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Research Letter

Occult serous carcinoma of fallopian tube presenting as supraclavicular lymphadenopathy

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Dear Editor,

Primary fallopian tube carcinomas (PFTCs) are rarely encountered gynecological neoplasms and account for 0.3–1% of female genital tract malignancies [1,2]. PFTCs most commonly occur in patients aged 40–65 years, with a median age of 55 years. Difficulties are encountered in the clinical and pathological diagnosis of PFTCs because they share the same clinical findings and pathological features as serous epithelial ovarian cancer and primary peritoneal serous carcinoma [1].

Similar to ovarian cancer, PFTC can spread by transcoelomic exfoliation of cancer cells in the abdominal cavity, which causes peritoneal carcinosis. Direct spread, transluminal migration, lymphatic and hematogenous metastasis have also been shown [2]. Distant metastases are more frequently seen in PFTC than in ovarian cancer [3].

PFTC is usually asymptomatic. The most common symptom is abdominal pain, which can be colicky due to tubal peristaltism, or blunt as a result of tubal distention. Patients are usually diagnosed at an advanced stage, accompanied by widespread pelvic metastasis due to nonspecific clinical signs and symptoms [4].

Isolated supraclavicular lymph node metastasis is a rare manifestation of tubal carcinoma. In the literature, only three patients [5–7] who presented with isolated supraclavicular lymph node were diagnosed as having PFTC. In this research letter, we aimed to discuss the diagnosis and follow-up of a patient who was diagnosed with PFTC with isolated supraclavicular lymph node metastasis.

A woman aged 60 years (gravida 7, parity 5) who had been postmenopausal for 12 years, was admitted to the general surgery department with a palpable left supraclavicular lymph node. An excisional biopsy of the supraclavicular lymph node was performed. Pathological examination of the biopsy material revealed papillary adenocarcinoma metastasis (Figure 1A). Immunohistochemical staining was performed to determine the origin of the primary tumor. The results showed diffuse-strong nuclear WT-1 and p53, cytoplasmic cytokeratin 7, focal-strong nuclear progesterone receptor, and sporadic nuclear estrogen receptor staining. cytokeratin 20, thyroid transcription factor-1 and thyroglobulin staining were not detected. According to the final pathology report, breast or ovarian tumors were preliminarily diagnosed according to the morphological and immunohistochemical results. The patient was re-evaluated in the general surgery department. Breast examination, mammography and breast ultrasound were performed to confirm absence of breast tumor. Both gastroscopy and colonoscopy revealed normal results. The patient was referred to our department for evaluation of gynecological oncology.

In the gynecological examination, there was no abnormal vaginal discharge or palpable mass in the pelvic palpation. No pathological finding was observed by transvaginal ultrasonography. The cervicovaginal smear and endometrial sampling were normal. The patient had only mild pelvic and back pain. Her family history was unremarkable. Serum carbohydrate antigen (CA)-125 level was 901 U/mL.

There were lymph nodes with pathological size and enhancement localized at L4-5 lumbar spine in thoracoabdominal computed tomography (CT). No other abnormality was found. The patient underwent positron emission tomography combined with CT (PET-CT). PET-CT revealed an intense 28 mm × 19 mm hypermetabolic area in the posterior soft tissue and a hypodense nodular lesion located in the left adnexal area. Multiple retroperitoneal lymphadenopathies were also detected in the right retrocaval area (Figure 1B).

The patient was diagnosed with advanced-stage ovarian tumor and underwent surgery in July 2011. The patient had a total

