

中文題目:以類似原發性子宮內膜癌為臨床表現之肺腺癌併子宮內膜轉移:一個稀有案例報告

英文題目: Endometrial metastasis of lung adenocarcinoma mimicking primary endometrial cancer : a rare case report

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Background:

The primary lung cancers most commonly metastasize to the brain, bones, liver, and adrenal glands, female genital tract involvement is very rare. Ovarian, adnexa with fallopine tube , uterine cervical, vagina metastases from pulmonary adenocarcinoma had been reported only in some literatures . The endometrium is an even rate site for metastases from primary lung cancer , and only 1 case of lung adenocarcinoma metastasizing to this site from literature review, other 2 cases are from small cell lung cancer.

Herein , we reported a rare case of NSCLC harboring the epidermal growth factor somatic mutation, exon 19 deletion, with endometrium ,bone and adrenal gland metastases. Difficulty may exist in determining the origin of the primary tumor in women with synchronous pulmonary and endometrial tumors because of the similar pathological features. Immunohistochemistry (IHC) may be helpful, but can't provide the exact evidence for final diagnosis TTF-1 positive endometrium cancer had been noted. We reviewed related literature and share the experience of using EGFR mutation to discriminate the primary origin or secondary metastatic endometrial cancer from lung.

Case :

A 53 year-old woman presents to our clinic with a recent history of abnormal vaginal spotting for 6 months. She had undergone 2 normal-term vaginal deliveries (gravid 2,para 2) , and had reached menopause four years ago.

On gynecologic examination, the external genitalia and the vulva were free of lesions. Vaginal ultrasound revealed 30 mm endometrial thickness. No obvious ovarian lesion was found. The laboratory data revealed normal value of hemoglobin, creatine, urea and electrolyte. Sexual hormone (*Follicle-stimulating hormone* (FSH), *Luteinizing hormone* (LH) and Estradiol (E2)) was compatible with menopause status. However, high cancer-related antigen-125 (CA-125) level 218 U/ml was found (normal range: 0~35 U/ml).

Endometrial biopsy was performed by use of the hysteroscope and displayed grade 3 adenocarcinoma with myometrial invasion. The immunohistochemical (IHC) study demonstrated diffusely and strongly positive Thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK-7).(Fig. 1). Negative staining of estrogen receptor(ER),p16 and CK20, which may imply the pulmonary origin related metastatic adenocarcinoma.

The chest radiograph accidentally revealed opacification over the left lower lung (LLL), with some small nodules at right upper lung(RUL). Computed tomography of the abdomen revealed bronchogenic tumor with central necrosis in the LLL (5.6cm in diameter) with metastatic lymphadenopathy in the bilateral hila, left lower paraesophageal, subcarinal, right precarinal regions , and aortopulmonary region. A left adrenal nodule about 2.26cm in size was also identified. (Fig.2) She then received CT-guide biopsy of left lung tumor, pathological report demonstrated adenocarcinoma, further IHC study revealed positive staining of TTF-1, but negative of P63. We also checked EGFR mutation analysis by cycleave polymerase chain reaction technique (cycleave-PCR)and exon 19 deletion was detected, which compatible with the non-small cell lung cancer. We further rechecked the EGFR mutation analysis from the tissue of endometrium, which also harboring exon 19 deletion.

We ultimately diagnosed that this female patient had lung adenocarcinoma , having exon 19 deletion with endometrium ,bone and adrenal gland metastasis.

We therefore treated her with gefitinib (250mg)therapy once daily. After gefitinib treatment for 3 months, the image follow up revealed mild shrinkage of the main tumor and endometrium lesion.

Discussion :

The lung cancer is well known to metastasize frequently and widely, close to 70% of patients with lung cancer present with locally advanced or metastatic disease at the time of diagnosis. There are only rare cases in the literature of gynecological manifestations of lung cancer. Vaginal, uterine cervical, and fallopian tube were also been reported [1]. The endometrium is an unusual site for metastases from primary lung cancer, only few case reports had been proposed. Concerning endometrial involvement, only one case is from SCLC [2], 1 case from well-differentiated pulmonary neuroendocrine carcinoma [3] and only one case of NSCLC adenocarcinoma [4] metastasizing to this site have been reported in the literature.

Thyroid transcription factor 1 (TTF-1) has been considered to be a useful marker to differentiate between primary pulmonary adenocarcinomas and metastases on the basis of morphologic features alone. However, a small proportion of endometrial carcinomas also show TTF-1 expression. Overexpression of EGFR has been documented in between 36% and 87% of the endometrial adenocarcinoma patients. However, The EGFR sequence in these patients' tumor tissue was found to be wild type, with no mutations on exons 18 to 21. Therefore, EGFR mutation can provide the information to differentiate the exact tumor origin, either primary origin or secondary metastatic endometrial cancer from lung.