GESTATIONAL TROPHOBLASTIC DISEASE

Rizal Sanif[1]

[1]Lecturer at department obstetric and gynecology of the Medical Faculty Universitas Sriwijaya Palembang

Email: izaaaliya@gmail.com

ABSTRACT

Gestational trophoblastic disease (GTD) is a group of tumors defined by abnormal trophoblastic proliferation. GTD is divided into hydatidiform moles (contain villi) and other trophoblastic neoplasms (lack villi).[1] The malignant forms of the disease are also collectively known as gestational trophoblastic tumors or neoplasia (GTN).GTN includes the invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. Southeast Asia and Japan have the highest reported incidence estimated to be two in 1000 pregnancies. In high-income countries, the incidence of a complete mole is approximately 1–3 per 1000 pregnancies, and the incidence of a partial mole is about 3 per 1000 pregnancies. Approximately 15–20% of patients will be treated for gestational trophoblastic neoplasia after the evacuation of complete hydatidiform mole. GTD develop from abnormal proliferation of trophoblastic tissue and form botryoid arranged vesicles. Risk factors include extremes of age, ethnicity, and a prior history of an HM, suggesting a genetic basis for its etiology. GTD causes a broad spectrum of different symptoms. The most frequent clinical symptom is abnormal vaginal bleeding. Other signs include uterine enlargement more significant than expected for gestational age, absent fetal heart tones, cystic ovary enlargement, hyperemesis gravidarum, and abnormally high level of β-hCG for gestational age. Ultrasound is the gold standard in non-invasive techniques, but histological examination is necessary to reach the final diagnosis. Different treatment modalities are available for gestational trophoblastic neoplasm depending on the type and stage; these include D&C (dilation and curettage), chemotherapy, hysterectomy, or a combination of these.[2] The prognostic score for GTN reported by FIGO is a score of 0–6 is the low-risk group and 7 is the high-risk group. All patients who have hydatidiform mole should be up for β-hCG surveillance and monitoring. Most relapses occur within the first year after completion of chemotherapy. A generally approved schedule of β-hCG surveillance indicates monitoring weekly for six weeks after chemotherapy followed by biweekly measurements until six months after chemotherapy. Afterward, a biannual measurement of β-hCG for five years is sufficient.[1] Seeing this, the determination of the diagnosis of GTD becomes very important. With the proper diagnosis, the management of the patient will also improve.

Keywords: Gestational trophoblastic disease, gestational trophoblastic neoplasm.

INTRODUCTION

Gestational trophoblastic disease (GTD) is a group of tumors defined by abnormal trophoblastic proliferation. GTD is divided into hydatidiform moles (contain villi) and other trophoblastic neoplasms (lack villi).[1] The malignant forms of the disease are also collectively known as gestational trophoblastic tumors or neoplasia (GTN).GTN includes the invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor[1,2] These malignancies can occur weeks or years following any pregnancy but occur most commonly after a molar pregnancy.[1]

Estimates for the incidence of various types of gestational trophoblastic disease vary. Southeast Asia and Japan have the highest reported incidence, estimated to be two in 1000 pregnancies.[1] In high-income countries, the incidence of a complete mole is approximately 1–3 per 1000 pregnancies, and the incidence of a partial mole is about 3 per 1000 pregnancies.[3] The prevalence of molar pregnancy in Indonesia has been reported 12 per 1000 pregnancies.[7] Women at the extremes of reproductive life are at increased risk, especially those older than age 45 years. Approximately 15–20% of patients will be treated for gestational trophoblastic neoplasia after the evacuation of complete hydatidiform mole.[4] Seeing this, the determination of the diagnosis of GTD becomes very important. With the correct diagnosis, the management of the patient will also improve.

Initially, GTD developed from abnormal proliferation of trophoblastic tissue and formed botryoid arranged vesicles.[5] Hydatidiform mole (HM) is associated with abnormal gametogenesis and fertilization. Risk factors include extremes of age, ethnicity, and a prior history of an HM, suggesting a genetic basis for its etiology.[1] History of a previous molar pregnancy increases the risk to 10 times that for sporadic moles.[3] The influence of hormonal factors such as late menarche, the usage of oral contraceptives, and light menstrual flow has been linked to the increased risk of GTN.[5] In 90% of cases, complete hydatidiform mole (CHM) arises when an empty ovum that lost its maternal chromosomes is fertilized by one sperm, which then duplicates its DNA, resulting in a "complete" 46-chromosome set.[7]

GTD causes a broad spectrum of different symptoms. The most frequent clinical symptom is abnormal vaginal bleeding. Other signs include uterine enlargement more significant than expected for gestational age, absent fetal heart tones, cystic ovary enlargement, hyperemesis gravidarum, and abnormally high level of β-hCG for gestational age. Ultrasound is the gold standard in non-invasive techniques. The most commonly described appearance of a molar pregnancy on ultrasound is the "snowstorm" or "bunches of grapes" pattern of the uterus.[1,5] As false negative and false positif rates are high with the use of ultrasonography, specifically in the case of partial hydatidiform mole, histological examination is necessary to reach the final diagnosis. As histological examination may not be practicable after every termination, testing the level of β-hCG 3–4 weeks after management to make sure it returned to the normal range is highly recommended.[6]