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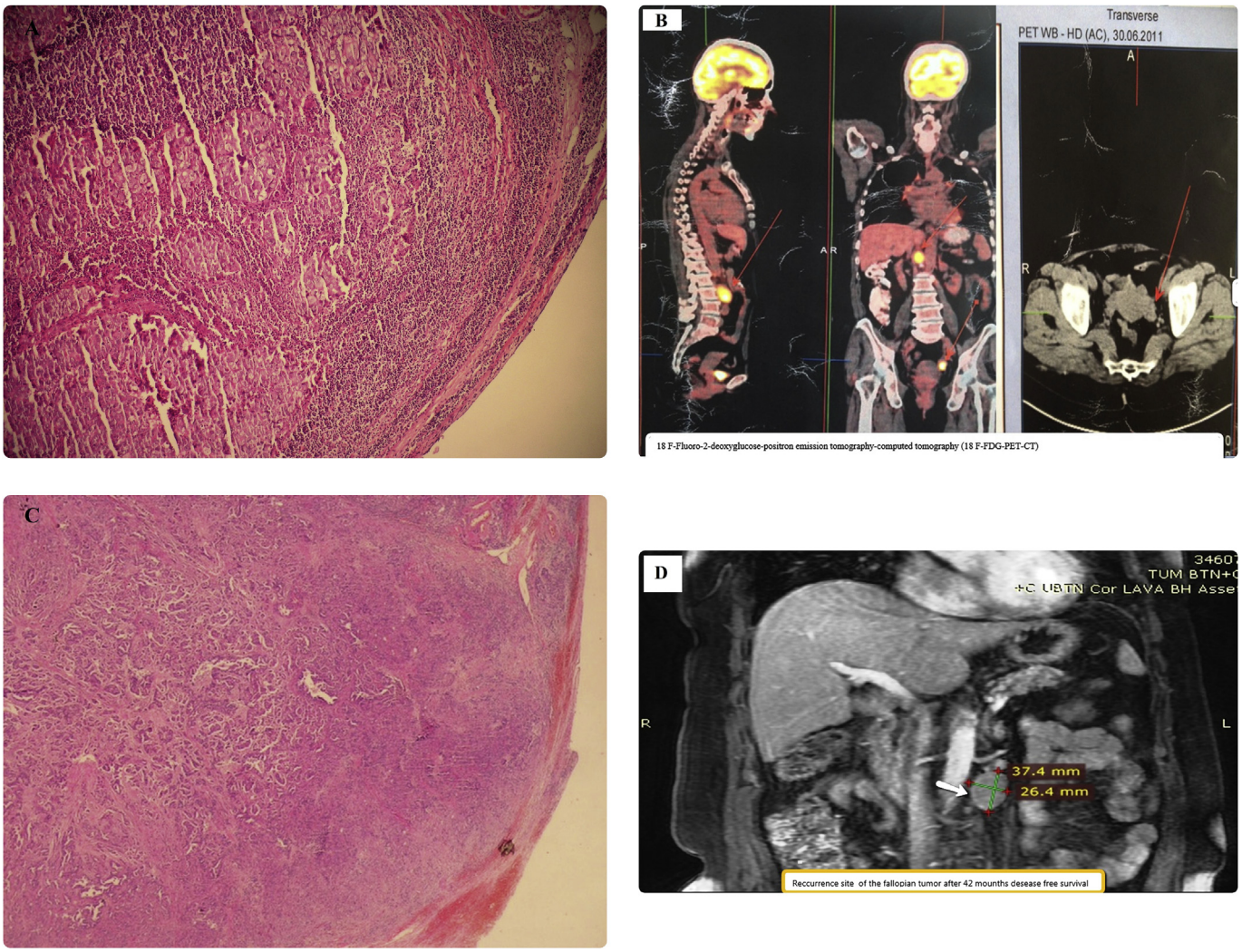

Figure 1. (A) Serous carcinoma metastasis of the fallopian tube in supraclavicular lymph node (hematoxylin and eosin, 100×). (B) Appearance of the tumor in positron emission tomography/computed tomography. (C) Serous carcinoma arising from the left fallopian tube lumen (hematoxylin and eosin, 40×). (D) Appearance of the recurrence site in magnetic resonance imaging.

abdominal hysterectomy and bilateral salpingo-oophorectomy, appendectomy, total omentectomy, and pelvic para-aortic lymphadenectomy (8 left pelvic lymph nodes, 12 right pelvic- and 12 para-aotric lymph nodes). No intraoperative macroscopic tumoral implant or ascites was observed. The right tuba and the omentum were normal. A lobulated-contoured lesion located in the ampulla of left fallopian tube was seen. A surgical specimen was sent for frozen section examination, which revealed a 2.5-cm diameter malignant tumor in the ampulla of the left fallopian tube. The diagnosis was tubal high-grade papillary serous adenocarcinoma in the final pathology report (Figure 1C).

We observed tumoral invasion of the muscular layer and serosa of the fallopian tube, but extension beyond the serosa was not observed. Also, serous tubal intraepithelial adenocarcinoma (STIC) was found in the right fallopian tube. There was no tumoral implant in the pelvic, para-aortic lymph nodes, omentum, or appendix. As a result of these evaluations, the patient was diagnosed with PFTC with isolated supraclavicular lymph node metastasis.

She underwent six cycles of combined paclitaxel and carboplatin chemotherapy after the primary surgery. Postoperative recurrence was monitored using serum CA-125 levels. When elevated serum CA-125 level (182 U/mL) was detected, the results of magnetic resonance imaging showed a solid mass of approximately 36 mm × 26 mm in the left para-aortic area, inferior to the renal artery (Figure 1D). Total disease-free survival was 42 months. The mass was considered as recurrent disease; therefore, secondary cytoreductive surgery and adjuvant chemotherapy was planned.

Advanced epithelial ovarian cancer will ultimately develop recurrent disease. However, the standard treatment of women with recurrent ovarian cancer remains poorly defined. Surgery for recurrent ovarian cancer is suggested to be associated with increased overall survival.

