

Spectrum of Gestational Trophoblastic Disease Secondary to Dilation and Evacuation - Our Experience at a Tertiary Care Centre in Mullana, Ambala

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ABSTRACT

BACKGROUND

Gestational trophoblastic diseases have varying clinical presentations with certain diagnostic signs and symptoms. A strong correlation between gestational trophoblastic diseases (GTD) and a previous history of dilation & evacuation (D & E) has been documented in the limited available literature. We wanted to study the spectrum of gestational trophoblastic disease secondary to dilation & evacuation.

METHODS

A two-year study including all the females who were admitted to MMIMSR Hospital in view of suspicion of gestational trophoblastic disease was conducted with all having a common history of dilatation and evacuation in the recent past.

RESULTS

Through the analysis we saw the spectrum of GTD including partial mole, complete mole, invasive mole and choriocarcinoma, as well as its complications in the form of arterio-venous malformation (AVM).

CONCLUSIONS

The two-year experience suggests that dilatation and curettage may predispose a female of reproductive age group to develop gestational trophoblastic disease in the future. Hence, a high index of suspicion is necessary for timely diagnosis and intervention. The study further helped us understand the wide spectrum of the disease and its associated complications.

KEY WORDS

Abortion, AVM, Dilatation and Evacuation, GTD, GTN

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BACKGROUND

Dilatation and evacuation are widely used methods for uterine evacuation following early pregnancy complications including abortions or GTD's. D & E is the method of choice for management of complete molar pregnancy as well as partial molar pregnancy except when the size of the fetal parts defers the use of curettage when medical management can be used.

Gestational trophoblastic diseases include a wide spectrum of presentations including partial as well as complete molar pregnancy, invasive mole, choriocarcinoma, placental site trophoblastic tumour and epithelioid trophoblastic tumour. The latter four entities are clubbed together and referred to as gestational trophoblastic neoplasia (GTN). Recently, the spectrum of GTD has been expanded to also include a new entity namely atypical placental site nodule (APSN) as few of these lesions may coexist with or develop into placental site trophoblastic tumour (PSTT) / epithelioid trophoblastic tumour (ETT).¹ A high incidence of correlation with previous history of D & E has often been described in the limited available literature.

We wanted to study the spectrum of gestational trophoblastic disease secondary to dilation & evacuation.

METHODS

This was a case series conducted over a period of two-years from September 2018 to September 2020.

Collection of Data

All patients referred to the Department of Radio Diagnosis with clinically / ultrasound diagnosed GTD or its spectrum were part of the study.

Inclusion Criteria

- All patients clinically suspected to have GTD or its spectrum disorder.
- All patients with diagnosed GTD or its spectrum on ultrasound / computed tomography (CT) /magnetic resonance imaging (MRI).

A complete detailed clinical history of the patient was taken. Chief complaints and a thorough clinical examination including local and systemic examinations were performed. Relevant biochemical and blood investigations were sent for. Ultrasonography (USG) was done in all cases as the first line imaging modality of choice. Further use of advanced imaging modalities including CT ± contrast or MRI ± contrast, depending on the provisional diagnosis, as per the need, patient's condition and feasibility at the moment, were performed.

After the scan, all the images were evaluated in axial, coronal and sagittal plane. Findings were recorded and correlated with clinical / biochemical / imaging / biopsy / surgical findings.

Appropriate management as per the protocol was recommended to the treating clinician as per the findings. A

detailed follow-up was done for all the patients included in the study and shall be mentioned in the text.

