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Case report

A case of pulmonary lymphangioleiomyomatosis complicated with uterine and retroperitoneal tumors

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ABSTRACT

A 39-year-old female experienced dyspnea on exertion for eight months. Chest CT demonstrated findings of Lymphangioleiomyomatosis (LAM), including diffuse thin-walled cystic lesions. A surgical lung biopsy revealed human melanoma black-45-positive cell infiltration and aggregation, resulting in a diagnosis of sporadic LAM without tuberous sclerosis complex. Pelvic MRI showed two large tumors, one of which was in the myometrium and the other was in the retroperitoneal space. Because we were not able to exclude the presence of malignant tumors using MR imaging, the tumors were surgically resected. The histopathology demonstrated the resected tumors to be composed of LAM cells. The patient's symptoms worsened, and sirolimus was administered, which improved the dyspnea and pulmonary function. The adverse effect was mild liver damage. Following the initiation of treatment with sirolimus, transient elevation of the serum KL-6 level was detected without interstitial pneumonia. This LAM case complicated with large uterine and retroperitoneal tumors was successfully treated with surgical resection and sirolimus.

1. Introduction

Lymphangioleiomyomatosis (LAM) is a rare, multiorgan disorder characterized by the proliferation of smooth muscle-like cells (LAM cells) primarily in the lungs and axial lymph nodes [1–6] Sporadic LAM is known to exclusively affect young females of reproductive age, with clinical manifestations such as progressive dyspnea on exertion, recurrent pneumothorax, hemoptysis, chylous pleural effusion and ascites [1,2]. Extrapulmonary involvement, including that of the kidneys and pelvic organs, is a common finding in patients with LAM; however, large uterine tumors are extremely rare. Although there is no conventional treatment, recent progress in research regarding the molecular pathogenesis of LAM has identified *TSC* gene abnormalities [7,8], indicating the participation of the mammalian target of rapamycin (mTOR) signaling pathway in the proliferation of LAM cells [9] and the potential for therapeutic approaches using mTOR inhibition. We experienced a case of sporadic LAM complicated with large uterine and retroperitoneal tumors that were treated with a surgical resection.

2. Case presentation

A 39-year-old Japanese female presented with a complaint of dyspnea on exertion that began eight months previously. Due to worsening of her symptoms, she consulted a general physician five months prior to visiting our department and was diagnosed with bronchial asthma. Inhaled corticosteroids (ICS) and a long-acting beta agonist (LABA) were initially introduced, without any apparent improvements in symptoms. The patient had no past medical history or smoking habits. A physical examination demonstrated no abnormal findings. In the laboratory findings obtained at the first visit, hypergammaglobulinemia and a mildly increased KL-6 level were observed. A blood gas analysis demonstrated hypoxemia (Table 1), and a pulmonary function test showed a moderate obstructive abnormality ($FEV_{1\%}$: 56.6%, $\%FEV_1$: 82.2%) with a reduced diffusing capacity of the lung for carbon monoxide (DL_{CO}) ($\%DL_{CO}$: 41.2%).

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Table 1
Laboratory data.

CBC		Biochemistry		Immunochemistry	
WBC	5300/μl	AST	17 IU/l	CEA	1.4 ng/ml
Neu.	57.9%	ALT	8 IU/l	SCC	1.2 ng/ml
Ly.	34.1%	LDH	186 IU/l	CA125	38 U/ml
Mo.	5.4%	ChE	265 IU/l	CA19-9	<1 U/ml
Eo.	1.9%	T.Bil	0.5 mg/dl	CA15-3	24 U/ml
Ba.	0.7%	ALP	160 IU/l	CA72-4	3 U/ml
RBC	5.14×10^6/μl	γ-GTP	14 IU/l	NSE	11.3 ng/ml
Hb	13.9 g/dl	TP	8.2 g/dl	AFP	8 ng/ml
Ht	42.2%	Alb	4.4 g/dl	KL-6	506 U/ml
Plt	275×10^3/μl	BUN	12 mg/dl		
		Cr	0.78 mg/dl	Blood gas analysis(room air)	
ESR1h	24 mm	Na	139 mmol/l	pH	7.448
PT	100< %	K	3.7 mmol/l	PaO_2	75.2 Torr
APTT	36.1 s	Cl	107 mmol/l	$PaCO_2$	28.1 Torr
Fbg	321 mg/dl	Ca	8.7 mg/dl	HCO_3^-	19.2 mmol/l
		CRP	<0.04 mg/dl	BE	−3.3 mmol/l
				SaO_2	96%

A chest X-ray image revealed bilateral reticular shadows and mild hyperinflation. Chest CT demonstrated diffusely distributed small cystic lesions, reticular opacity and micronodular lesions (Fig. 1A, B). These CT findings were suspicious to be LAM with lymphatic edema; hence, a histopathological evaluation was required to make a precise diagnosis.

