



Case Series

Gestational trophoblastic disease a perplexing challenge: A case series

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Abstract

Hydatidiform mole (HM) is classified under gestational trophoblastic disease (GTD). Molar pregnancies originate in villous trophoblasts and are characterized by abnormal chorionic villi with trophoblast hyperplasia as a consequence of overexpression of paternal genes. Gestational trophoblastic neoplasia (GTN) is the subtype of GTD which are invasive or metastatic. The disease process possesses a challenge to manage these cases due to its varied presentations and associated complications. This case series of 6 cases in a tertiary care hospital describes different presentations of hydatiform moles such as haemorrhagic shock, thyrotoxicosis; different types of HM like invasive/ complete/ partial moles and how intraoperative/ postoperative management of Hydatiform moles changes with each case. The Preoperative optimization, intraoperative and postoperative management of HM is challenging for Anaesthesiologist. The role of the multidisciplinary approach in the management is crucial.

Keywords: Hydatidiform mole, Gestational trophoblastic disease, Beta-hCG, Hyperthyroidism.

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1. Introduction

Hydatidiform mole (HM) is a group of diseases classified under gestational trophoblastic disease (GTD), which originate from placenta due to abnormal proliferation of trophoblast cells. The two different types of HM, complete mole and partial mole are mentioned. HM are considered benign but they are premalignant and can become invasive.¹ Gestational trophoblastic neoplasia (GTN) is the subtype of GTD which are invasive or metastatic and includes invasive mole, choriocarcinoma, placental site trophoblastic tumour, and epithelioid trophoblastic tumour. The different group of diseases classified under GTD have different karyotypes, histopathology, clinical presentations, management, complications and prognoses. The disease process can be complicated due to associated hyperthyroidism, hemodynamic changes, hyperemesis gravidarum, preeclampsia etc. It possesses challenge to manage these cases for anaesthesia and post operative care. Surgical removal of the HM is the treatment of choice and can be accomplished by either uterine evacuation or hysterectomy. Postoperative patient can complicate due to hyperthyroidism,

trophoblastic embolization, massive fluid replacement or preeclampsia and can develop various cardiopulmonary symptoms.^{2,3} This case series of six cases in a tertiary care hospital describes different presentations of hydatiform moles and how management of Hydatiform moles changes with each case. It also highlights the role of the multidisciplinary approach in the management of affected patients.

2. Case Series

2.1. Case 1

31yr/ Female patient Gravida 6, Para 3 with previous 3 caesarean section was referred from local hospital with complains of bleeding per-vaginum since last 15 days, pain in abdomen since last night and history of amenorrhoea. She also had progressive fever, associated with shivering. On Examination she was pale with pulse rate around 140/ min and respiratory rate of 30/min. Per abdomen uterus 16 weeks and relaxed. Per -speculum examination revealed grape like vesicles mixed with clots. Ultrasound (USG) was suggestive of bilateral ovarian cyst, endometrial

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heterogenous multiple cystic area likely complete hydatiform mole and free fluid. Her hemogram showed haemoglobin (Hb) 5.9 g/dL, Platelets 1.5 lakh, Thyroid stimulating hormone (TSH) 0.02 mIU/ml, beta-human chorionic gonadotropin (beta-hCG) 58182 IU/L, rest liver (LFTs) & renal function tests (RFTs), coagulation parameters were within normal range.

Emergency suction and evacuation was done under general anaesthesia with intractable bleeding not responding to uterotonics. Patient further required exploratory laparotomy with bilateral uterine artery ligation and subtotal obstetric hysterectomy under general anaesthesia. Intraoperative patient had persistent tachycardia; blood pressure (BP) was maintained with vasopressor support. Intraoperative and postoperative patient required multiple transfusions. She received steroids, oxytocin infusion. Post-operative patient was shifted to intensive care unit. She was started on Propylthiouracil and Metoprolol in view of hyperthyroidism. She was persistently tachycardiac, tachypnoeic with saturation around 90%. 2D Echo was done to rule out cardiorespiratory complications secondary to thyrotoxicosis or embolization of trophoblasts; which was reported normal. HRCT & MRI abdomen were done. On post-operative day (POD) 1 she developed features suggestive of transfusion related acute lung injury (TRALI) and was difficult to wean off the ventilator. Vasopressor infusion was tapered and patient was sedated with Dexmedetomidine infusion; Benzodiazepines/ Opioids intermittently. POD 3 patient was extubated & was managed with non-invasive ventilation intermittently. Invasive vesicular mole was ruled out by radiological investigations. Sign/ symptoms secondarily to hyperthyroidism subsided and she was subsequently shifted to ward.