Case Details

Patient 1

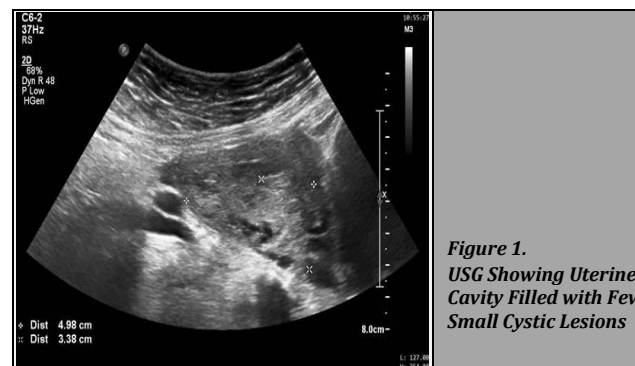


Figure 1.
USG Showing Uterine Cavity Filled with Few Small Cystic Lesions

A 32-year-old-female presented with amenorrhoea of 2 months and bleeding per vaginal for last 5 days. She had a history of incomplete abortion 8 months back for which D & E was performed. Her B-Hcg level was 3200 mIU / ml and USG showed few small cystic lesions occupying part of the uterine cavity with no appreciable fetal tissue, s / o complete molar pregnancy. She was taken up for D & E and the curettings were sent for histopathology which was suggestive of molar pregnancy. Sequential reduction in B-Hcg levels were observed on weekly follow ups.

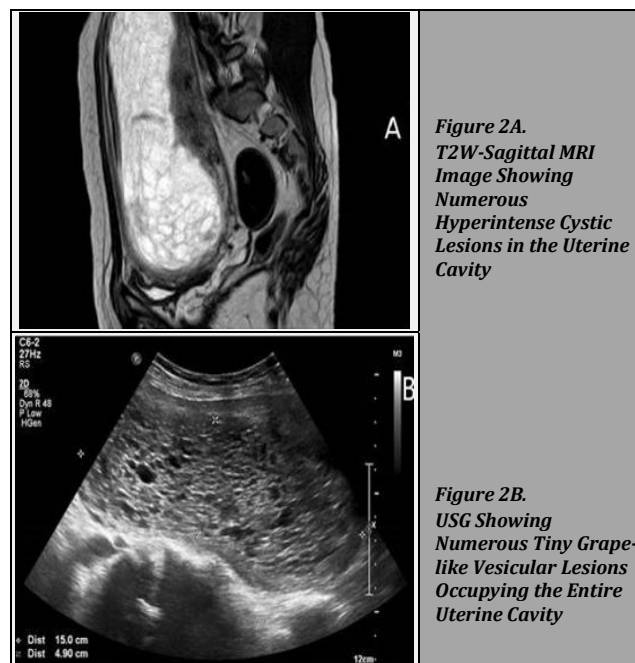


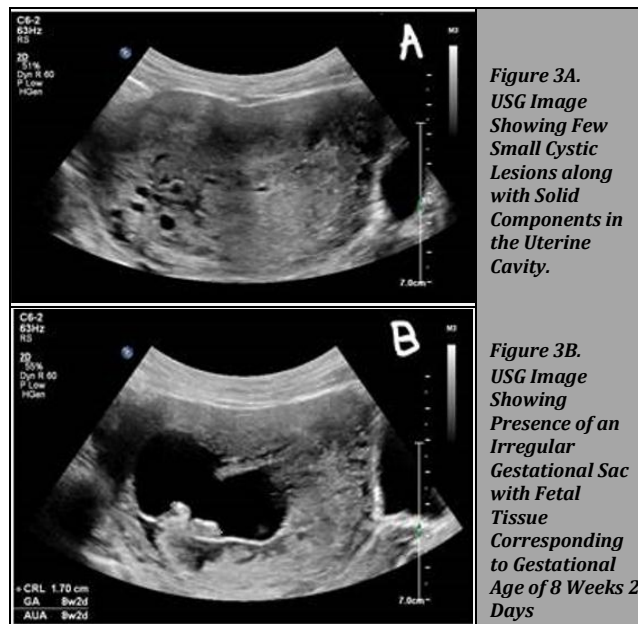
Figure 2A.
T2W-Sagittal MRI Image Showing Numerous Hyperintense Cystic Lesions in the Uterine Cavity

Figure 2B.
USG Showing Numerous Tiny Grape-like Vesicular Lesions Occupying the Entire Uterine Cavity