Different treatment modalities are available for gestational trophoblastic neoplasm depending on the type and stage; these include D&C (dilation and curettage), chemotherapy, hysterectomy, or a combination of these. Most of the patients (about 95%)

diagnosed with a hydatidiform mole who develop neoplasia have a low risk of resistance. For most of these patients, mono-chemotherapy with methotrexate or dactinomycin is the treatment of choice. Using prophylactic chemotherapy instead of monitoring β-hCG levels until disease clearance criteria are met will decrease the use of intense chemotherapy regimens and boost the chance of complete healing.[6]

There are three known systems to stage gestational trophoblastic diseases; 1. The World Health Organization (WHO) prognostic index score, 2. The Clinical Classification system by the National Institutes of Health (NIH), and 3. The FIGO staging system was revised and edited in 2000.[6] The prognostic score for GTN reported by FIGO is that 0–6 is the low-risk group and 7 is the high-risk group. Variables included in the prognostic score were 1. Tumor condition (β-hCG level, size, and a number of metastases), 2. Site of metastasis 3. History of chemotherapy and 4. age and time interval with previous pregnancies.[2] High-risk groups for GTN require combination chemotherapy.[2]

All patients who have hydatidiform mole should be up for β-hCG surveillance and monitoring.[6] Besides a variety of different protocols for follow-up, the recommendation of FIGO has been generally accepted. According to FIGO, women with PHM should be followed up by weekly β-hCG controls to record a normal level of β-hCG in two consecutive measurements, followed by monthly check-ups for the next 3 to 6 months. CHM requires monthly check-ups for an entire year.[5] Follow-up following the evacuation of a hydatidiform mole is vital to detect trophoblastic sequelae (invasive mole or choriocarcinoma), which occurs in nearly 15 to 20% with complete mole and 1 to 5% with partial mole.[6] For a woman with GTN, after chemotherapy, a follow-up including post-treatment images has to be initiated to guarantee continuous monitoring of clinical processes. Duplex ultrasonography plays an important role in the follow-up of low-risk disease, and careful surveillance with serum β-hCG is crucial. Most relapses occur within the first year after completion of chemotherapy. A generally approved schedule of β-hCG surveillance indicates monitoring weekly for 6 weeks after chemotherapy followed by biweekly measurements until 6 months after chemotherapy. Afterward, a biannual measurement of β-hCG for 5 years is sufficient.[1]

METHODS

This community service activity is conducte d in an online educational seminar through the Zoom conference application on Saturday, 14 August 2021, commemorating the 58th DIES Natalis of the Faculty of Medicine, Sriwijaya University. This activity was also held in collaboration with the Research and Community Service Unit of the Faculty of Medicine, Sriwijaya University, PNPB Faculty of Medicine, Sriwijaya University, Indonesian gynecological oncology association. This online educational seminar participants were all obstetric and gynecology residents, general practitioners, nurses, and midwives.

DISCUSSION

GTD causes a broad spectrum of different symptoms. The most frequent clinical symptom is unexpected vaginal bleeding. Nowadays, imaging, including ultrasonography can diagnose GTD even before the onset of symptoms such as anemia, hyperemesis, pre-eclampsia, uterine enlargement, hyperthyroidism and respiratory distress. β-hCG surveillance plays an important role in the clinical management of a woman with GTD.[5]

The role of CT is limited in the evaluation of molar pregnancy. It is typically used to stage a suspected malignancy and evaluate for metastatic disease in cases of GTN. Moles are seen at contrast-enhanced CT as an intrauterine mass of low attenuation relative to the enhancing myometrium, with thin enhancing septa. Bilateral ovarian theca lutein cysts may be seen as enlarged ovaries containing multiple fluid-attenuation cysts separated by thin septa in a classic "spoke-wheel" pattern. The MR imaging appearance of GTN is nonspecific, and differentiation between the various types of GTN is limited. Accurate differentiation between GTN and benign processes such as retained products of conception is likewise complicated.[7]

The gold standard in treating HM is suction dilation and curettage performed under ultrasonographic vision to avoid uterus perforation. The diagnosis of GTN and the subsequent indication for systemic chemotherapy is made by three or more equivalent elevated β-hCG levels over at least three weeks or a rise in β-hCG of 10% or greater. Histological verification of CC and metastases (especially brain, liver, or lung) of excluded other origins, as well as radiologically abnormal findings larger than 2 cm, are further reasons for chemotherapeutic treatment. Women with heavy vaginal bleeding, gastrointestinal hemorrhage requiring transfusions, or β-hCG levels above 20000 IU/l after four weeks following HM evacuation should receive chemotherapy.[5]

CONCLUSION

GTD is a rare group of trophoblast-derived diseases with an overall favorable survival rate. Some patients may develop a malignant disease resulting in death. Therefore, patients should be treated in specialized centers experienced in the management of women with GTD. Imaging plays an important role in the diagnosis and management of GTD.

CT plays an important role in the staging of suspected systemic metastatic disease in the chest and abdomen. MR imaging allows reliable assessment for the spread of extrauterine disease and local complications. It is important to properly manage molar pregnancies to minimize acute complications and promptly identify post- molar gestational trophoblastic neoplasia. It is important to individualize treatment for women with all forms of gestational trophoblastic neoplasia based on known risk factors, using less-toxic therapy for patients with low-risk disease and aggressive multiagent therapy for those with high-risk disease.

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