Short communication

Incidental lymphangioleiomyomatosis in pelvic lymph nodes associated with malignant neoplasm of the ovary – two case reports

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To the Editor,

Lymphangioleiomyomatosis (LAM), a rare, destructive and progressive neoplastic disease, generally arises in the lung and occurs predominantly in women of childbearing age or premenopausal age [1]. Primary extrapulmonary LAM is extremely rare, with only a handful of cases being reported, leading to limited information being available regarding the pathologic characteristics. Here we report two cases of LAM of the pelvic lymph node, accidentally discovered after surgical staging of ovarian malignancy. This report shows that occult LAM can be detected in surgical staging of pelvic tumors. The diagnosis should be based on clinicopathological features and immunohistochemical examination, to avoid a missed diagnosis or misdiagnosis.

Written informed consent was obtained from the patient described in this letter, and the investigation was conducted in accordance with the Declaration of Helsinki (1975). The ethics committees of the Affiliated Hospital of Southwest Medical University approved this study.

The first case was of a 55-year-old postmenopausal woman admitted to the hospital with abnormal uterine bleeding for more than 2 months. Doppler ultrasound suggested mixed cystic-solid echogenicity in the posterior uterus with a size of 10 × 9.5 × 7.5 cm, leading to a differential diagnosis of malignant tumor with pelvic lymph node metastasis. The second case was of a 54-year-old woman, who presented with a mass in her right ovary. The patient underwent an oophorectomy ten years ago, for clear cell carcinoma of the left ovary. After reviewing the abdominal computed tomography, a space-occupying lesion was seen in the right ovary, but no further treatment was given at the time and the tumor gradually enlarged. Total hysterectomy, bilateral adnexectomy and lymph node dissection were performed in both patients. Their past and family histories were unremarkable.

Final pathological examination revealed that the right ovarian lesion of the first patient was consistent with high-grade serous carcinoma, and the right ovarian lesion of the second patient was consistent with clear cell carcinoma. No lymph node metastases were found in either of the patients, although multifocal spindle cell proliferation was an unexpected finding. A total of 91 lymph nodes were dissected in the first patient, out of which 18 showed spindle cell proliferation, including left pelvic lymph node (3/32), right pelvic lymph node (2/13), paraaortic lymph node (7/28), anterior sacral lymph node (5/15), and common iliac lymph node (1/3). In the second patient, a total of 20 lymph nodes were found after surgery, and a small focus of spindle cell proliferation was found in 1 left pelvic lymph node. In all affected lymph nodes, the lesions mainly affected the parenchyma and extended beyond the capsule (Fig. 1A).

Histologically, the spindle cells in lymph nodes are arranged in bundles, trabeculae, and papillae, and are associated with slit-like vascular channels. Cytologically, spindle cells are mild, with weak eosinophilic cytoplasm and small nucleoli (Fig. 1B). There is no atypia, necrosis, or mitosis. Microscopically, the size of the lesion was evaluated as 4 mm while the diameter was in the range < 1 –10 mm.

Immunohistochemical studies showed that these spindle cells were positive for HMB45 (Fig. 1C), spinal muscular atrophy and smooth muscle marker antibody duo, but negative for Melan A. D2-40 show lymphatic endothelium (Fig. 1D) and the Ki-67 proliferation index was less than 1%.

Therefore, combined with morphological and immunohistochemical results, the 2 patients were ultimately diagnosed with lymph node LAM. Neither