Patient 2

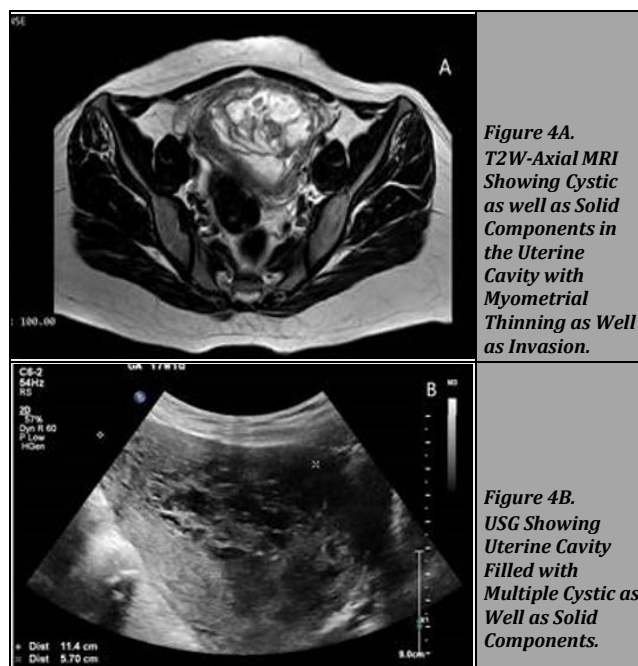
30-year-old-female P2L1A1 presented with amenorrhoea of 4 months and bleeding per vaginal for last 2 days. She gave a history of delivering an intrauterine fetal demise (IUFD) fetus at 9 months gestation wherein due to adherent retained products of conception (RPOC) she underwent D & E. B-Hcg level was 21,000 mIU / ml. USG and MRI revealed cystic lesions occupying the entire uterine cavity with no signs of myometrial invasion. A diagnosis of complete molar

pregnancy was made for which she underwent D&E and was discharged in a satisfactory condition with sequential reduction in the levels of B-Hcg on weekly follow-up.



Patient 3

24-year-old-female G2P1L1 presented with amenorrhoea of 4 months, severe abdominal pain and recurrent episodes of vomiting for the last 2 days. She had a history of D & E, I / v / o RPOC's following a normal vaginal delivery 3 years back. B-Hcg level was 43,200 mIU / ml. USG showed uterine cavity filled with multiple cystic as well as solid components with an irregular gestational sac with fetal tissue corresponding to gestational age of 8 weeks 2 days with absent cardiac activity. A diagnosis of partial molar pregnancy was made. She underwent D & E for the same and was discharged in a satisfactory condition with sequential reduction in the levels of B-HCG.



Patient 4

A 30-year-old G3P2L2 female presented with amenorrhoea of 4 months and bleeding per-vaginam for the last 7 days. She gave a history of medical termination of pregnancy (MTP) pill intake one year back followed by D & E, I / v / o incomplete abortion. Her B-Hcg levels were 2,59,315 mIU / ml. USG and MRI showed numerous cystic lesions occupying the entire uterine cavity with areas of myometrial invasion. A diagnosis of complete molar pregnancy with invasive component was made. She underwent hysterectomy and was discharged in a stable condition.