2.2. Case 2

29 year/ Female patient Gravida 2, Para1 presented with complains of per-vaginal bleeding post-coitus associated with passage of clots. Patient had history of amenorrhoea for two months and pulmonary tuberculosis three years back. USG showed thickened endometrium with multiple cystic lesions and septations suggestive of hydatiform mole. On examination patient was vitally stable and laboratory parameters were within normal range. TSH- 2.6 mIU/ml, beta-hCG 56500 IU/L. Emergency Suction and Evacuation was done under spinal anaesthesia. Intraoperative patient was vitally stable. Inj Oxytocin infusion was started. Procedure was uneventful.

2.3. Case 3

18 yrs./ Female Gravida 2, Para1 with previous FTND came with complains of bleeding per-vaginally and pain in abdomen. USG showed grossly thickened endometrium with multiple cystic areas within suggestive of molar pregnancy. Her hemogram was normal, TSH on lower side, beta-hCG

200000 IU/L, rest LFTs, RFTs coagulation parameters were within normal range.

Emergency Suction and Evacuation was performed under spinal anaesthesia. Intraoperative patient had tachycardia; rest vitals were stable. Inj. Metoprolol (5mg diluted) and Inj Dexmedetomidine (0.5 mcg/kg) bolus was given slowly intravenously. Inj. Oxytocin infusion was started. Procedure was uneventful. Postoperative patient received prophylactic methotrexate. Serial beta-hCG were in decreasing trend.

2.4. Case 4

20 yrs./ Female primigravida presented with Complains of bleeding per-vaginally, nausea and vomiting. Amenorrhoea for 3 months. Per abdomen uterus was 16 weeks and relaxed. USG revealed Bulky uterus with heterogenous echotexture. Post-superior uterus didn't show clear differentiation of Endo-myometrial junction was suggestive of invasive mole. Her hemogram was normal, thyroid hormone (free T3- 9.34 ng/ml, T4- 2.45 ng/dl), TSH 0.012 mIU/ml; beta-hCG – 575142 IU/L; rest of parameters were within normal range.

Preoperatively patient received Anti-thyroid medication and Beta blockers. She underwent suction and evacuation surgery under spinal anaesthesia (Inj. Bupivacaine plus Inj. Dexmedetomidine). Intraoperative patient was agitated had pulse around 150-160/ minute which was controlled by Beta blockers -Inj. Esmolol I.V. infusion; Inj. Oxytocin infusion, Inj. Dexmedetomidine infusion were started. Postoperative patient was shifted to high dependency unit and Carbimazole and Metoprolol were continued. Serial blood tests revealed high beta-hCG. Patient was diagnosed with invasive vesicular mole and was started on chemotherapy.

2.5. Case 5

40 years/ Female patient Gravida 4, Para3 presented with complains of severe nausea, vomiting and pain in abdomen. History of amenorrhoea for 2 months. USG showed echogenic mass in endometrium with multiple cystic spaces suggestive of hydatiform mole. On examination patient was vitally stable except tachycardia and laboratory parameters were within normal range. TSH-0.98 mIU/ml, beta-hCG 1,50,000 IU/L. Emergency suction and evacuation was performed under spinal anaesthesia (Inj. Bupivacaine plus Inj. Dexmedetomidine). Intraoperative patient vitals were stable. Inj. Oxytocin infusion was started. Procedure was uneventful.

2.6. Case 6

35 year/ Female patient Gravida 4, Para3 presented with complains of nausea, vomiting, per-vaginal bleeding. Patient had history of amenorrhoea for two and half months. USG was suggestive of hydatiform mole, it showed thickened endometrium with multiple cystic lesions and septations. On examination patient was vitally stable and laboratory parameters were within normal range. TFTs – were normal,

beta-hCG 65000 IU/L. Emergency suction and evacuation was performed under spinal anaesthesia (Inj. Bupivacaine plus Inj. Dexmedetomidine). Intraoperative patient was vitally stable. Inj. Oxytocin infusion was started. Procedure was uneventful.

