Epithelioid Trophoblastic Tumor: An Unusual Malignancy of Ovary
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ABSTRACT
Epithelioid Trophoblastic Tumor (ETT) is a distinct but rare variety of gestational trophoblastic tumors. Misdiagnosis delays effective treatment and affects the survival. The case being reported here involved a 43 years old lady presented with 4 months history of intermenstrual per vaginal bleeding and 6 weeks amenorrhea. Workup has revealed pelvic mass. The patient underwent laparotomy with transabdominal hysterectomy and bilateral salpingo-oophorectomy. Histopathology turned out to be clear cell carcinoma of the ovary. Patient was put on chemotherapy but there was progression of disease. Review of histopathology and immunohistochemistry revealed it as Epithelioid Trophoblastic Tumor; serum β-hCG was also raised. The case was really challenging for histopathologist. By the time final diagnosis was made, patient developed extensive metastases in lungs and liver and expired. Such an uncommon yet distinct trophoblastic tumor should be kept in mind by pathologists and treating physicians.

Key Words: Epithelioid trophoblastic tumor. Choriocarcinoma. Ovary.

INTRODUCTION
Epithelioid Trophoblastic Tumor (ETT) is a rare variety of gestational trophoblastic tumors distinct from placental site trophoblastic tumor and choriocarcinoma. It usually occurs in women in reproductive age group. A high level of serum β-hCG in ETT is reported to be associated with a large tumor mass and unusually high mitotic activity.1,2 Rising levels of β-hCG after therapy may be an indication of failure of treatment.

Ovarian involvement with ETT can be challenging to pathologists and may be potentially confused with ovarian epithelial carcinoma, particularly of clear cell differentiation. The patient being reported here was initially diagnosed as having clear cell carcinoma of the ovary. Final review and immunohistochemical analysis proved it to be epithelioid trophoblastic tumor. To authors’ knowledge, ovarian involvement of ETT with initial presentation as an ovarian tumor has not been reported in Pakistan.

CASE REPORT
A 43 years old married, normotensive and normoglycemic lady presented at NORI in July 2013. She had no family history of cancer. Her age at menarche was 14 years and she had 4 children. Her age at first childbirth was 26 years and at last childbirth she was 33 years old. She had breastfed her children and had never taken any hormonal treatment. She presented with 4 months history of intermenstrual per vaginal bleeding and 6 weeks amenorrhea to gynecologist. In gynecology department, her ultrasound abdomen and pelvis showed a 12.6 x 8.3 x 11.5 cm pelvic mass pushing uterus superolaterally and both ovaries could not be visualized separately.

The patient underwent laparotomy with transabdominal hysterectomy and bilateral salpingo-oophorectomy in July 2013. Peroperative findings were left adnexal fungating, multi-loculated necrotic and friable mass infiltrating parametrium and rectal wall. Left fallopian tube was attached to the mass. There was no involvement of urinary bladder and ascites. Histopathology revealed clear cell carcinoma. Among serum tumor markers, β-hCG was 3265 IU/ml and CA 125 was 63.8 IU/ml. Other tumor markers including CEA and Alpha-Fetoprotein (AFP) were in normal range. Immunohistochemically tumor cells showed positivity for Cytokeratin (CK) AE1/AE3 and CD 10 whereas there was focal positivity for CK 7. The presence of germ cell tumor was ruled out by immunohistochemistry. Epithelial markers were positive.

The patient's postoperative CT scan showed multiple liver metastases, para-aortic and left iliac lymphadenopathy and a solitary metastatic lesion in lower lobe of right lung (Figure 1). Considering epithelial carcinoma of ovary chemotherapy comprising of Paclitaxel and Carboplatin was started. After 3 cycles of chemotherapy, interim assessment revealed progressive disease with increase in the size and number of liver and lung metastases and large recurrent pelvic mass (Figure 2). β-hCG rose to 18687 IU/ml.

In view of no response to otherwise highly effective chemotherapy in epithelial carcinoma of ovary, we advised review of histopathology and immunohisto-
chemistry from another laboratory. Final diagnosis was epithelioid trophoblastic tumor as syncytiotrophoblasts were abundant with diffuse positivity for CK, CK 7 and EMA and focal positivity for β-hCG (Figure 3). The patient was advised another chemotherapy regimen (EMACO) comprising of etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine but she expired before chemotherapy could be started.

DISCUSSION

Epithelioid Trophoblastic Tumor is a recently described with variety of trophoblastic tumors. It arises from neoplastic proliferation of intermediate trophoblasts. In view of the history of prior molar pregnancies, in most patients ETTs are most often confused with choriocarcinoma. Presentation is usually with vaginal bleeding, sometimes with amenorrhea and serum β-hCG is usually mildly raised (< 2500 mIU/ml). Patients are usually in reproductive age group as reported in different international studies. One case described a 66 years old postmenopausal woman with ETT.

This patient was also in reproductive age group and presented with vaginal bleeding and amenorrhea with raised β-hCG. Initially, she was considered to be pregnant but investigations done later has revealed no products of conception yet ovarian mass was detected. The average interval between antecedent gestation and the development of tumor is 6.2 years. But this patient had last childbirth 10 years before the development of ETT.

ETT can present as isolated uterine/cervical disease isolated extraterine disease or as a primary uterine tumor with metastasis. Most often the uterus is the primary site of ETT (40%), followed by the cervix (31%). The lung is the most common extraterine site, accounting for 19% of cases. Other cases of extraterine disease have been reported in the small bowel, vagina, fallopian tube, broad ligament, and gallbladder. In literature, very few cases of ovarian ETTs have been reported. Recently, a 75 years old woman has been reported who was initially diagnosed as squamous cell carcinoma lung and later turned out to be ovarian ETT with lung metastases. Diagnosis of ETT is really a challenge as in this patient. Delay in diagnosis affects prognosis and treatment. Histological features of tumor in this patient mimicked epithelial tumor, therefore, it was labeled as clear cell carcinoma of ovary. Although, β-hCG was high but the presence of germ cell tumor was ruled out by immunohistochemistry. No clinical evidence of uterine involvement was identified at diagnosis or follow-up. The patient had no previous history of hydatidiform mole.

ETT may present as metastatic disease in up to 35% of cases. The majority of metastases involve the lung, liver or vagina though rare sites such as brain, spine and gallbladder have been reported. ETT has been shown to have a very aggressive course with a previous reported mortality rate of 13%. This patient presented with stage-IV disease with liver and lung metastases. ETT had a very aggressive course in this patient as she succumbed to her disease few days after final diagnosis. One reason for the dismal prognosis in this case could be the delay in diagnosis due to her atypical clinical picture and disease progressed very rapidly.

An awareness of clinical presentation with elevated serum β-hCG, the characteristic histological features of ETT and a panel of immunohistochemical markers are helpful in reaching the correct diagnosis of this uncommon, yet distinct trophoblastic tumor.
REFERENCES


