A Young Lady with Severe Dyspnea in Postpartum Period After Long Term Infertility Treatment

Uzun Dönem İnfertilite Tedavisinden Sonra Postpartum Döneminde Ciddi Dispne ile Başvuran Genç Kadın Hasta

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ABSTRACT

Lymphangioleiomyomatosis (LAM) is a disease that predominantly affects young females and generally progresses to respiratory failure and death. A 33-year-old postpartum woman was admitted with progressive dyspnea and high CA-125 levels. She had bilateral chylopneumothorax, chylous ascites and was diagnosed as LAM by open lung biopsy. Her management was very complex as her chylous ascites and pleural effusions were very resistant to therapy. Betadine pleurodesis was very successful in the management of chylothorax. There were no LAM cases presenting with high CA-125 levels. We believe that CA-125 levels could be used as a useful parameter in patient follow-up. *(Tur Toraks Der 2011; 12: 127-30)*

Key words: Lymphangioleiomyomatosis, pleurodesis, betadine, CA-125

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ÖZET

Lenfanjioleimyomatozis (LAM) çoğunlukla genç kadınları etkileyen, genellikle solunum yetmezliği ve ölüme ilerleyebilen bir tablodur. 33 yaşında postpartum periyodda kadın hasta ilerleyici nefes darlığı ve yüksek CA-125 seviyeleri ile başvurdu. Hastada bilateral şilopnömotoraks, şilöz asit mevcut idi ve açık akciğer biyopsisi ile LAM tanısı aldı. Hastanın takibi oldukça karmaşıktı ve şilöz asit ve plevral efüzyonlar tedaviye çok dirençliydi. Betadin plörodezisi şilotoraksların tedavisinde oldukça başarılı oldu. Literatürde yüksek CA-125 seviyeleri ile başvuran LAM vakası sunulmamıştır. Takipte CA-125 seviyelerinin yararlı bir parametre olabileceğini düşünmekteyiz. *(Tur Toraks Der 2011; 12: 127-30)*

Anahtar sözcükler: Lenfanjioleyiomyomatozis, plörodezi, betadin, CA-125

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CASE

A 33-year-old chemistry teacher was referred in December 2006 with a one month history of progressive breathlessness in the last trimester of her first pregnancy. She had a history of intense hormonal therapy for infertility for the previous six years and she gave birth to twins after invitro fertilization by cesarian section one day earlier.

Physical examination showed orthopnea, tachypnea, tachycardia, dullness and diminished breath sounds in both hemithoraxes. There was no fever, cyanosis or clubbing.

Her arterial blood gas analysis in room air was pH: 7.47, PCO_2: 30 mmHg, PO_2: 50 mmHg and $SatO_2$: 80%. Biochemical tests showed only two abnormal results: high triglycerides (760 mg/dl) and Ca-125 (250U/ml) in her serum which was otherwise normal.

Radiologic examination revealed a left-sided hydropneumothorax and right sided hydrothorax. HRCT scan of the chest showed diffuse bilateral thin walled microcysts in the lung parenchyma (Figure 1). Abdominal CT revealed multiple paraaortic lymhadenopathies and massive peritoneal fluid.

We inserted bilateral chest tubes immediately and air with white opaque fluid drained from both sites at an average of 800 cc per day for each site. High triglyceride, low cholesterol level, cholesterol/triglyceride ratio<1 were detected in both pleural fluid and peritoneal fluid and total parenteral nutrition was started. After 14 days, as the chylous drainage continued in the same degree, we performed thoracic duct ligation and open lung biopsy with right thoracotomy (Figure 2).

Pathologic examination confirmed the diagnosis of lymphangioleiomyomatosis (LAM) (Figure 3).