3. Discussion

Molar pregnancies originate in villous trophoblasts and are characterized by abnormal chorionic villi with trophoblast hyperplasia as a consequence of overexpression of paternal genes. Hydatidiform mole (HM) is classified under gestational trophoblastic disease (GTD) which can be of two types complete mole and partial mole. Complete moles are diploid whereas partial moles are triploid.⁴ Also, complete moles produce higher levels of beta-hCG in comparison with partial moles. High beta-hCG levels which can produce complications like hyperemesis, hyperthyroidism, preeclampsia, cardiorespiratory distress, stroke etc. in patients with HM. Preeclampsia before 20 weeks is evident in HM. Severe hypertension if present should be treated to reduce the risk of stroke. High circulating levels of beta-hCG with their TSH like activity may result in a slightly low TSH and an increase in maternal free T4 concentration.⁵

Many life-threatening complications like thyroid storm, shock, cardiorespiratory distress, takotsubo cardiomyopathy etc have been reported with HM. Its management remains a challenge to concerned team. Surgical Uterine evacuation is treatment of choice for molar pregnancy which need to be followed by serial beta-hCG levels to confirm complete resolution of disease or to identify development of gestational trophoblastic neoplasia (GTN). GTN is the invasive or metastatic form of GTD which includes invasive mole, choriocarcinoma, placental site trophoblastic tumour, and epithelioid trophoblastic tumour. GTN has an excellent prognosis with chemotherapy.

In this case series we present patients with both complete and partial moles and one case of invasive mole. We came across varied presentation of hydatiform mole from completely asymptomatic patients to patient with thyrotoxicosis, haemorrhagic shock and impending thyroid storm. Presenting signs/ symptoms for HM were history of amenorrhoea, bleeding per vaginum, hyperemesis, hyperthyroidism etc. On physical exam, uterine size and date discrepancy was usually seen. Many of our patients presented with deranged TFT, low TSH. Hyperthyroidism due to high levels of beta-hCG can present in HM from asymptomatic state to thyroid crisis as beta-hCG is a weak human thyrotropin. Various adrenergic symptoms (palpitations, heat intolerance, diaphoresis, tremor etc); Neuromuscular symptoms, Psychiatric symptoms or Cardiovascular complications [atrial fibrillation,⁶ Takotsubo Cardiomyopathy⁷ or heart failure] etc are to be looked for. Wayne's index of sign and symptoms scoring or Burch and Wartofsky to assess the degrees of dysfunction in various major systems were used for thyrotoxicosis scoring.³

Ultrasound was used to diagnose complete molar pregnancies based on the presence of a "snowflake" pattern and certain placental characteristics such as cystic changes or overt masses seen. Although the gold standard is based on the gross morphology of the specimen, histopathologic features, and karyotype.

Surgery is the mainstay for management of Hydatiform mole either in form of Suction and Evacuation or hysterectomy.⁸ Preoperative preparations were made which include evaluating preoperative conditions of patients, blood tests, electrocardiography, chest x-ray. All patient should be optimised for preeclampsia, shock but in certain emergency situations as in case 1 when the patient is profusely bleeding emergency surgery is needed. Hemodynamic stability should be obtained prior to surgery. Anti-thyroid drugs and beta-blockers should be started for optimizing the state of hyperthyroidism. Cardio selective or nonselective beta blockers needs to be started depending on cardiac status.[9] Case 4 presented with invasive mole, very high levels of beta-hCG and clinical features of thyrotoxicosis. She received anti-thyroid drugs and beta-blockers preoperatively which were continued post operative for 3-4 weeks.

The main management of hydatidiform mole is evacuation by suction curettage carried out under ultrasound guidance to avoid uterine perforation. In the case of hydatidiform mole with life threatening bleeding, hysterectomy is recommended. Sometimes patients present in catastrophic conditions as in case 1 described above; where the patient presented with haemorrhagic shock and impending thyroid storm.⁸ She required emergency exploratory laparotomy with bilateral uterine artery ligation and subtotal obstetric hysterectomy under general anaesthesia. Sedation, total intravenous anaesthesia (TIVA), general anaesthesia, and spinal anaesthesia are various anaesthetic techniques of molar pregnancy evacuation.¹¹ Choice of anaesthesia technique depends on the presenting symptoms and extent of disease. β -blockers for weakening sympathetic activity, emergency drugs such as lidocaine for ventricular arrhythmias, steroids, temperature monitoring / measures to control and hypotensive agents must be kept ready in cases of thyrotoxicosis. We encountered 3-4 cases with clinical features of thyrotoxicosis. Blood bank needs to be notified for need of massive blood transfusion in cases of bleeding. Anaesthesiologist needs to be vigilant for any complications from stroke to cardiorespiratory distress.