The theoretical benefit from cytoreductive surgery relates to removing large tumor volumes that have a decreased growth fraction and poor blood supply, thereby improving the efficacy of chemotherapeutic agents.

Primary fallopian tube carcinomas are rarely encountered malignancies and there is little information on their etiology and treatment. Some data suggest that chronic tubal inflammation, infertility, tuberculosis salpingitis, and tubal endometriosis play a role in the etiology of PFCT [8].

Histopathologically, the presence of p53 in the fallopian tube epithelium indicates proliferative lesions named serous tubal

intraepithelial lesions [9]. These lesions are dysplastic lesions and cause STIC [10]. STIC might be a precursor of fallopian tube, ovarian and peritoneal high-grade serous carcinoma [10]. In our case, although high-grade serous carcinoma was found in the left fallopian tube, STIC was present in the right fallopian tube.

Lymphatic discharge of the fallopian tubes may differ according to the affected portion of the fallopian tube. Anatomically, lymphatic drainage of fallopian tube to the pelvic lymph nodes occurs through the lymphatic channels located in the proximal part of the uterus, and para-aortic lymph node drainage occurs through the lymphatic channels located in distal tube and fimbria [11]. Sometimes, lymphatic drainage of the medial part occurs through the round ligament lymphatics to the inguinal region [12]. Both positive para-aortic and pelvic lymph node involvement is seen 42–59% of patients [2].

Similar to the surgical treatment of epithelial ovarian cancer, the aim in the treatment of PFTC is complete removal of the tumor [13]. The standard surgical treatment is total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, infracolic omentectomy, pelvic- and para-aortic lymph node dissection, and abdominal washing and peritoneal sampling [14].

International Federation of Gynecology and Obstetrics (FIGO) staging is the most coherent prognostic factor related to survival [15]. For patients at an advanced stage, it is necessary to remove as much tumor mass as possible and perform aggressive cytoreductive surgery [16]. Although widespread intra-abdominal tumoral implant was not observed in this patient, the presence of supraclavicular lymph node metastases was evaluated as Stage 4 disease, and the most extensive surgical resection was performed to maximize survival. Supraclavicular lymph node metastasis without widespread intra-abdominal disease is a rare event. In the literature, metastases were reported in only three patients who presented with isolated supraclavicular lymph nodes. Piura et al [5] reported the first in 1989; their patient presented with isolated supraclavicular metastasis and was diagnosed as having fallopian tube carcinoma. The second was a woman aged 70 years reported by Scholz et al [6]. Their patient was diagnosed with a left supraclavicular mass with PFTC at Stage IV. The patient was successfully treated with carboplatin after surgery. Sakurai et al [7] reported a patient aged 76 years who presented with a supraclavicular lymph node. Biopsy of the lesion revealed metastatic adenocarcinoma and the primary lesion originated from the right fallopian tube. Two years of disease-free survival was reported. Our patient was elderly, similar to the patients in the literature, and had no gynecological symptoms.

CA-125 is the most widely used tumor marker in the diagnosis and follow-up of PFTC. Elevated pretreatment levels were reported in 80% of patients with PFTC [17]. In our case, the CA-125 level was increased; there was an isolated supraclavicular metastasis, and no intra-abdominal disease. Also, recurrence after 42 months was determined by an increase in serum CA-125 levels.

Secondary cytoreductive surgery is defined as the removal of recurrent masses after remission. The aim of cytoreductive surgery is to extend survival; it is not a curative treatment. The obvious benefits of optimal primary surgery in advanced-stage ovarian cancer have led researchers to investigate secondary cytoreductive surgery for recurrent disease after clinical remission. Additionally, various chemotherapeutic agents containing platinum have been administered to patients after secondary cytoreductive surgery [18].

A meta-analysis published in 2009 revealed that complete cytoreductive surgery independently increased overall survival in patients with recurrent ovarian cancer [19]. A prospective study by Eisenkop et al [20] reported 87% decreased mortality after secondary cytoreductive surgery in disease-free patients as compared with patients with residual disease. The median survival rate was reported as 44.4 months in the complete secondary cytoreduction group, whereas it was 19.3 months in the suboptimal cytoreduction group.

Our patient's disease-free survival time after primary surgery was 42 months. Platinum-based chemotherapy following secondary cytoreductive surgery was planned due to recurrence.

PFTC should be considered as a systemic disease because it may be accompanied with distant lymph node metastases without widespread pelvic disease; its treatment and follow-up should be scheduled accordingly. Furthermore, we believe that it is appropriate to use CA-125 in the diagnosis and follow-up of patients with isolated supraclavicular lymph node metastasis; however, if metastases originate from other primary origins, such as lung and breast, CA-125 may not be a good marker.

Conflicts of interest

The authors have no conflict of interest relevant to this article.

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