Bilateral chylous drainage had persisted in large amounts from the chest tubes although we continued total parentheral nutrition (TPN). We then decided to

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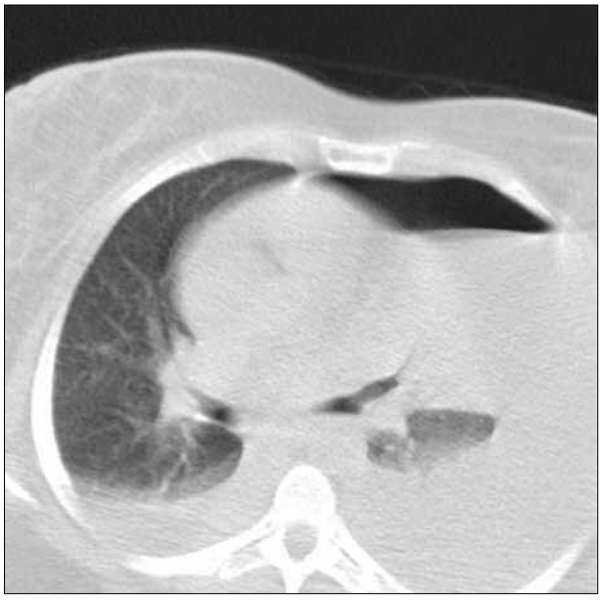

Figure 1. Posteroanterior chest radiography of the patient showing left-sided hydropneumothorax and right sided hydrothorax

Figure 2. Thoracic duct ligation and open lung biopsy with right thoracotomy

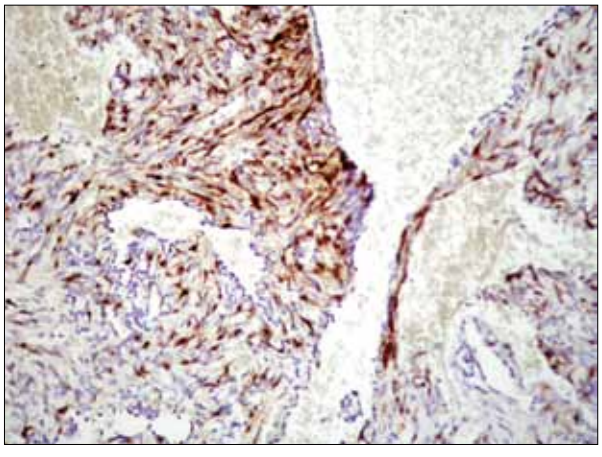

Figure 3. Pathologic examination of lung biopsy. Immunohistochemical stains for HMB-45 highlight the LAM cells. Appropriate original magnification X 400

perform right thoracotomy for thoracic duct ligation and to obtain a lung biopsy (Table 1). Thoracic duct ligation eliminated the left chylothorax but right chylothorax persisted. Firstly talc pleurodesis was tried but unfortunately this was unsuccessful. A good pleurodesis was followed by betadine.

We started an octreotide infusion at 2 mg/kg/hour and planned to give this for 5 days as suggested in the literature when chylous ascites was over 10 liters. Two days later, the dose was increased to 4 mg/kg/hour. The chylous drainage gradually diminished from day 2 to day 5 of octreotide infusion. Her chylous ascites persisted in a minimal amount.

In the second month of her hospitalization she was diagnosed as acute pulmonary embolism with spiral tomography of thorax. Her anticoagulation therapy was ended at 6 months as her congenital thrombophilic markers were found negative.

While CA-125 levels were very high (250 U/ml) on admission, it decreased to normal limits (0-35 U/ml) with therapy.

She is still in follow-up for 2.5 years with medical therapy with GnRH analogue. She has mild exertional dyspnea and we performed high resolution computerised tomography (HRCT) of the lungs, pulmonary function tests (PFT), diffusion capacity of lungs (DLCO) and abdominal USG at her clinical visits. Pneumothoraxand chylothorax did not rcurt, and minimal abdominal chylous ascites persisted, her last DLCO showed a moderate decrement. She is now clinically stable and working as a chemistry teacher.

DISCUSSION

LAM is a disease that predominantly affects young females and generally progresses to respiratory failure and death. The clinical features result from progressive cystic destruction of the lungs and the accumulation of LAM cells within the lungs and axial lymphatics. The disease tends to present between the menarche and the menopause, with the mean age of onset being 34 yrs. Occasionally, post-menopausal females will present with the disease; however, these patients are often receiving oestrogen replacement therapy. The disease is rare (termed sporadic LAM) with a prevalence of 1 in 1,000,000 population [1,2].