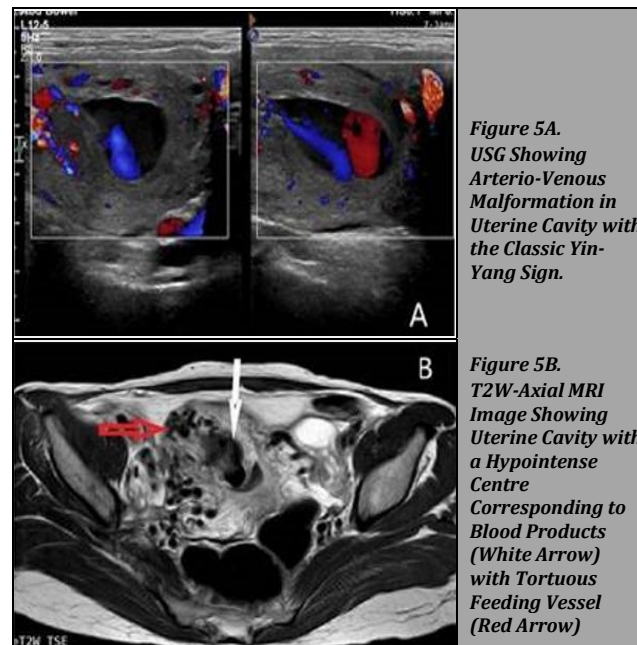




Figure 6B.
USG Showing Uterine Cavity Filled with Numerous Cystic Lesions (Red Arrow) with a Soft Tissue Component along the Right Lateral Uterine Wall (White Arrow)



Figure 6C.
Sagittal CECT Image Showing Irregular Heterogenous Hyper-Enhancing Areas with Soft Tissue Component along the Right Lateral Uterine Wall with wall Dehiscence (Black Arrow) with Numerous Dilated and Tortuous Vascular Channels (Red Arrow) with Massive Haemoperitoneum (White Arrow)

Patient 5

A 40-year-old female presented to the emergency with profuse bleeding per-vaginum for the past 1.5 months. She gave a history of incomplete abortion 8 months back for which she had undergone D & E. USG showed presence of an irregular ulcerated hyper-vascular lesion along the right lateral uterine wall and an invasive molar component was suspected. 6 months later, patient presented to us with the above said complaints. B-Hcg level was 73,500 mIU / ml. USG and MRI done at our institute showed conversion of the previous ulcerated uterine wall hypervascular mass into arterio-venous malformation. USG guided dilatation and curettage was done which on histopathology confirmed invasive molar component, however, during the procedure there was torrential bleeding for which hysterectomy had to be performed. She was later discharged in a stable condition.

Patient 6

A 26-year-old female P1L1A1 with previous 1 lower segment Caesarean section (LSCS) presented in a state of shock with progressive abdominal distention and tenderness, amenorrhoea of 7 months and bleeding per-vaginum for last 2 days. 4 months prior to presentation, she underwent D & E, I / v / o incomplete abortion following MTP pill intake. The histopathology report was suggestive of molar pregnancy. She presented to our institute with the above said complaints and a B-HCG level of 4,59,817 mIU / ml. USG and contrast enhanced computed tomography (CECT)-abdomen showed uterine cavity filled with numerous cystic lesions with a soft tissue component along right lateral uterine wall with wall rupture, multiple dilated and tortuous vascular channels, s / o AVM with massive haemoperitoneum. Diagnosis of complete molar pregnancy, myometrial invasion, uterine rupture, bleeding AVM with massive haemoperitoneum was made. She was taken up for emergency laparotomy, but due to excessive

blood loss, patient collapsed intra-operatively and could not be revived post- cardiopulmonary resuscitation (CPR).



Figure 7A.
CECT Abdomen: Axial Section Image Showing Image Showing Rent (White Arrowhead) in the Uterine Fundus with Peri-Uterine Fluid / Collection and Heterogenous Hyperdense Content likely RPOC (Red Arrowhead) along with Bowel Loops Showing Air-Fluid Levels s/o Bowel Obstruction (Green Arrowhead)



Figure 7B.
USG Image-Post-Embolic Status with Coil In-Situ Giving the Posterior Acoustic Shadowing

