Case Report

Janina Słodkowska[1], Jan Patera[2], Jan Breborowicz[3], Agnieszka Jarzemska[4], Maria Korzeniewska-Kosela[5], Krystyna Siemiątkowska[6], Elżbieta Radzikowska[7], Grzegorz Przybylski[4], Wojciech Kozłowski[2]

Extrapulmonary Lymphangioleiomyomatosis Presented as the Asymptomatic Retroperitoneal Tumours – Two Cases Report

[1] Department of Telepathology, National Institute of Tuberculosis and Lung Diseases, Warszawa,
[2] Department of Pathology, Military Institute of Medicine, Warszawa,
[3] Department of Pathology, Wielkopolskie Center of Oncology, Poznań,
[4] Department of Lung Diseases, Nicolaus Copernicus University, Bydgoszcz,
[5] I Department of Lung Diseases, National Institute of Tuberculosis and Lung Diseases, Warszawa,
[6] Department of Pathology, Kujawsko-Pomorskie Center of Pulmonology, Bydgoszcz, III Department of Lung Diseases, National Institute of Tuberculosis and Lung Diseases, Warszawa

Lymphangioleiomyomatosis [LAM] is a rare lung disease affecting women and characterized by abnormal smooth muscle cells (LAM cells) proliferation along lung and lymphatic channels. The frequent occurrence of extrapulmonary LAM [e-LAM] has been reported as abdomenpelvic lymph nodes involvement, angiomyolipomas, lymphangioleiomyomas or lymphangiomas in LAM patients. An extrapulmonary manifestation as the initial LAM presentation preceding pulmonary disorders and as asymptomatic extrapulmonary LAM lesions are unusual. We report two women presented with asymptomatic retroperitoneal cystic masses accidentally found on ultrasound examination. The tumours were surgically removed and diagnosed as: 1-*malignant mesothelioma* and 2-*lymphangiomyoma*. The microscopical sections were reviewed and re-diagnosed as e-LAM at advanced pulmonary LAM development. *Mesotheliosis* present in e-LAM morphology is unique and was misleading for malignancy diagnosis. The second case illustrates the hormone dependent growth of *lymphangiomyoma* and LAM development in young women. It is difficult to prove the presence of pulmonary LAM at the time of tumours excision but both cases demonstrate importance of appropriate LAM diagnosis and being aware of such diagnosis in cases presenting with extrapulmonary extension of the disease.

Introduction

Lymphangioleiomyomatosis [LAM] is a rare multisystem disease with the incidence estimated as 1 in 1 million people [3]. This disorder is characterized by abnormal smooth muscle cells proliferation (LAM cells) in the lymphatics and the lymph nodes, blood vessels and lung airways, mediastinum and abdomen. It exclusively affects women during reproductive period; appeared worsen or be diagnosed during pregnancy or with of exogenous estrogens. The typical LAM presentations are respiratory disorders. The frequent occurrence of extrapulmonary LAM [e-LAM] has been reported as abdomenpelvic tumours in LAM patients [7]. However an extrapulmonary manifestation as the initial LAM presentation is unusual [2, 5, 6]. We report 2 cases of asymptomatic retroperitoneal tumours excised prior to the pulmonary LAM manifestation which subsequently were shown to be e-LAM. The unique presence of *mesotheliosis* within one e-LAM lesion and estrogen-dependent growth of LAM lesions are interesting points of the presented cases.

Report of the Case 1

A 43-year-old women was referred to the ITB&LD for a consultation of the lung lesions suggestive of LAM. The patient past history revealed left-sided spontaneous pneumothorax, 5 years ago. No invasive treatment nor other diagnostic lung procedures were performed that time. Three years later an asymptomatic, left abdominal mass was diagnosed during ultrasound [USG] routine gynaecological examination. On computerized tomography [CT], the retroperitoneal mass measured 9x6x7cm; con-

tained solid and cystic components with fluid levels (drained 500 ml of chylous). Mild paraaortical lymphadenopathy was noticed. No other abnormalities in the abdomen, pelvis nor lungs were present. The patient had no pulmonary symptoms and no assessment of lung function was done. The excised tumour was diagnosed as *malignant mesothelioma* and chemotherapy was recommended. A progressive exertional dyspnoea appeared one month after laparotomy. High resolution CT [HRCT] showed multiple small cysts in both lungs, two years later. The lung function tests indicated severe airflow obstruction and air trapping. The chronic obstructive lung diseases was diagnosed and therapy was continued. Six months later, lung HRCT showed multiple polymorphic cysts up to 2 cm in diameter. No mesothelioma progression was seen after 30 months. The clinical data were reviewed and the patient was referred for the consultation.

