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Lymphangioleiomyomatosis observed in the dissected lymph node and myometrium in a patient that underwent radical operation for endometrial cancer

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Summary

Lymphangioleiomyomatosis (LAM) is a rare disease that afflicts mostly young women. It is characterized pathologically by the appearance of interstitial collections of atypical smooth muscle cells and cyst formation in the lungs, lymph node, kidney, and so on. A case was presented that underwent radical operation with the diagnosis of endometrial cancer, in which were found LAM cells in dissected lymph node and myometrium. *Case:* A 40-year-old woman underwent radical operation with the diagnosis of endometrial cancer. Although the dissected pelvic and para-aortic lymph nodes did not show the metastases of cancer, immunohistochemical study revealed the LAM cells among the dissected lymph nodes. Further histological study showed the LAM cells were in the uterine myometrium as well. Physical examination excluded the diagnosis of tuberous sclerosis. Since pulmonary LAM were observed as well, the physician followed the patient. *Discussion:* Sporadic LAM, without a complication of tuberous sclerosis, rarely shows LAM cells systemically as in this case. *Conclusions:* When LAM is observed coincidentally in operated dissected lymph node, it is important to examine for tuberous sclerosis and also to follow up the findings in the lung.

Key words: Lymphangioleiomyomatosis; Endometrial cancer; Lymph node; Myometrium; Tuberous sclerosis.

Introduction

Lymphangioleiomyomatosis (LAM) is a rare disease that afflicts mostly young women [1, 2]. It is characterized pathologically by the appearance of interstitial collections of atypical smooth muscle cells and cyst formation in the lung, lymph node, kidney, and so on. It is sometimes complicated with tuberous sclerosis complex (TSC) and is called TSC-associated LAM. LAM is categorized as a generally benign mesenchymal neoplasm [3]. However, pulmonary LAM should be observed carefully, because it sometimes causes severe pneumothorax and develops into a life -threatening event.

As LAM is a rare disease, there is no accurate data about prevalence rate or morbidity. In Japan, the prevalence rate of LAM is estimated to be 1.9~4.5 per one million according to the Japanese intractable diseases information center. In pulmonary LAM, the normal architecture of the lung is distorted by multiple small cysts up to several centimeters in diameter [4], as the growth of LAM cell producing matrix metalloproteinases (MMPs) [5].

Recently, LAM cells were sometimes found coincidentally in the dissected lymph node at the time of gynecological operation [6-8]. In most cases, LAM cell is confined to the dissected lymph node. A case that underwent radical operation with the diagnosis of endometrial cancer, had LAM found coincidentally in dissected lymph nodes, myometrium, and lung is presented.

Case Report

A 40-year-old nulligravida woman visited the present hospital with a chief complaint of abnormal genital bleeding. Her menstruation cycle was regular and 28 days. She had no appreciable medical history.

During her visit, endometrium biopsy was performed. The result revealed endometrioid adenocarcinoma G1 and estrogen receptor positive. Uterine endometrial cancer was diagnosed. MRI and PET-CT examination showed that the tumor lesion was confined to the corpus uteri. The Wertheim's radical hysterectomy with pelvis and para-aortic lymph node dissection was performed (Figure 1). Histopathological examination revealed that the tumor was confined to the corpus uteri and showed less than half myometrial invasion. No metastases were found in the dissected pelvis and para-aortic lymph nodes. Postoperatively, FIGO Stage I A G1, UICC pT1aN0M0 was confirmed.

During histological examination, characteristic abnormal spindle cell proliferation was noted in subcapsular area of the lymph node. The proliferating cells had minimally atypical nuclei with light eosinophilic cytoplasms and arranged in fascicular, nested, and whorling patterns. Tumor cell nests were surrounded by channel-like spaces (Figures 2A, B). Moreover, a microscopic lesion with same histology was found in the uterine myometrium (Fig-

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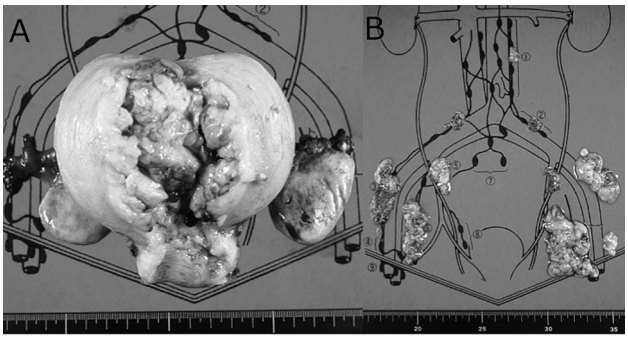

Figure 1. — Resected uterus (A), and pelvis and para-aortic lymph nodes (B).

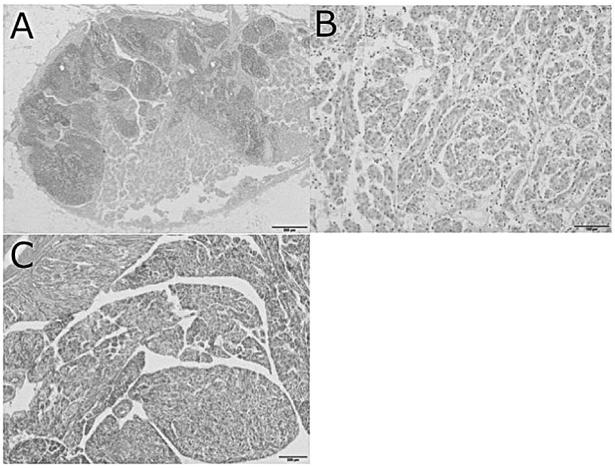

Figure 2. — HE stain of the dissected lymph node (A, B). LAM lesion is distributed in subcapsular area of the lymph node with spindle cell proliferation arranged in nested pattern (A). In the LAM lesion, immature smooth muscle-like spindle cells (LAM cells) with minimal cytological atypia are arranged in fascicular, nested, and whorl pattern surrounded by channel-like spaces (B). LAM lesion is also noted in the uterine myometrium (C).