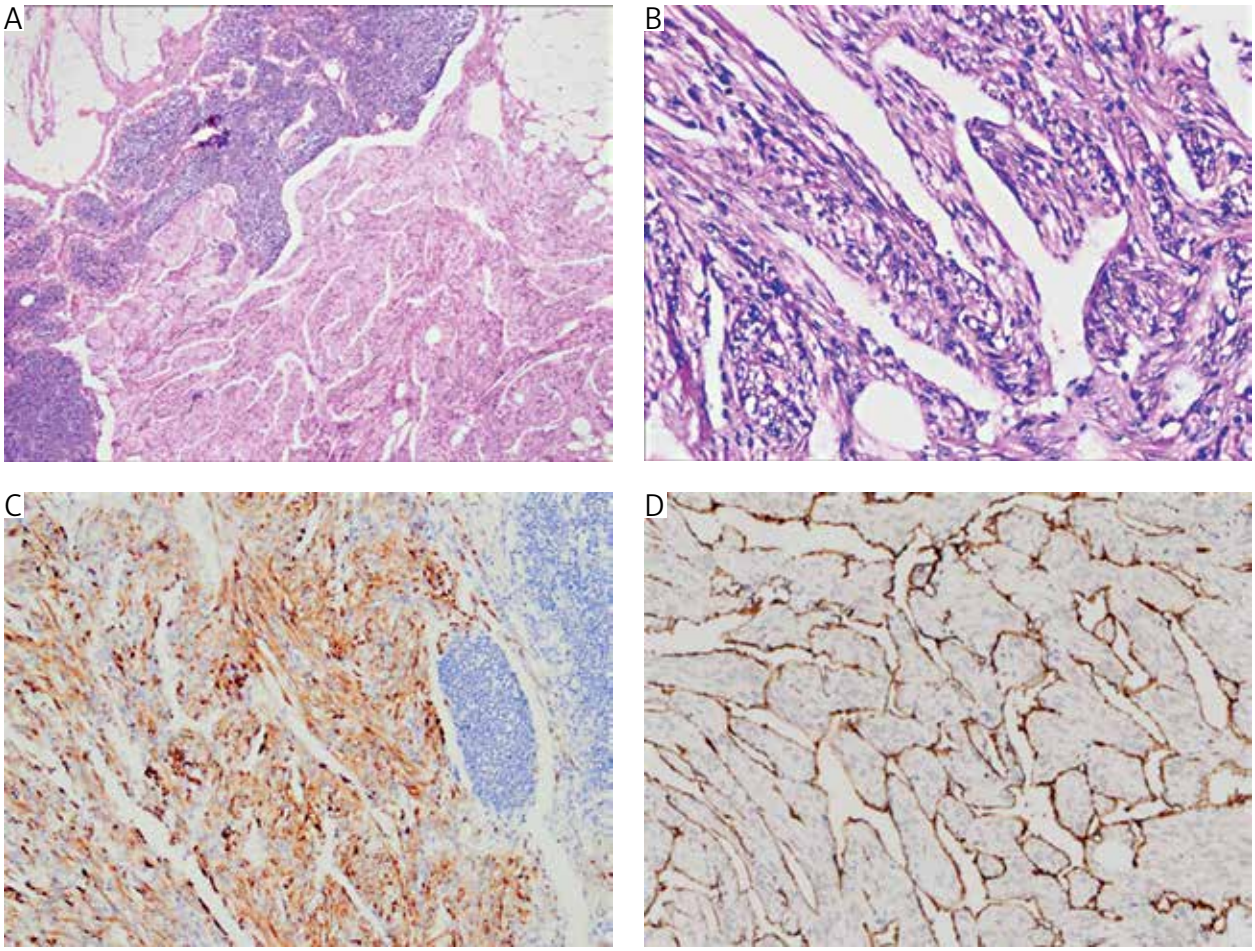

Fig. 1. A) Spindle cells are located in the parenchyma of the lymph node and infiltrated into adjacent adipose tissue (HE 40×); B) high magnification view showing proliferation of plump spindle-shaped myoid cells arranged in short fascicles with weak eosinophilic cytoplasm and no atypia or pathological mitosis (HE 200×); C) the plump myoid cells in lymphangioleiomyomatosis (LAM) are positive for HMB-45; D) D2-40 was particularly useful to highlight compressed lymphatic channels within areas of more solid-appearing, fascicular growth patterns of LAM

of the patients received any further treatment. No abnormalities were found in other organs, including the uterus, lung, and kidney, and no nodular sclerosis was observed in either of the patients. Both patients were followed up for 30 and 16 months, respectively, and no disease was observed.

Lymphangioleiomyomatosis belongs to the family of perivascular epithelioid cell neoplasms [2]. Extrapulmonary LAM is a rare tumor, which occurs in middle-aged adults, with a female predominance, the uterus or an adjacent locale in the retroperitoneum or pelvic cavity being the primary site of origin [3]. Although the origin of LAM is unknown, the pathogenic mechanism has been attributed to functional loss of tuberous sclerosis complex (TSC) genes, leading to neoplastic proliferation of cells [4]. Lymphangioleiomyomatosis can occur sporadically or in association with the genetic syndrome TSC.

Due to the rarity of LAM and limited treatment experience, no effective treatment currently exists for this and management must be based on clinical experience. The usual adequate local treatment is resection of the extra-pulmonary mass or cyst. At the pathological level, LAM is associated with mutations in tumor suppressor genes TSC1 and TSC2, leading to activation of the mTOR pathway, which is currently the main therapeutic target. As the disease occurs in women of childbearing age, some have suggested that estrogen may play a role in the pathogenesis. Moreover, LAM cells express hormone receptors. Therefore, steroids, hormone therapy (antiestrogen), and mTOR inhibitors (sirolimus and everolimus) are currently used clinically to treat LAM [5].

In summary, the treatment of extrapulmonary LAM is challenging. Surgical resection is an appropriate option for disease control and symptom relief. Currently, the prognosis of extrapulmonary LAM is good. However, sufficient data are needed to confirm this. Lymphangioleiomyomatosis is an aggressive disease, and close follow-up is necessary.

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The authors declare no conflict of interest.

References

1. Xu KF, Xu W, Liu S, et al. Lymphangioleiomyomatosis. Sem Respir Crit Care Med 2020; 41: 256-268.
2. Xuan LL, Wei JG, Liu HG: [Pathological diagnosis and new progress of perivascular epithelioid cell tumor]. Zhonghua Bing Li Xue Za Zhi 2021; 50: 282-287.
3. Hayashi T, Kumasaka T, Mitani K, et al. Prevalence of uterine and adnexal involvement in pulmonary lymphangioleiomyomatosis: a clinicopathologic study of 10 patients. Am J Surg Pathol 2011; 35: 1776-1785.
4. Ando H, Ogawa M, Watanabe Y, et al. Lymphangioleiomyoma of the uterus and pelvic lymph nodes: a report of 3 cases, including the potentially earliest manifestation of extrapulmonary lymphangioleiomyomatosis. Int J Gynecol Pathol 2020; 39: 227-232.
5. McCarthy C, Gupta N, Johnson SR, Yu JJ, McCormack FX. Lymphangioleiomyomatosis: pathogenesis, clinical features, diagnosis, and management. Lancet Respir Med 2021; 9: 1313-1327.

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