The pulmonary symptoms tend to dominate the clinical course, with the most common features being pneumothorax, progressive dyspnoea and chylous pleural effusions [2-4].

Chylothorax may contribute to symptomatic dyspnoea in LAM and occurs by one of three mechanisms: 1) obstruction of the thoracic duct and its tributaries; 2) leakage from pleural lymphatics; and 3) transdiaphragmatic flow from chylous ascites. Treatment is aimed at obliterating the pleural space to prevent lymphatic accumulation, or ligation of the thoracic duct. The natural history of chylous collections is variable; while some will

Table 1. Clinical progress of the patient

Date	Problem	Treatment	Result
08.12.2006	Infertility	Six year intense hormonal therapy+*in vitro* fertilization	Gave birth with cesario section
09.12.2006	L hydropneumothorax	Chest tube	Air and chylous leakage
01.12.2006	R hydropneumothorax	Chest tube	Chylous drainage
	High amount chy	14 days TPN	No response
22.12.2006	Sustained bilateral chy	R thoracotomy (Ductus thorasicus lig+Open lung biopsy)	L chylothorax succesful, R chylothorax no response
31.12.2006	R hydropneumothorax	Talc pleurodesis	Failure for chy, successful for px
02.01.2007	R chylothorax	Betadine pleurodesis	Successful
16.01.2007	Chylous ascites	Drainage (10 liter)	Failure
	Sustained chylous ascites	Somatostatin infusion (4mg/kg iv for 5 days)	Successful
17.01.2007	Pulmonary embolism	Anticoagulation	Successful
30.04.2007	L pneumothorax	Betadine pleurodesis	Successful

R: right, L: left, chy: chylous effusion, lig: ligation, px: pneumothorax, İv: intravenous, TPN: total parenteral nutrition

have small persisting effusions that require no treatment, for moderate or large effusions associated with dyspnoea, treatment is required. In most cases, simple aspiration or chest tube drainage results in re-accumulation in a short time. Patients with persisting effusions after aspiration have been successfully treated by pleurodesis, pleurectomy and, in some cases, thoracic duct ligation. Early experience with thoracic duct ligation was poor; however, this now appears to be a relatively safe procedure in patients with LAM [5].

Ooopherectomy is generally performed for LAM, and gonadotrophin-releasing hormone agonists can produce the same reduction in oestrogen levels as ovarian ablation; however, evidence for their use is restricted to case reports [6].

In the literature, a case report about exacerbation of pulmonary LAM by exogenous oestrogen used for infertility treatment was reported earlier [5,7]. The presence of LAM should be considered before initiating infertility treatment.

Although we know that talc pleurodesis is very effective, in this case betadine (povidone-iodine) produced good results in pleurodesis [8,9]. We consider that betadine, a very acidic agent, could have destroyed lipid particles in the chylothorax.

While CA-125 levels were very high (250 U/ml) on admission, it decreased to normal limits (0-35 U/ml) with therapy. Zahner et al. reported that CA-125 could be a suitable screening parameter for LAM, which might additionally be of prognostic value, and he recommended further studies for sensitivity and specificity of CA-125 [10]. We did not find any LAM case presenting with high CA-125 levels. In our case, while CA-levels continued high, it decreased to normal limits when the patient was in a stable clinical condition. We believe that CA-125 levels could be used as a useful parameter in follow-up.

As is clearly seen from our patient's progress table above, diagnosis and management of LAM cases could be a very chaotic process and it often requires emergency decisions and an efficient team to cope with this disease.

In this new millennium, great progress has been achieved for infertility problems and women have a tendency to give birth to their first babies in their late thirties or even forties. However, these intense therapies could produce some hormone-related pathologies in women. For this reason, both gynecologists and pulmonary physicians should be aware of such problems in these patients.

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