Extraterine Epithelioid Trophoblastic Tumor (ETT) Presenting as Malignant Pericardial Effusion: Cytological and Immunohistochemical Observation of a Case.

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Introduction

Epithelioid trophoblastic tumor (ETT) is a rare gestational trophoblastic disease (GTD) arising from the chorionic-type intermediate trophoblast, first described by Shih and Kurman1, with approximately 110 cases reported in the literature. ETT usually occurs in reproductive-aged women following a preceding gestation and commonly occurs in the cervix and uterus. Metastasis occurs in approximately 25% of patients and death in 13%. Rarely, ETT can occur in extraterine sites such as lung, orbit, small bowel or spine with or without evidence of cervical or uterine corpus disease, masquerading a primary non-trophoblastic malignancy6.

Clinical History

- The 46-year-old Taiwanese woman, G3P3A0, last term-pregnancy: 18 years ago.
- Cough, dyspnea and puffy face for three months (SVC syndrome).
- Extraterine effusion, tapping was done due to impending cardiac tamponade at ER.

Initial Clinical Diagnosis

- Primary lung cancer with lung-to-lung and brain metastasis.
- Uterine Leiomyoma.

Cytology and Cell block of Pericardial effusion

- Smear shows a few small clusters of atypical cells, with irregularly enlarged, hyperchromatic and sometimes multi-lobulated nuclei with one or more prominent nucleoli. Abundant cytoplasm with ill-defined cytoplasmic borders, and occasional cytoplasmic vacuolation were found.
- In cell block, numerous epithelioid trophoblast tumor nests were characterized by comedo necrosis and hyaline material deposits.

Immunohistochemical profile and special stains

- Positive: CK7, p40, GATA-3, HSD3b1, Ki-67 (20%)  
- Negative: Cairetin, HMB45,CK20, PAX8, Uroplakin-III, TTF-1, mucicarmine, PASD

Final Pathological Diagnosis

- Extraterine Epithelioid Trophoblastic Tumor (ETT) in lung and pericardium, with brain metastasis.
- Negative for malignancy in Endometrial D.C.

Discussion

Extraterine ETT in the absence of a uterine tumor has been documented in the lung, parametrium, periaxial soft tissue, broad ligament, spine, orbit, lymph nodes, small bowel, fallopian tube, ovary, gallbladder. The existence of extraterine ETT apparently limited to specific organ requires more data to explain. Possible etiology includes the de novo transformation of trophoblast cells transmitted to the lung during pregnancy or the spontaneous resolution of an antecedent uterine ETT6. Cytological features of ETT were only described in three case reports3,4,5. In the smears of endometrial brushings, a few solitary or small clusters of atypical giant cells were scattered in the background of the secretory endometrium. These cells were mononucleate with irregularly enlarged and hyperchromatic nuclei with one more inconspicuous nucleoli. HSD3B1 is a highly specific trophoblast-associated marker that assists in the differential diagnosis of trophoblastic tumors and tumor-like lesions. In practice, a tumor with more than 50% tumor cells positive is a trophoblastic lesion.

P63 is expressed in ETT in a strong diffuse pattern and it is only focally present in choriocarcinoma and absent in PSTT. In addition, Whitney A. al.demonstrated P40 as an equivalent to P63 in the diagnosis of lesions of chorionic-type intermediate trophoblast origin.

GATA-3 is frequently expressed in normal and lesional trophoblastic tissues2. It is important to recognize the expression of GATA-3 in trophoblastic tumor, because it can present a diagnostic pitfall in the assessment of suspected metastatic bladder or breast carcinoma.

Conclusions

It is difficult to make a definite diagnosis of ETT using only the cytologic specimen in the extraterine sites, especially in the absence of cervical or uterine corpus disease; however, our case demonstrated that the cell block could be key to identifying the comedo necrosis and hyaline-like material and also a source for the application of immunohistochemical stains. In addition, awareness of the co-expression of GATA-3 and P63/P40 in ETT is important, because it could be a diagnostic pitfall in the assessment of suspected metastatic breast or urothelial carcinomas involving either gynecologic tract or extraterine sites.

References