Report of the Case 2

A 26-year-old pregnant woman (2nd month of pregnancy) was presented to a hospital with the right adnexal mass accidentally found on USG investigation. During following months of her pregnancy, she has been hospitalised several times due to abdominal uterine bleeding; the slow growth of the tumour has been observed. Four months after a delivery the retroperitoneal solid and cystic mass (with fluid collections) measured 10x5x4 cm on CT scan. No pelvic adenopathy was identified. A needle biopsy diagnosis was: an benign (hamartomatous) lesion. The pedunculated tumour was excised and diagnosed as: *lymphangiomyoma*. Two years after laparotomy the spontaneous right-sided pneumothorax occurred. During recurrent pneumothorax the patient was admitted to ITB&LD for the pleurectomy with lung biopsy. At the histopathological diagnosis of LAM, the pulmonary function tests were normal except of small decrease of DLCO. HRCT showed small cysts distributed through the lung fields, compatible with LAM. Screening for tuberous sclerosis was negative. The patient has been given therapy of medroxyprogesterone (once monthly) which stabilized pulmonary LAM but the retroperitoneal mass re-grew (up 2,5 cm). After 4 years of follow up the results of pulmonary tests deteriorated; the recurrent retroperitoneal lesion extended up to 4,5 cm.

Material and Methods

The microscopic sections of the excised tumours were prepared at the outside institutions and were reviewed at ITB&LD. The additional immunostains were done for: Smooth Muscle Actin [SMA], Desmin [Des], HMB–45, CD34, Estrogens [ER] and Progesterone [PrR] Receptors. Additionally for the case 1: cytokeratyn (AE1/AE3), Vimentin [Vim], Ki-67 antigen (MIB-1) and mesothelial cell antigen (HBME-1) (Dako, Denmark) were prepared.

Results of Pathological Findings

Case 1. The tumour cavity was lined by the proliferating typical mesothelium (positive for Vim and cytokeratyn; negative for HBME-1; the Ki-67 proliferation index <5%) – consistent with *mesotheliosis*. The solid part of the tumour was composed of irregular bundles of proliferating LAM cells (SMA+, Des+, HMB-45+), surrounded a ramifying network of endothelium (CD34 +) lined spaces (Fig. 1). The

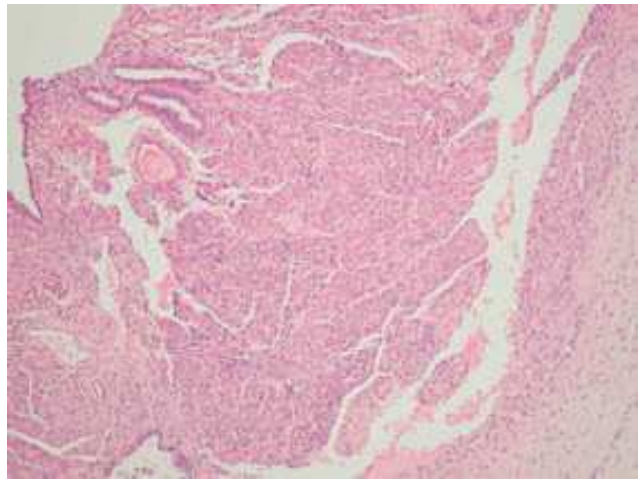

Fig. 1. The case 1. The traverse section of the tumour wall mainly composed of the irregular bundles of the proliferating smooth muscles cells (LAM cells). Slit-like spaces within the LAM bundles are seen. The tumour cavity is lined by the narrow mesothelium (the upper left corner). H&E stain, 10×.

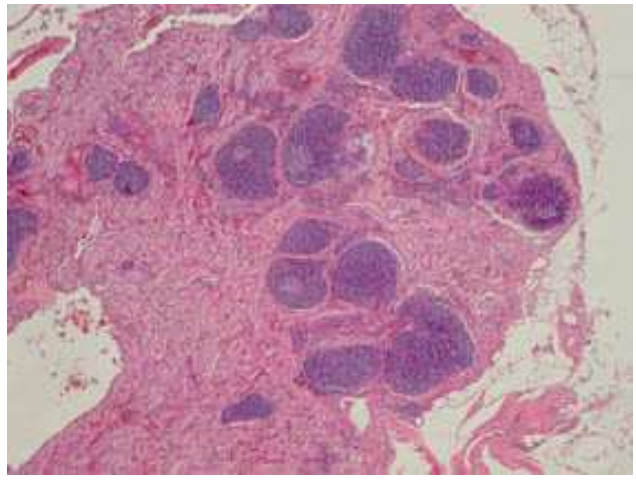

Fig. 2. The case 2. Histology of the tumour peduncle: fascicles of proliferating LAM cells separated by narrow lymphatic channels, with the rich component of lymphoid cells froming follicular centres. H&E stain, 10×.

nuclear immunoreaction for ER and PrR in LAM cells showed various intensities.

