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Gestational trophoblastic disease

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Most women with gestational trophoblastic disease are of reproductive age. Because the disease is readily treatable with favourable prognosis, fertility becomes an important issue. Hydatidiform mole is a relatively benign disease, and most women do not require chemotherapy after uterine evacuation. A single uterine evacuation has no significant effect on future fertility, and pregnancy outcomes in subsequent pregnancies are comparable to that of the general population, despite a slight increased risk of developing molar pregnancy again. If women develop persistent trophoblastic disease, single or combined chemotherapy will be needed. Although ovarian dysfunction after chemotherapy is a theoretical risk, a term live birth rate of higher than 70% has been reported without increased risk of fetal abnormalities. Successful pregnancies have also been reported after choriocarcinoma. Only a few case reports have been published on fertility-sparing treatment in placental-site trophoblastic tumour, and the successful rate is about 67%. Women are advised to refrain from pregnancy for at least 6 months after a molar pregnancy, and at least 12 months after a gestational trophoblastic neoplasia. Most of the contraceptive methods do not have an adverse effect on the return of fertility. Finally, at least one-half of these women suffer from some form of psychological or sexual problems. Careful counselling and involvement of a multi-disciplinary team are mandated.

Introduction

Gestational trophoblastic disease (GTD) is a pregnancy-related disorder, consisting of hydatidiform mole, invasive mole and metastatic mole, choriocarcinoma, placental-site trophoblastic

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tumour (PSTT) and epithelioid trophoblastic tumour. Gestational trophoblastic neoplasia (GTN) is diagnosed when a woman's human chorionic gonadotropin (hCG) level fails to return to normal after a pregnancy. In order to diagnose GTN, using the recommendation from the International Federation of Obstetrics and Gynecology (FIGO), hCG should either plateau, with at least four persistently elevated hCG values on days 1, 7, 14 and 21, or rise sequentially for 2 weeks on days 1, 7 and 14 or longer; lung metastases should be diagnosed by chest X-ray.[1] Gestational trophoblastic disease also includes invasive mole, choriocarcinoma and PSTT.[2] In FIGO's 26th report, most women with GTN are between 25 and 29 years of age, and 82.7% are younger than 40 years.[1] It is therefore important to preserve the fertility of this group of women. For this chapter, we conducted a literature search from PubMed, and reviewed references of articles on fertility and GTD. These will be discussed below.

Fertility after gestational trophoblastic disease

Hydatidiform mole

Hydatidiform mole includes partial mole and complete mole. Both conditions are regarded as benign, and most women do not require additional treatment after uterine evacuation. Several studies from different centres have investigated the pregnancy outcomes after a molar pregnancy; all showed no difference from the general population.[3–7] In particular, the rate of subsequent term live pregnancy was in the range of 68–83% for both partial and complete moles, whereas the rates of stillbirth rate, spontaneous miscarriage and congenital abnormalities were 0.3–1.3%, 9–20%, and 1.8–3.9%, respectively.

The treatment of choice for molar pregnancy is uterine evacuation, curettage, or both.[8–11] Although most women with hydatidiform mole can retain their fertility, it is essential to pay extra caution in carrying out uterine evacuation, as it may lead to torrential bleeding, necessitating hysterectomy. First, it is advised to avoid using misoprostol for cervical priming because of a small risk of uterine contraction, which may result in tumour embolism into the venous system.[8,9] Second, the procedure should be conducted by an experienced gynaecologist because the uterus tends to be bigger and more vascular and than the usual uteri. Third, it is usually not necessary to give an oxytocic agent. If heavy bleeding occurs, this can be given after the evacuation is completed.[8] In the USA, some centres advocate using intravenous oxytocin infusion starting at the onset of the uterine evacuation until several hours after the operation to increase uterine contractility.[10] Medical abortion is not recommended because of risks of bleeding, incomplete abortion, and tumour embolisation, which may, in turn, increase the need of subsequent chemotherapy.[11,12] Nevertheless, medical abortion may be considered in partial mole at second trimester because the fetal parts may obstruct the evacuation, and the risk of persistent trophoblastic disease is low.

Some investigators have evaluated the effectiveness and safety of prophylactic chemotherapy with either methotrexate or actinomycin-D for high-risk molar pregnancy. Prophylactic chemotherapy is considered on the basis of age, uterine size, presence of intra-uterine mass and ovarian cysts. A woman's history and presentation, during or shortly after uterine evacuation, is taken into account in order to decrease the chance of post-molar GTN and the potential side-effects of chemotherapy, which may affect the ovarian function.[13–18] Although most studies have shown a reduction in the incidence from 18–50% to 7–18%, with occasional tolerable side-effects, only two were randomised-controlled trials with about 30 women in each arm.[13,16] The criteria of high-risk molar pregnancy, however, differed in different centres. Currently, chemo-prophylaxis is usually considered in countries with limited resources for follow up, or in women with poor compliance to follow up.[11,16]

Hysterectomy is rarely carried out for women who have completed their families or with life-threatening haemorrhage. Hysterectomy can provide permanent sterilisation and prevent local myometrial invasion, but it cannot obviate the risk of metastasis and the need of chemotherapy.[9,11]

As there is a small risk of developing persistent trophoblastic neoplasia, women should be counselled to refrain from pregnancy for at least 6 months (see below). If women happen to conceive