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Case Report

# Perimenopausal invasive complete hydatidiform mole: a rare encounter

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## ABSTRACT

Invasive mole, classified under the gestational trophoblastic diseases, comprises hydropic chorionic villi invading the underlying myometrium, blood vessels, or extra-uterine sites. They are usually suspected clinically when serum beta HCG levels are persistently high and are labeled as persistent gestational trophoblastic disease. They are then treated with chemotherapy. Definite diagnosis of invasive mole requires histopathologic examination. Surgery is rarely performed owing to good response to chemotherapy and preservation of fertility since most women are of reproductive age. However, in perimenopausal females, surgery can be considered. Thus, these specimens are a rare encounter for pathologists. Here, we report a case of a persistent gestational trophoblastic disease in a 48-year-old perimenopausal female with persistent elevation of serum beta HCG levels and completed family status who underwent hysterectomy and was diagnosed as a case of an invasive mole on histopathologic examination.

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## INTRODUCTION

Gestational trophoblastic diseases (GTDs) include a spectrum of diseases from abnormal trophoblastic proliferation associated with a villous enlargement (moles) or neoplasms without villi (e.g. choriocarcinoma).[1] The former category of GTDs includes partial mole (PM), complete mole (CM) that are commonly encountered, and invasive mole (IM) which is a rare entity.[2] When hydropic villi invade the myometrium or blood vessels, the term invasive mole is used. The villous or trophoblastic tissue may also extend to the broad ligament or metastasize to extra-uterine sites such as the lungs, vagina, or vulva.[3] Women of reproductive age are commonly affected with rare occurrence in perimenopausal women.[2]

The definite diagnosis of IM is done on a hysterectomy specimen but surgical treatment is rarely done as patients are usually young. These cases are clinically labeled under persistent gestational trophoblastic disease and are treated with chemotherapy which successfully treats even metastatic lesions.[3] However, in cases with a completed family; hysterectomy can be performed rather than undergoing chemotherapy.

## # CASE STUDY

A 48 years old gravida 5, para 4 lady presented to the gynecology OPD with complaints of amenorrhoea for 3 months and per vaginal bleeding for 3 days. Her previous obstetric history was unremarkable. The patient's beta HCG was more than 150,000 mIU/ml (performed by Chemiluminescent immunoassay method) and radiologic features were consistent with molar pregnancy. Thus, diagnosis of molar pregnancy was suspected and suction and evacuation (S and E) were performed and sent for histopathology. The histologic features were consistent with Complete Hydatidiform mole. After the evacuation, serum beta HCG persisted at 39,000mIU/ml. After 5 days a second S and E was mandated after which the beta HCG level dropped to less than 2mIU/ml.

The patient was kept on close follow-up and serial beta HCG monitoring. Her beta HCG values showed a rising trend from 195 mIU/ml at 1 month, 607 mIU/ml at 2 months to 1,807 mIU/ml at 3 months. Ultrasonography did not reveal any significant findings. A clinical diagnosis of persistent GTD was made. Because of her completed family and no evidence of invasive disease on radiology, she underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy for a definite diagnosis.

Gross examination of the specimen revealed an unremarkable endometrial cavity. However, on serial sectioning of the uterine body, a single small hemorrhagic cavity was noted in the myometrium towards the uterine fundus measuring 1.5 cm. The cavity was seen connected to the overlying endometrium at a single focus which was barely visible. No perforation to the serosa or any other metastatic deposits were noted elsewhere in the specimen. Since the cavity was very small, it was entirely submitted for microscopic examination and thus, the gross picture is not available. The cervix, parametrium, tubes, and ovaries were unremarkable. Microscopic examination revealed the myometrial cavity containing few hydropic villi with extensive trophoblastic proliferation showing hyperchromasia and atypia (fig. 1). No lymphatic invasion was noted. Focally, connection with endometrial lining was noted. No chorionic villi or trophoblasts were identified elsewhere. A diagnosis of Invasive complete hydatidiform mole was made. Two weeks after the surgery, her beta HCG levels were reduced to 0.67mIU/ml.