Case 2. The tumour and peduncle showed more solid morphology, composed of bundles of the proliferating LAM cells, separated by thin-walled vascular channels – focally extended into adjoining tissue. The variable component of lymphoid tissue (containing germinal centres) involved by smooth muscles proliferation was present (Fig. 2). The immunophenotype of LAM cells was the same as in the previous case. No mitotic activity was seen. The excised lymph nodes showed normal architecture.

Conclusions

The abdomenpelvic masses as extrapulmonary LAM lesions (lymphangioleiomyomas, angiomyolipomas or lymphadenopathy) in LAM patients occur frequently [1, 6, 8]. Renal angiomyolipomas are the most frequent abdominal lesions, usually manifest as asymptomatic, small, bilateral tumours. Lymphangiomas are the cystic retroperitoneal masses that occur in up to 20% of LAM patients. Other CT findings are hypo- or hyperattenuating lymph nodes, a dilated thoracic duct, and ascites [8]. The primary manifestation of e-LAM is unusual and is accounted for 10% [3, 5]. Extrapulmonary LAM can proceed pulmonary manifestation by 1–2 years [6]. We described two cases of asymptomatic retroperitoneal tumours re-diagnosed as e-LAM at the pulmonary manifestation of the disease. The microscopical sections were reviewed and re-diagnosed as e-LAM at advanced clinical stage of pulmonary LAM. The LAM diagnoses were delayed by 30 months. *Mesotheliosis* present in one of the e-LAM lesion is unique and was misleading for malignancy diagnosis. This case and the casual reports about e-LAM with endosalpingiosis [7] or with HMB-45 negative LAM cells [2] illustrate rare and unusual spectrum of extrapulmonary LAM morphology.

The second case emphasizes a significance of sex steroids in LAM aetiology and hormone dependent growth of *lymphangiomyoma* in the young pregnant women, who subsequently presented the pulmonary LAM. The long follow up of the patient indicates inefficiency of the implemented hormonal therapy in LAM patient.

It is difficult to prove the presence of pulmonary LAM at the time of tumours excision, but both cases demonstrate importance of appropriate LAM diagnosis and being aware of such diagnosis in extrapulmonary extension of the disease.

References

1. *Chu SC, Horiba K, Usuki J et al:* Comprehensive evaluation of 35 patients with lymphangioleiomyomatosis. Chest 1999, 115, 1041–1052.
2. *Jaiswal VR, Baird J, Fleming J et al:* Localized retroperitoneal lymphangioleiomyomatosis mimicking malignancy. A case report and review of the literature. Arch Path Laboratory Medicine 2004, 127, 879–882.
3. *Johnson SR, Tattersfield AC:* Clinical experience of lymphangioleiomyomatosis in the UK. Thorax 2000, 55, 1052–1057.
4. *Lam B, Ooi GC, Wong MP et al:* Extrapulmonary presentation of asymptomatic pulmonary lymphangioleiomyomatosis. Case report. Respirology 2003, 8, 544–547.
5. *Lu H-Ch, Wang J, Tsnag Y-M et al:* Lymphangioleiomyomatosis initially presenting with abdominal pain. A case report. Clin Imaging 2003, 27, 166–170.
6. *Matsui K, Tatsuguchi A, Valencia J et al:* Extrapulmonary lymphangioleiomyomatosis (LAM): clinicopathologic features in 22 cases. Hum Pathol 2000, 31, 1242–1248.
7. *Matsui K, Travis WD, Gonzales R et al:* Association of lymphangioleiomyomatosis (LAM) with endosalpingiosis in the retroperitoneal lymph nodes: report of two cases. Int J Surg Pathol 2001, 9, 155–162.
8. *Pallisa E, Sanz P, Roman A et al:* Lymphangioleiomyomatosis: pulmonary and abdominal findings with pathologic correlation. Radiographics 2002, 22 Spec No: S185–198.

Address for correspondence and reprint requests to:
Prof. Janina Słodkowska
Department of Telepathology,
National Institute of Tuberculosis and Lung Diseases,
Ul. Płocka 26
01–138 Warszawa
E-mail: j.slodkowska@igichp.edu.pl