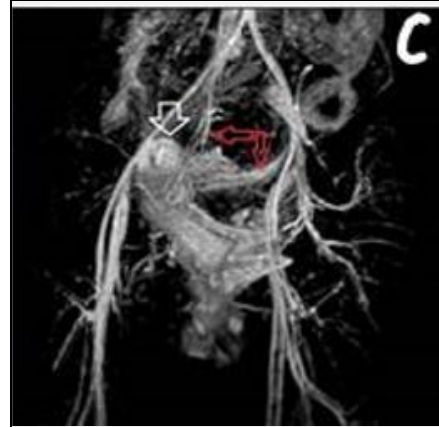


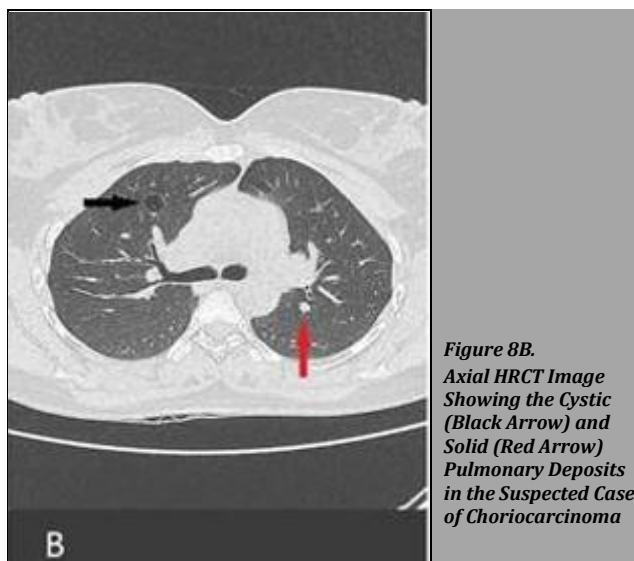
Figure 7C.
CEMR-Angiography: Coronal Section Image Shows Hyperintense Lesion at the Level of Fundus of Uterus (White Arrowhead) with Feeding Vessels (Red Arrowheads) Arising from the Right and Left Internal Iliac Arteries and Draining into the Internal Iliac Vein

Patient 7

A 35-year-old female P0L0A1 presented to the emergency in a state of shock with progressive abdominal distention and absent bowel sounds. The patient was tachypnoeic having a PR-116 / min, BP-90 / 60 mmHg, RR - 35 bpm, temp. - 100.2° f with SPO2-78 % on room air. There was a history of D & E 1 month prior to presentation. Incomplete abortion at an amenorrhoea of 7 weeks. 21 days following D & E the patient complained of pain abdomen and vomiting. Her urine pregnancy test (UPT) was positive, and her previous USG was suggestive of right ruptured ectopic pregnancy with hemoperitoneum with ulcerated uterine wall along the fundus.

She underwent exploratory laparotomy followed by right salpingectomy. Her condition worsened and was referred to our institute for further management. USG (using Doppler and spectral analysis) and CECT showed bulky uterus with heterogeneous and highly vascular infiltrating mass in fundus and body of uterus with myometrial invasion; perforation

along right lateral wall and fundus of uterus; peri-uterine collection; intestinal obstruction and progressively enlarging cystic lesions in the left adnexa with embedded left ovary. Her B-Hcg level was 81000 mIU / ml. She was taken up for exploratory laparotomy followed by uterine repair; products of conception seen coming out via the uterine breach were removed and sent for histopathological analysis which was suggestive of H. mole.



Following this chemotherapy was initiated. During the course of her treatment, the fundal infiltrating mass converted into a bleeding AVM which was confirmed on CEMR pelvis with angiography. Finally, a diagnosis of invasive mole with conversion to AVM was made. She underwent total of 6 cycles of chemotherapy for invasive mole with eventual resolution of the mass and sequential drop in levels of B-Hcg; and uterine artery embolisation for resolution of AVM.

Patient 8

A 24-year-old female presented with complaints of on-and-off bleeding per-vaginum for the past 3 months. She underwent D

& E for missed abortion 8 months back. Her B-Hcg level was 91,000 mIU / ml. USG and MRI showed infiltrative heterogenous mass invading the myometrium with area of extension just beyond the parametrium but not into the adnexa. High contrast computed tomography (HRCT)-chest showed metastatic deposits. A provisional diagnosis of choriocarcinoma was made. Patient refused further investigations or management and hence, no definite diagnosis could be made and was lost to follow-up.

