CASE REPORT

Postmenopausal choriocarcinoma: A rare case report

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ABSTRACT

Choriocarcinoma is a highly malignant epithelial tumor originating from trophoblast. It primarily occurs during the fertile period. Postmenopausal uterine choriocarcinoma is very rare. We present a case of choriocarcinoma in a postmenopausal lady developing 5 years after menopause. She presented with heavy postmenopausal bleeding along with passage of vesicles per vaginum. Serum beta-hCG was 96,484 mIU/ml. Emergency abdominal hysterectomy with bilateral salpingo-oopherectomy was done due to intractable bleeding following suction and evacuation. Histopathology revealed uterine choriocarcinoma. She was treated with EMACO regimen following which her beta-hCG returned to normal in five cycles. The patient is under regular follow-up and is doing well.

Key Words: Uterine choricarcinoma, postmenopausal bleeding, beta-hCG

INTRODUCTION

Choriocarcinoma is an aggressive neoplasm usually arising in the body of uterus. Most cases present within 1 year of the antecedent pregnancy (molar or non-molar).[1] To date, there are very few case reports in the global literature of gestational diseases in postmenopausal women. Reports of choriocarcinoma are even rarer.[1]

This tumor is a biphasic proliferation of cytotrophoblast and syncytiotrophoblast, with morphology similar to primitive trophoblast of the placental previllous stage; chorionic villi are absent in this tumor type.[2] The syncytiotrophoblast is the differentiated hormone secreting component.[1]

Choriocarcinoma shows variable clinical signs and symptoms, the most frequent being abnormal uterine bleeding. However, signs linked to metastasis, often pulmonary, can sometimes be the first to suggest the diagnosis. Other secondary locations also include brain, liver, gastrointestinal or urinary tract.[3]

CASE REPORT

A 52-year-old woman, P7L3 admitted to Emergency department with chief complaints of heavy postmenopausal bleeding and passage of vesicles per vaginum of 2-days duration. She attained menopause 5 years ago and her last pregnancy was 12 years back. There was no past history of molar pregnancy or abortion.

On general examination she was severely pale with pulse rate 110/minute and blood pressure of 90/60 mm of Hg. Clinical examination revealed uterus of 16-weeks size, cervix was long, soft; os open with passage of fleshy vesicles [Figure 1]. She was resuscitated with crystalloids and three units of blood transfusion. Blood investigations showed hemoglobin to be 6.4 gm% and serum beta-hCG was 96,484 mIU/ml. Chest X ray, thyroid profile, liver function, renal function tests and coagulation profile were within normal limits. Ultrasound showed a large moderately echogenic mass with numerous cystic spaces seen filling the central uterine cavity with bilateral normal ovaries. She was diagnosed as a case of gestational trophoblastic disease and suction and evacuation was planned. During evacuation there was intractable bleeding for which emergency total abdominal hysterectomy with bilateral salpingo-oophorectomy was done.

Grossly uterus was 14 × 10 × 9 cm and cut section showed cavity filled with soft dark brown polyps.
Microscopic examination revealed wide areas of hemorrhagic necrosis with clusters of trophoblastic cells having intermediate trophoblasts, bizarre nuclei among these cells having increased mitotic activity with dilated vesicular spaces lined by trophoblasts and filled with fibrinoid material. Villus pattern was completely absent and there was no evidence of myometrial invasion. Histopathology of uterus was suggestive of choriocarcinoma whereas cervix showed features of chronic cervicitis.

Post-operatively abdominal and cranial CT scan revealed no metastasis and she was finally diagnosed as a case of high-risk gestational trophoblastic neoplasia (GTN) with FIGO (International Federation of Gynecology and Obstetrics) score 11.