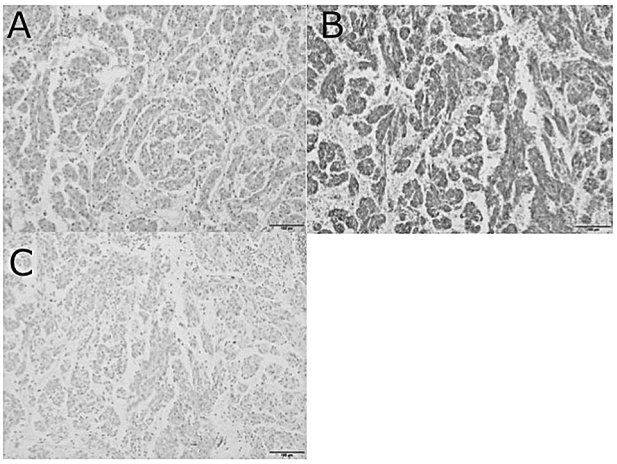

Figure 3. — Immunohistochemical stain of the LAM cells in the lymph nodes. HE stain (A). LAM cells are diffusely and strongly positive for α-SMA (B). A few scattered HMB45 positive LAM cells were also observed (C).

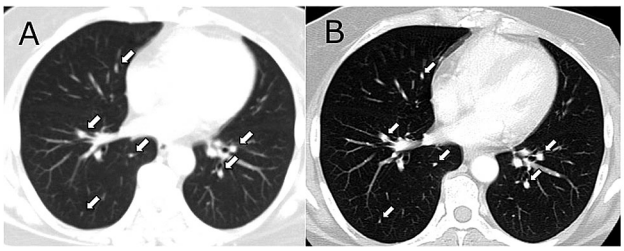

Figure 4. — Chest CT examination: (A) pre-operation (B) post-operation. Multiple small cysts (arrows) permeate the entire lung parenchyma, indicating pulmonary LAM.

ure 2C). Immunohistochemically, proliferating cells showed diffuse and strong positivity of α-SMA suggesting their smooth muscle nature. In addition to that, they were focally positive for melanocytic marker, HMB-45 (Figure 3). Based on the histology and immunohistochemical staining pattern, the authors diagnosed the lesion of the lymph node and myometrium lesion as LAM.

The physical examination excluded the diagnosis of tuberous sclerosis. Chest CT examination revealed multiple small cysts permeating the entire lung parenchyma and indicated pulmonary LAM (Figure 4B). Preoperatively, cancer metastases were not found in the lung. However, the existence of pulmonary LAM was unclear. Retrospectively, with modifying preoperative CT image into the lung window, the existence of pulmonary LAM was indicated preoperatively (Figure 4A). Pulmonary LAM was followed up by the physician every three months. CT image showed almost no change with the LAM lesions or no symptom of pneumothrax. Postoperative course of endometrial cancer was also followed up well (no evidence of disease for two years).

Discussion

LAM is a rare disease that mostly afflicts young woman of childbearing age. There are two types of LAM, sporadic LAM (non-TSC-associated LAM) and TSC-associated LAM. In both types of LAM, most patients have the mutations in TSC1 or TSC2 genes. TSC patient shows inherited neurocutaneous disorder that is characterized by the development of variety of tumors in multiple organs, including hamartomas of the brain, eyes, heart, lung, liver, kidney, and skin. Both LAMs are characterized pathologically by the appearance of interstitial collections of atypical smooth muscle cells and cyst formation [4, 9].

It is likely that estrogen plays a central role in disease progression of LAM [10-12]. In this case, immunohisto-

chemical study revealed that the LAM cells were estrogen receptor positive. Recently, LAM cells were sometimes found coincidentally in the dissected lymph node at the time of gynecological operation [6-8]. Eighteen out of 30 (60%) of coincidentally found LAM cases were operated for endometrial tumor. In these 30 cases, two cases were clinically diagnosed as tuberous sclerosis. A case of incidentally found lymph node LAM associated with endosalpingiosis, besides the retroperitoneum lymph nodes, was reported [4]. In the other 29 cases, LAM cells were confined to the dissected lymph node. It is very rare that LAM is found systemically in lymph node, myometrium, and lung at the same time in sporadic LAM, as in this case.

Once LAM cells are found coincidentally in the dissected lymph node, the examination for tuberous sclerosis should be done. At the same time, the examination aims to find LAM systemically, especially for pulmonary LAM, because sometimes pulmonary LAM develops into a life threatening disease. In this case, complication of tuberous sclerosis was excluded by physician. Meanwhile, pulmonary LAM was found since preoperative CT image. Pulmonary LAM showed no development for two years postoperatively. Estrogen is thought to play a main role in disease progression, because the disease only rarely presents after menopause. One of the reasons why it showed no development in this case, might be the lack of estrogen because of the operation. If the pulmonary LAM develops, one of the management options is to use the mechanistic target of rapamycin (mTOR) inhibitor, such as the sirolimus [13]. Lung transplantation may be required eventually for the patient showing progressive respiratory failure [14].

In conclusions, once LAM cells are coincidentally observed in dissected lymph node, it is important to examine for tuberous sclerosis and also to assess the pulmonary findings.

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