RESULTS

Amongst our study group all the patients included (N = 8), had a common history of undergoing D & E in the recent past, either for incomplete abortion or for RPOC.

Diagnosis

- 12.5 % (N = 1) of the patients were diagnosed with partial mole.
- 37.5 % (N = 3) of the patients presented with complete mole and out of these, 33 % (N = 1) had simultaneous presence of invasive component.
- 37.5 % (N = 3) patients presented with invasive mole and 100 % of these cases complicated into arterio-venous malformation.
- 12.5 % (N = 1) of the patients presented with a suspicion of choriocarcinoma.

Management

- Patients with partial or complete mole underwent D & E and were discharged satisfactorily.
- Those with invasive mole were given chemotherapy and responded well with no signs of recurrence even on follow-up scans.
- The patient with AVM who underwent timely embolisation, their condition improved with complete resolution of the vascular malformation.
- 33 % (N = 1) of the patients with AVM could not be saved because of excessive blood loss due to late presentation.
- 33 % (N = 1) of the patients with AVM underwent hysterectomy due to torrential bleeding.

The patient with suspicion of choriocarcinoma did not undergo any confirmatory studies or any treatment and was lost to follow-up.

DISCUSSION

All the patients included in the study series presented to us with excessive bleeding per vaginal and had a common history of undergoing D & E sometime in the near past. On examination, all of them had Hb level well below the normal range and a uterine size large for their respective gestational age.