A combination of etoposide, methotrexate, and dactinomycin, followed by cyclophosphamide and vincristine (EMA/CO regimen) was initiated. Our patient responded well to the regimen; her beta-hCG decreased to 341.63 mIU/ml after first cycle and she was advised to come for follow-up. The chemotherapy regimen was repeated every 2 weeks for five cycles. After five cycles of chemotherapy, her beta-hCG level dropped below 5 mIU/mL. Then she was followed-up weekly till three consecutive normal values of serum beta-hCG. After that additional two cycles of chemotherapy were given according to FIGO guidelines for treatment of high-risk cases of GTN.[4] Now our patient is being followed up monthly in our institute and is doing well. Follow-up plan is monthly serum beta-hCG for 1 year followed by 6-12 months for life or at least 3-5 years.

DISCUSSION

Majority of choriocarcinoma cases are intra-uterine and of gestational origin. Gestational choriocarcinoma has an incidence of one in 20,000 to one in 25,000 in western countries.[9] One report from India quotes the incidence of choriocarcinoma as one in 2958 pregnancies.[6]

Extraterine gestational choriocarcinomas may also arise at a site of ectopic pregnancy. The non-gestational choriocarcinomas are believed to develop from pluripotent germ cells, most commonly arising in the gonads. However, very rarely, choriocarcinoma can develop from germ cells or from dedifferentiation of endometrial carcinoma into choriocarcinoma.[1]

Choriocarcinoma has been reported in association with endometrial carcinoma as well as liver, lung and urinary bladder carcinomas.[5] These types of choriocarcinomas can be diagnosed based on histology that is, coexisting malignant cells other than choriocarcinoma cells.

Desai et al. reported choriocarcinoma in a 73-year-old woman, 23 years after menopause.[1] Khuu et al. reported a case of uterine carcinosarcoma with choriocarcinomatous dedifferentiation in a 71-year-old woman.[7] In that case, histology results suggested choriocarcinoma intermixed with adenocarcinoma and stromal sarcoma. While, in our patient, there was no evidence of endometrial adenocarcinoma; the non-lesional endometrium showed decidualization. These findings rule out dedifferentiation within an endometrial carcinoma. Immunohistochemistry tests positive for beta-human chorionic gonadotrophin as well as cytokeratin and negative for alpha-fetoprotein also supports the diagnosis of choriocarcinoma.[1]

Tsukamoto et al. reported three postmenopausal patients with choriocarcinoma, with the interval between the last pregnancy and development of tumor being 11, 15 and 18 years.[8] O’Neill et al. and Okamoto et al. reported choriocarcinoma 22 and 23 years after last...
pregnancy, respectively.[5,9] A report from Chumworathayi et al. described cervical choriocarcinoma with metastatic transformation from squamous cells.[10]

The molecular mechanism behind the long latent period between development of a choriocarcinoma and last pregnancy has not been described. It is theoretically possible that our patient became pregnant after her last known gestation (before 12 years) but without clinical symptoms which she considers unlikely. Evsen et al. reported a case which had a history of a molar pregnancy 3 years after her menopause at the age of 52 years and subsequently developed choriocarcinoma at the age of 58 years.[11] Even if we consider the possibilities of asymptomatic gestation developing in choriocarcinoma, our patient has an established menopause of 5 years.

OCT-3/4, CD-30 and AFP are markers of various germ cell tumors.[12] Various serum tumor markers (beta-hCG, AFP and CA-125) are also useful in the differential diagnosis of choriocarcinoma. It is well known that elevated AFP and CA-125 levels are seen in non-seminomatous germ cell tumors and ovarian carcinomas, respectively.[13]

Fisher et al. demonstrated DNA polymorphism studies are the most specific to confirm a gestational origin of tumor.[14] These studies compare microsatellite polymorphism between the patient, tumor and partner’s DNA (if available) by examination of restriction fragment length polymorphisms (RFLPs) using locus specific microsatellites. Genetic studies are useful when the patient’s history and pathological review are insufficient for diagnosis.[10] But patient management should not be delayed while awaiting DNA analysis results. Germ cell choriocarcinoma confirmed by DNA analysis is extremely rare and has previously only been reported in women of child-bearing age.[1,13]

CONCLUSION

In this case, response to chemotherapy along with histology and serum tumor markers suggested gestational origin of choriocarcinoma which was effectively managed by surgery followed by chemotherapy.

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