CASE REPORT

Extensive trophoblastic differentiation in case of an endometrial carcinoma

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ABSTRACT

Trophoblastic differentiation of endometrial carcinoma is extremely rare, till date 18 cases reports are there in the literature. A 68-year-old postmenopausal female presented with abnormal vaginal bleeding. Histopathologically, there were areas of serous carcinoma with trophoblastic differentiation (~90%). On immunohistochemistry, the trophoblastic component was positive for β-human chorionic gonadotropin (hCG), HPL and EMA. IHC confirmed the diagnosis of serous carcinoma with trophoblastic differentiation. The clinicopathological features of 18 previously reported cases of trophoblastic differentiation in the uterine tumor were analyzed in addition to the present case.

KEY WORDS: Endometrium, serous carcinoma, trophoblast

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INTRODUCTION

Trophoblastic differentiation in nongonadal tumors is relatively uncommon and is reported in tumors of lung, breast, gastrointestinal tract, and urinary system.[1] Trophoblastic differentiation in endometrial carcinomas is very rare. An extensive literature search revealed 18 cases of trophoblastic differentiation in endometrial carcinomas.[1-7] The most common histopathological type was endometrioid adenocarcinoma. Herein, we describe an unusual case of papillary serous carcinoma of the endometrium, displaying extensive trophoblastic differentiation.

CASE REPORT

A 68-year-old postmenopausal female presented with abnormal vaginal bleeding for 15 days. Her hemoglobin was 7 g/dl. Ultrasonography of her pelvis revealed thickened endometrial cavity. Magnetic resonance imaging demonstrated a relatively well-circumscribed tumor measuring 14 mm in diameter, in the fundus and the right lateral wall of the uterus [Figure 1a]. There was no other organomegaly or lymphadenopathy. The patient underwent an endometrial biopsy. The biopsy showed a tumor composed of large pleomorphic cells with clear cytoplasm and large nuclei with irregular distribution of the chromatin. A few intermingled multinucleated cells with eosinophilic cytoplasm were also noted. The cells with clear cytoplasm showed immunopositivity for human placental lactogen (HPL). There was focal immunopositivity for beta human chorionic gonadotropin (HCG). Tumor cells were negative for estrogen receptor (ER) and progesterone receptor (PR). Serum beta HCG level was 4.2 ng/ml (<2 ng/ml).

The patient underwent the total abdominal hysterectomy and bilateral salpingo-oophorectomy with dissection of pelvic and para-aortic lymph nodes. On gross examination, a tumor growth was arising from the fundus and the right lateral wall of the uterus, measuring 3 cm × 2 cm × 1 cm [Figure 1b]. On microscopic examination, the tumor had two distinct components. The predominant component (exceeding 90%) was composed of large cells with abundant eosinophilic cytoplasm (intermediate trophoblast) [Figure 2a], along with multinucleated cells (syncytiotrophoblast). The second component comprising <10% of the tumor showed glands and papillary structures with fibrovascular cores, lined by stratified epithelium showing atypia [Figure 2b]. The trophoblastic component was invading the myometrial muscle bundles. There was the lymphovascular invasion [Figure 2c]. The right side ovary showed metastatic

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deposits, whereas the left side adnexa, bilateral parametria, and paracervical tissue were free from the tumor.

Immunohistochemistry findings

Epithelial membrane antigen (EMA) and pan cytokeratin (AE1/AE3) were diffusely expressed in both the areas of papillary and trophoblastic differentiation. The trophoblastic component showed strong positivity for HPL [Figure 3a] and focal positivity for beta HCG [Figure 3b]. The serous component was strongly positive for p53 [Figure 3c]. Tumor cells were negative for ER and PR.

The final diagnosis was serous papillary carcinoma with trophoblastic differentiation. The patient underwent chemotherapy and was free of disease 4 months thereafter.

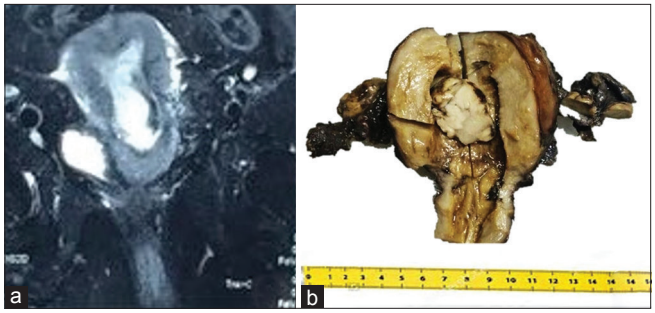

Figure 1: (a) Contrast-enhanced computed tomography scan showing the tumor in the endometrial cavity. (b) The gross image of the tumor in the endometrial cavity arising from the fundus

DISCUSSION

Trophoblastic differentiation in endometrial carcinoma was first reported by Civantos and Rywlin in 1972.[3] After an extensive review of literature, 17 cases of endometrial carcinoma with trophoblastic differentiation were found.[1-7] The patients' age ranged from 34 to 88 years, with a mean age of 61 years. The most common presenting symptom was abnormal vaginal bleeding. The serum beta HCG levels varied widely and were normalized after surgery. The percentage of the trophoblastic component was highest in our case (90%). The majority of the trophoblastic component was of intermediate trophoblast which explained the near-normal level of beta HCG, in the present case. The differential diagnoses were clear-cell carcinoma, urothelial carcinoma, poorly differentiated carcinoma, and undifferentiated sarcoma.