Case No.	Age (Yrs.)	Past History	Clinical Presentation	β-HCG Levels	Radiological Investigations	Radiological Diagnosis	Histopathological Diagnosis	Management	Follow-up
1	32	Incomplete abortion 8 months back followed by D & E	Amenorrhoea bleeding per vaginum	3,200 mIU / ml	USG: Few small cystic lesions occupying part of the uterine cavity. No fetal tissue.	Complete molar pregnancy	Complete molar pregnancy	D & E	Serial reduction in B-HCG levels on weekly follow-up.
2	30	Full term IUD delivery 9 months back D & E for adherent RPOC's post delivery	Amenorrhoea bleeding per vaginal	21,000 mIU / ml	USG: Numerous cystic lesions occupying the entire uterine cavity. MRI-Pelvis: Cystic lesions occupying the entire uterine cavity with no myometrial invasion	Complete molar pregnancy	Complete molar pregnancy	D & E	Serial reduction in B-HCG levels on weekly follow-up.
3	24	D & E for RPOC's	Amenorrhoea pain abdomen recurrent episodes of vomiting	43,200 mIU / ml	USG: Uterine cavity filled with multiple cystic and solid components with significant internal vascularity on doppler. Presence of an irregular gestational sac with fetal tissue corresponding to gestational age of 8 weeks 2 days with absent cardiac activity	Partial molar pregnancy	Partial molar pregnancy	D & E	Followed up weekly
4	30	D & E for RPOC's	Amenorrhoea bleeding per vaginum Expulsion of clots and few globular contents	2,59,315 mIU / ml	USG: Uterine cavity filled with multiple cystic and solid components with significant internal vascularity and myometrial thinning. No signs of metastatic deposits. MRI-Pelvis: Cystic lesions occupying entire uterine cavity with areas of myometrial invasion. HRCT chest: Normal with no signs of metastatic deposits. NCCT-Head: Normal with no signs of metastatic deposits	Complete molar pregnancy with invasive mole	Complete molar pregnancy with invasive mole	Total abdominal hysterectomy	Discharged in stable condition
5	40	D & E for incomplete abortion 8 months back outside USG: irregular ulcerated hyper-vascular lesion along the right lateral uterine wall: invasive molar component suspected	Profuse bleeding per-vaginam	73,500 mIU / ml.	USG: Arterio-venous malformation along uterine wall CEMRI: Conversion of previous ulcerated uterine wall mass into arterio-venous malformation with its feeding vessels arising from both internal iliac arteries.	Conversion of suspected invasive mole into AVM	AVM with areas of trophoblastic proliferation.	Chemotherapy with uterine artery embolization	Complete resolution of the uterine lesion. No signs of recurrence
6	26	D & E I / v / o incomplete abortion Previous 1 LSCS	Shock acute abdomen abdominal distention amenorrhoea bleeding per-vaginam	4,59,817 mIU / ml.	USG: Uterine cavity filled with numerous cystic lesions with soft tissue component along right lateral uterine wall with multiple dilated, tortuous vascular channels s / o arterio-venous malformation with massive hemoperitoneum. CECT: Uterine cavity filled with numerous cystic lesions with soft tissue component along right lateral uterine wall with wall dehiscence with numerous dilated and tortuous vascular channels and massive hemoperitoneum.	Complete molar pregnancy with myometrial invasion with uterine wall dehiscence with ruptured AVM with massive haemo-peritoneum.	Invasive mole with AVM	Exploratory laparotomy followed by TAH	Patient collapsed per-operatively and could not be revived
7	35	1 month prior to presentation: Amenorrhoea Multiple episodes of bleeding per-vaginal. D & E for suspected incomplete abortion. 1 week prior to presentation: Pain abdomen, vomiting and UPT (+). USG-Whole abdomen: right adnexal ruptured ectopic pregnancy haemoperitoneum ulcerated uterine wall along the fundus s / o heterotopic pregnancy. Exploratory laparotomy with right salpingectomy	Shock progressive abdominal distention absent bowel sounds	81,000 mIU / ml	USG- Whole abdomen: Highly vascular infiltrating mass in uterus with myometrial invasion. Visible rent in uterine fundus and body with visible spillage of contents. Peri-uterine collection intestinal obstruction mild haemoperitoneum X-ray chest AP: bronchitis CECT-whole abdomen: Irregular heterogenous myometrium in uterine fundus. Contained uterine perforation peri-uterine collection organised haematoma in left ovary intestinal obstruction mild haemoperitoneum	Invasive mole with conversion to AVM with contained uterine rupture and haemo-peritoneum	Invasive mole	Exploratory laparotomy Uterine repair 6xcycles of chemotherapy	During the course of her treatment, the fundal infiltrating mass converted into a bleeding AVM which was confirmed on CEMR pelvis with angiography. Uterine artery embolisation was performed for the same. Eventual resolution of the mass and sequential drop in levels of B-Hcg
8	24	D & E for missed abortion 8 months back	On-and-off bleeding per-vaginam for the past 3 months	91,000 mIU / ml	USG and MRI -infiltrative heterogenous mass invading the myometrium with extension just beyond the parametrium HRCT-Chest- metastatic deposits	Provisional diagnosis of Choriocarcinoma	Patient refused	Patient refused	Patient refused

Table 1. Summary of All the Cases

Molar pregnancies present commonly in the form of bunch of grapes like vesicles and giving the characteristic snow-storm appearance on USG with or without the presence of any fetal tissue. Most common symptom being irregular vaginal bleeding which is preceded by amenorrhoea.

20 % of complete moles can become invasive. Invasive moles are characterised microscopically by trophoblastic invasion of the myometrium with identifiable villous structures and rarely metastasize. The clinical presentation may overlap with several other entities such as retained products of conception as well as postpartum endometritis.² Patients have persistent vaginal bleeding with elevated beta human chorionic gonadotropin (HCG) titres post evacuation. The first line of treatment for invasive and persistent moles is chemotherapy which tends to show spontaneous regression post-treatment.

Choriocarcinoma is a highly malignant, necrotic, haemorrhagic, and locally invasive type of GTN with early and extensive vascular invasion resulting in metastases to distant sites even when the primary tumour is small.^{3,4}

Persistent trophoblastic neoplasia is presumed to be invasive mole unless there is presence of metastases which would suggest choriocarcinoma.⁵

Nearly 30 % of patients with GTN have metastases at the time of diagnosis, with the most common locations being to the lungs (80 % of cases), vagina (30 %), liver (10 %), and brain (10 %).⁶ Few of the complications of GTD and GTN include uterine AVM and pulmonary AVF.