A lung biopsy specimen exhibited airspace dilatation with α-smooth muscle actin (αSMA) and human melanoma black (HMB)-45-positive smooth muscle-like cell (LAM cell) infiltration and aggregation. The immunohistochemical examination of the LAM cells was positive for both estrogen and progesterone receptors(ER, PR, respectively) (Fig. 2A–F). No multifocal micronodular pneumocyte hyperplasia (MMPH) lesions were observed in the specimen. Due to the absence of typical manifestations, which is consistent with the diagnostic criteria [10], and absence of family history of tuberous sclerosis complex (TSC), the patient was diagnosed with sporadic LAM.

Transabdominal and transvaginal ultrasound examinations showed a suspected leiomyoma of the uterus, but during systemic surveillance, pelvic MR imaging showed two large tumors with a very strong contrasting effect in the myometrium of the uterine corpus and retroperitoneal space (Fig. 1C–E). The CT of the abdomen shows paraaortic lymphnodes (not shown). There was a low possibility of leiomyoma due to the very strong contrasting effect in the early phase on MR imaging. Hence the proposed differential diagnoses were malignant tumor with hypervascularity and uterine LAM lesion. However, there was no report about large tumor to be composed of LAM cells in the myometrium. We discussed with gynecologists about non-surgical modality of treatments for these lesions, we were not able to exclude the presence of malignant tumors with rapid growing on MR imaging and thus the tumors were surgically resected. Total hysterectomy with bilateral salpingo-oophorectomy (BSO) was performed due to bleeding and tumor adhesion to the pelvic wall.

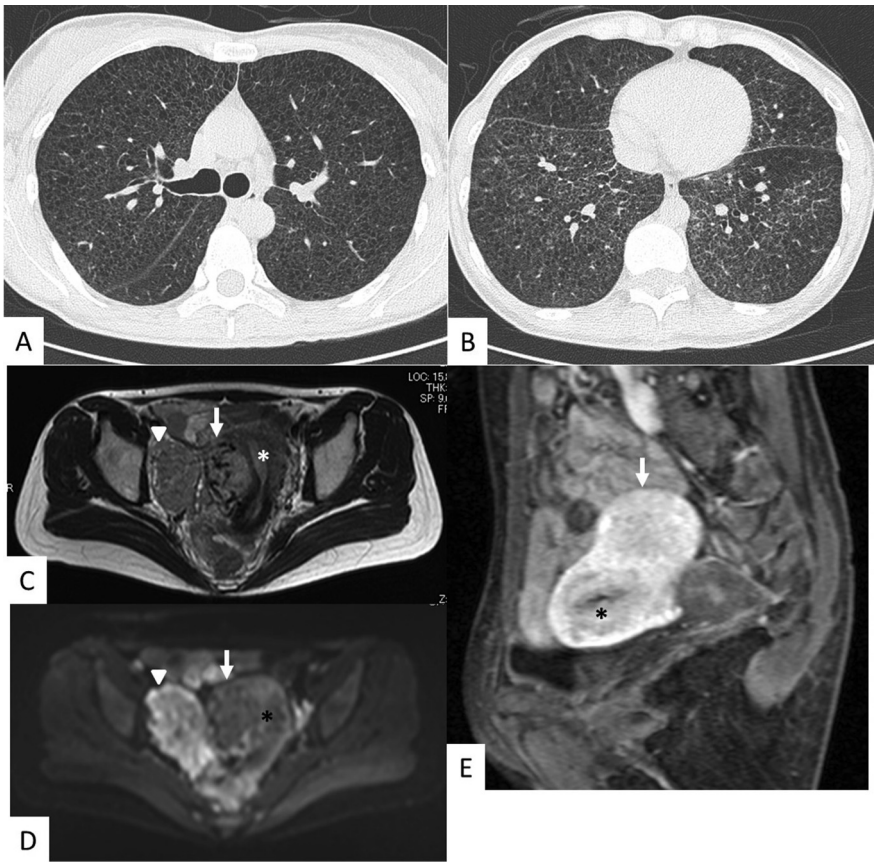

Fig. 1. Chest CT and pelvic MRI. **A and B**. Chest CT demonstrates diffusely distributed small cystic lesions with reticular opacity. **C and D**. T2-weighted (**C**) and diffusion-weighted (**D**) MRI show two large tumors, one of which (*arrow*) is located in the myometrium and the other (*arrowhead*) is located adjacent to the pelvic wall. The diffusion-weighted MRI reveals that the two tumors have different patterns. The retroperitoneal tumor(*arrowhead*) is higher intensity than the uterine tumor. **E**. A sagittal section of pelvic MRI shows a tumor (*arrow*) in the myometrium of the uterus (*asterisk*) with a very strong contrasting effect.