IHC was helpful in diagnosing this tumor. HPL is expressed only in the trophoblastic tumors. EMA and AE1/AE3 are expressed in the areas of papillary and trophoblastic differentiation,[1,2] urothelial carcinoma, and clear-cell carcinoma. Clear-cell carcinoma is invariably negative for p53 and HPL.

Trophoblastic differentiation in such cases has a highly aggressive clinical course. Of the 18 previously reported cases, 15 had metastases, and the common metastatic sites were lung, liver, and lymph nodes.[2] Seven patients succumbed to the disease.

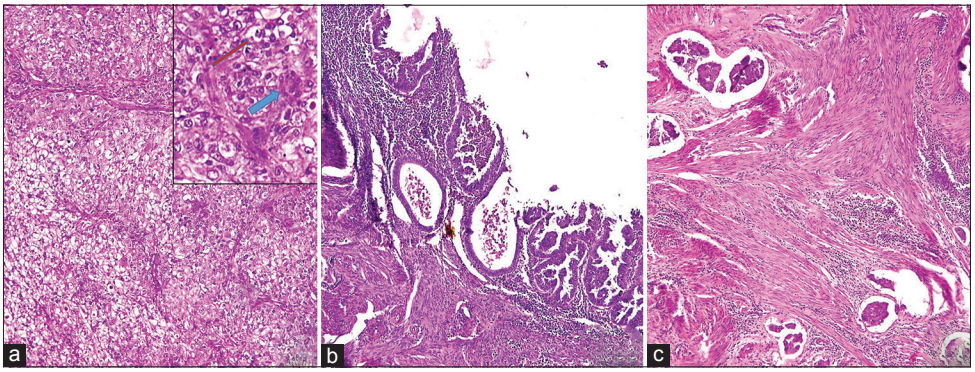

Figure 2: (a) Photomicrograph of the tumor showing trophoblastic differentiation (H and E, ×400). Inset showing the high power of tumor comprising intermediate trophoblastic cells (red arrow) and syncytiotrophoblastic cells (blue arrow). (b) Focal areas of papillary serous carcinoma (H and E, ×400). (c) Lymphovascular invasion shown by the tumor cells (H and E, ×200)

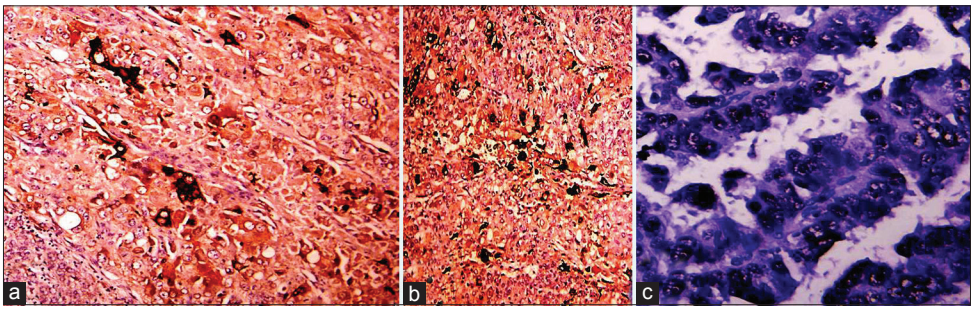

Figure 3: (a) Immunohistochemical staining by human placental lactogen confirms the trophoblastic component (×400). (b) Focal positivity of trophoblastic component for beta human chorionic gonadotropin immunohistochemistry (×400). (c) Strong immunohistochemical expression of p53 by the focal papillary serous component (×400)

The histopathology of the metastatic sites was variable; some showed features as the primary tumor (adenocarcinoma with choriocarcinomatous components), while in two cases, there was only choriocarcinomatous component. In the present case, the tumor metastasized to the right ovary.

The trophoblastic neoplasms are classified into three groups according to their origins: (1) the most common are gestational trophoblastic tumors, developing from neoplastic transformation of trophoblastic stem cells, mostly cytotrophoblastic cells; (2) the nongestational trophoblastic neoplasms arise from the carcinoma or germ cell tumor (teratoma, embryonic carcinoma, and yolk sac tumor), seen in carcinoma of breast, lung,[1] kidney, bladder, and gastrointestinal tract; and (3) the trophoblastic tumors arising outside the uterus as primary tumors, without other neoplastic components. The origin of this rare group is not well understood, as these tumors are not related to a gestational event. It can be due to the neoplastic transformation of residual germ cells which fail to migrate to the developing urogenital ridge. It is important to identify the two components as management involves treatment of both the components.

There are various hypotheses postulating the origin of the nongestational trophoblastic tumor: (1) dedifferentiation of epithelial cells into trophoblastic;[6] (2) failure of complete migration germ cells to the gonads; and (3) multidirectional differentiation from a common stem cell.[6] Studies have disclosed that there is a small population of endometrial epithelial stem/progenitor cells in normal human endometrium and a subpopulation of tumor-initiating cells with stem-like properties in endometrioid adenocarcinoma cell line.[8]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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