Acquired Uterine Arterio-Venous Malformations

Uterine arterio-venous malformation with GTD as well as later, is a very uncommon disorder which can be diagnosed by arteriography, colour Doppler or MRI. The incidence of uterine AVM is difficult to estimate as most of the cases go unnoticed. Fewer than 150 cases have been reported in the literature.⁷

They may occur after a median interval time of 5 months to 13 years after the completion of chemotherapy for prior GTN. They often present with profuse, long lasting, unexplained, intermittent episodes of vaginal bleeding occurring with or without pelvic pain or dyspareunia.^{6,8} Colour Doppler with spectral analysis followed by angiography acts as the tool for definitive diagnosis.⁶

The success of trans-arterial embolisation in treating such lesions and in maintaining fertility has led to its ascendance as the treatment modality of choice; with hysterectomy being reserved as the last resort therapy.^{6,7}

Pulmonary Arterio-Venous Fistula (AVF)

These can develop within pulmonary metastases of choriocarcinoma after successful completion of chemotherapy. Usually these nodules resolve, however if there is a persistence, this should raise the possibility of a pulmonary AVF.⁶

The various types of GTD and GTN as mentioned prior are often indistinguishable on imaging modalities alone. A detailed history, clinical examination, B-HCG values, histopathological correlation as well as post-treatment response helps us to make the final diagnosis.

Seckl MJ et al. in their study found that gestational trophoblastic neoplasms most commonly develop after a previous or a pre-diagnosed GTD, after a previous history of any intervention like D & E or Caesarean and can also develop after live birth, miscarriage or termination of pregnancy.⁹

Tools for Investigation of Gestational Trophoblastic Neoplasia¹

- Chest x-ray is enough to diagnose lung metastases and can be used for counting the number of lung metastases to evaluate the risk score. CT-chest may then be used for a more accurate depiction.
- Liver metastases can be diagnosed by ultrasound or CT scanning.
- Brain metastases can be diagnosed by MRI or CT scanning.

Moodley M found that in their audit, 66.7 % of the patients had a previous normal term pregnancy and only 1.8 % of the patients had previous molar pregnancies.¹⁰

Kitange B et al. in their study found a prevalence of 12.8 % for hydatidiform mole amongst a study group of 180 patients with history of incomplete abortion.¹¹

Contractor S found in his report of a similar presentation of formation of a uterine arterio-venous malformation after performing intervention in the form of D & E in a case of molar pregnancy.¹²

Ahmed Samy El-Agwany found in his report that in case a patient undergoes any intervention like D & E for an underlying GTD there are high chances to convert into an AVM.¹³

CONCLUSIONS

A history of uterine curettage followed by excessive bleeding in a woman of reproductive age group should raise the suspicion of GTD, wherein the radiologist plays a key role in the initial diagnosis and in guiding the disease management.

Prompt recognition of a molar pregnancy may lead to a less extensive disease process and associated treatment expenditure. Patient compliance likely results in fewer complications and early disease resolution.

Although serum β -hCG is a highly useful biochemical marker for diagnosing GTD, it is not diagnostic when considered in isolation. Ultrasound is the first line radiological investigation in confirming the diagnosis of GTD in a case suspected on the basis of clinical findings and β -hCG levels. Ultrasound in combination with Doppler is also a useful tool for diagnosing invasive disease, assessing treatment response, and detecting local recurrence. MRI is invaluable to assess extrauterine disease spread and complications. Chest radiograph, brain MRI, and body CT are primarily used to rule out any metastatic disease. Conventional angiography can be used to manage patients with heavy bleeding or for chemoembolisation. Prudent use of these imaging techniques permits an early diagnosis and appropriate management, contributing to excellent cure rates of the disease.

The results from our study group, even though small, represent a striking 100 % correlation of the presenting

spectrum of GTD with a prior history of having undergone D & E in the near past for early pregnancy related complications.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jemds.com.

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