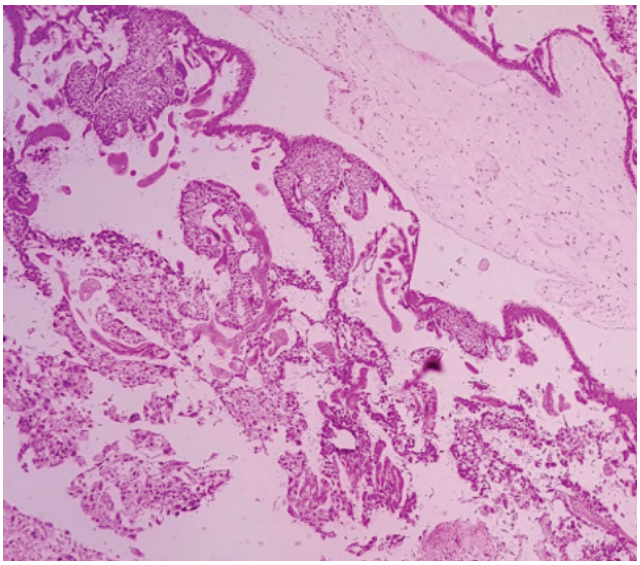

***Figure 1: Section showing hydropic villi with circumferential trophoblastic proliferation with adjacent decidua and myometrium. (HE stain; X100)***

## DISCUSSION

Hydatidiform mole is a pathologic conceptus where there is marked enlargement of the placental villi.[1] These can be complete or partial depending upon morphologic, cytogenetic, and clinicopathological features. Morphologically, most of the villi in CM are large and show hydropic changes along with circumferential trophoblastic proliferation. The trophoblasts can show cribriform, solid, or finger-like proliferation. Cytologic atypia is marked and fetal parts, nucleated red blood cells are absent. Stromal apoptosis and mucin can be seen. In PM, there is a dual population of the chorionic villi with some of them showing hydropic changes and polar trophoblastic proliferation whilst the other population appearing normal in size and morphology. Trophoblastic hyperplasia is mild to moderate and present in polar ends or sometimes circumferential. Fetal parts, fetal blood vessels, and nucleated red blood cells are often present. Also, CM has normal DNA content and most have a karyotype 46, XX. Scalloping of the villi, trophoblastic pseudo-inclusions are commonly noted. p57 immunostain helps distinguish the two types as the stain is present in the cytotrophoblasts and villous stromal cell nuclei in partial moles while the nuclear stain is absent in those cells of complete mole. Only intermediate trophoblasts and decidual tissue will be stained in a complete mole.[3]

Around 7 to 17% of moles undergo invasive change with 2-5% progressing to choriocarcinoma.[4] Invasive feature is more commonly seen in CM with a 15% risk of transformation while it is only 0.5 to 1% in PM.[5] This invasiveness appears to be linked to the male origin of the DNA in some studies6 while some show moles arising from two sperms fertilizing an empty egg seem to have a

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higher risk of malignant transformation.[7] In perimenopausal women, defective fertilization of immature ova may be the initiating event for GTNs.[2]

Clinically, IM presents with a history of molar pregnancy followed by features such as persistent abnormal vaginal bleeding, high serum beta HCG levels, an enlarged uterus. Hence, they are noted in women of reproductive age group and are rare in perimenopausal women.[2] The interval between antecedent molar pregnancy and the diagnosis of the IM is usually less than 6 months.[2] It is preceded by a hydatidiform mole in about 95% of cases. Factors like age more than 40 years, uterine size, B-Hcg level >1,00,000 mIU/ml, large theca lutein cyst, and history of previous GTD indicate risk of persistent GTDs. Age and beta-HCG levels were the risk factors present in this case.

On gross examination, IM appears as a hemorrhagic lesion in the uterine cavity and myometrium with the presence of grape-like molar vesicles. In our case, the hemorrhagic cavity was noted in the myometrium only after serial sectioning, however, molar villi were not grossly noted, likely because S and E were previously performed twice with the evacuation of all the villi within the endometrial cavity. Uterine perforation and extra-uterine deposits may be present in some cases. Microscopically, there is myometrial or vascular or extra-uterine invasion by the molar villi.

The major differential diagnosis is choriocarcinoma as both diseases can present after molar evacuation with PV bleeding or elevated beta HCG levels or extra-uterine deposits. However, chorionic villi are conspicuously absent in choriocarcinoma with the proliferation of sheets of trophoblasts with extensive hemorrhage and necrosis.

Management of IM includes chemotherapy and serial beta HCG monitoring. Hysterectomy is an option in perimenopausal women with no desire to preserve parity, in chemoresistant lesions, hemoperitoneum, or coexistence of other uterine diseases.[8]

## CONCLUSIONS

Invasive mole is infrequently encountered as a pathological specimen. Although common in women of reproductive age group, it has been noted in perimenopausal women. Beta HCG levels help in suspecting and monitoring the disease. S and E specimens cannot diagnose invasive mole and diagnosis can be made only on hysterectomy specimen.

**Conflict of Interest:** None

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