6. O'Neill CJ, Houghton F, Clarke J, McCluggage WG. Uterine gestational choriocarcinoma developing after a long latent period in a postmenopausal woman: the value of DNA polymorphism studies. Int J Surg Pathol. 2008;16:226-229.
7. Okamoto T, Nomura S, Nakanishi T, Yamada S, Tomoda Y: A case of uterine choriocarcinoma with spontaneous rupture twenty-three years following the antecedent pregnancy. J Obstet Gynaecol Res. 1997;23:189-195.
8. Marcu M, Chefani A, Sajin M: Postmenopausal choriocarcinoma: A case report. Rom J Morphol Embryol. 2005;46:145-148.
9. Sonobe H, Taguchi K, Ogawa K, Yoshioka T: Latent vaginal choriocarcinoma in a postmenopausal woman. Acta Pathol Jpn. 1976;26:611-618.
10. Kurman RJ, Schully RE, Norris HJ. Trophoblastic pseudotumor of the uterus: Anexaggerated form of syncytial endometritis simulating a malignant tumor. Cancer. 1976;38:1212-1226.
11. Twiggs LB, Oagaki T, *et al*. Trophoblastic pseudotumor-evidence of malignant disease potential. Gynecol Oncol. 1981;12(2 t 1):238-248.
12. Piura B, Shaco-Levy R. Placental site trophoblastic tumor. Harefuah. 2007;146:62-67.
13. Luiza JW *et al*. Placental site trophoblastic tumor: Immunohistochemistry algorithm key to diagnosis and review of literature. Gynecol Oncol Case Rep. 2013;7:13-15.
14. Ahmed Samy *et al*. Inavsive mole of the uterus: a description of two cases managed by hysterectomy. The Egyptian Journal ofRadiology and Nuclear Medicine. 2015;46:1267-1270.
15. Zohreh Yousoufi *et al*. Postmenopausal choriocarcinoma: Case report and literature review. Int J Cancer Manag. 2017 May;10(5):e-4400.
16. Fisher *et al*. the impact of molecular genetics on management of women with HCG producing malignancies. Gynecol Oncol. 2007;107(3)413-9.
17. Khuu *et al*: carcinosarcoma of the uterus associated with a nongestational choriocarcinoma. South Med J. 2000;93:226-228.
18. Garcia, *et al*. A hydadtiform mole in a postmenopausal woman. A case report and review of literature. Arch Pathol Lab Med. 2004;128(9):1039-42.
19. Kaabia *et al*. The uterine choriocarcinoma in postmenopausal women: Specificities of diagnosis and treatment. Pan Afr Med J. 2014;19:176.
20. Evsen *et al*. A rare case of postmenopausal bleeding: Choriocarcinoma. J Clin Gynecol Obstetr. 2012, 1.
21. Bazinet *et al*. Choriocarcinoma in a post menopausal nulligravida. Can Med Assoc J. 1970;102(2):150-1.
22. Xianling Zeng *et al*. Placental site trophoblastic tumor: A case report and literature review. Intractable and rare diseases Research. 2015;4(3):147-151.
23. Kucuk Z, *et al*. A rare case of uterine rupture due to a placental site trophoblastic tumor in the rudimentary horn. J Obstet Gynecol. 2015;35:97-98.
24. Felmate CM, *et al*. Placental site trophoblastic tumor: A 17 year experience at the New England Trophoblastic Disease Centre. Gynaecol Oncol. 2001;82:415-419.
25. Lan C, *et al*. Placental site trophoblastic tumor: Lymphatic spread and possible target markers. Gynecol Oncol. 2010;116:430-437.
26. Martonffy Al *et al*. First trimester complications. Prim Care. 2012;39:71-82.
27. Laul *et al*. Two interesting cases of gestational trophoblastic disease with methotrexate failure. Int Journal of Reproduction, Contraception, Obstetrics and Gynaecology. 2016;5(9)3215-3252.
28. Matsui *et al*. Relapse rate of patients with low risk GTT initially reated with single agent chemotherapy. Gynecol Oncol. 2005;96(3):616-20.
29. Growdon *et al*. Low risk GTN and methotrexate resistance: predictors of response to treatment with actinomycin D and need for combination therapy. J Reproduct Med. 2010;55(7-8):279-84.
30. Katke RD. Atypical presentation of uterine choriocarcinoma, a case report and review of literature. Clin Cancer Invest J. 2015;4(6):713-716.