Anaesthesiologists should avoid drugs that stimulate the sympathetic nervous system and must assure adequate depth of anaesthesia before any surgical procedure. We used Dexmedetomidine in our cases as adjuvant in spinal anaesthesia, as intravenous bolus & infusion, for ICU sedation & delirium. Dexmedetomidine appears to be promising drug in thyrotoxicosis.^{12,13} Dexmedetomidine is used in patients on mechanical ventilation for ICU sedation and for delirium.¹⁴ Intraoperative it is used for attenuation of

haemodynamic responses to sympathetic stimulation; as an anaesthetic adjunct in regional and general anaesthesia and was effective in suppressing catecholamine levels in pheochromocytoma.¹⁵ The intraoperative use of dexmedetomidine also maintains adequate depth of anaesthesia and controls the sympathetic hyperactivity during surgery.¹⁰ Dexmedetomidine has been found hazardous in patients with cardiogenic shock secondary to thyrotoxicosis but is beneficial in patients with tachyarrhythmias due to same.

Many cases require intensive care management in postoperative period. A postoperative serious complication that often occurs is cardiopulmonary distress including chest pain, dyspnoea, tachypnoea, tachycardia or even pulmonary oedema as we encountered in case number 1. Thyrotoxicosis can lead to thyroid storm.¹⁶ Cardiogenic shock, tachyarrhythmias, Stress cardiomyopathy etc. have been described.⁷ Respiratory distress after uterine evacuation is usually attributed to trophoblastic embolization. Respiratory problems can also be due to massive fluid replacement, complications of thyroid storm, or preeclampsia can develop in patients. The use of a combination of anti-thyroid drugs, β -blockers, and corticosteroids returns thyroid hormone concentrations to the normal range within 2 to 3 days. Modalities like Plasmapheresis have also been used to rapidly control hyperthyroidism.¹⁷

The International Federation of Gynaecology and Obstetrics (FIGO) recommends beta-hCG levels monitoring every one to two weeks until beta-hCG normalization and then monthly till normal beta-hCG levels for six months.¹⁸ National Comprehensive Cancer Network (NCCN) guidelines also have similar suggestion. Persistent high levels or rising levels of beta-hCG post-surgery is suggestive of GTN & necessitates chemotherapy.¹⁹ Case number 4 had persistent high beta-hCG, was diagnosed with invasive mole & required chemotherapy post operative. We used prophylactic chemotherapy in case number 3. Prophylactic chemotherapy can be considered in patients with high risk for developing GTN but supporting data are weak. Prophylactic chemotherapy may increase drug resistance and is associated with toxicities. Patients with molar pregnancy should be advised to use reliable contraception during the entire interval of beta-hCG monitoring.

4. Conclusion

Hydatiform moles have varied presentations from completely asymptomatic to devastating conditions like haemorrhagic shock, thyroid storm, cardiorespiratory failure, preeclampsia etc. and management also changes with every case. The role of the multidisciplinary approach in the management of affected patients of Hydatiform moles is thus crucial. The intraoperative and postoperative management of HM remains a challenge for Anaesthesiologist. Preoperative optimization is equally essential. Newer challenges and modalities in management are coming up. Drugs like Dexmedetomidine

have been tried successfully intraoperative and postoperative in complication like thyrotoxicosis. Further studies are required to prove its beneficial effects. Dexmedetomidine is also use in patients on mechanical ventilation for ICU sedation and for delirium. Newer challenges like Takotsubo Cardiomyopathy, disseminated hydatidiform mole with the development of acute pulmonary oedema are described with hydatiform mole. Different modalities of treatment like plasmapheresis are also been tried.

5. Source of Funding

None.

6. Conflict of Interest

None.

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