CEOG Clinical and Experimental Obstetrics & Gynecology

Case Report

Pulmonary lymphangioleiomyomatosis as an uncommon cause of recurrent early pregnancy loss

E.H. Comert, H. Sal, E.S. Guvendag Guven, S. Guven

Department of Obstetrics and Gynecology, School of Medicine, Karadeniz Technical University, Trabzon (Turkey)

Summary

Pulmonary lymphangioleimyomatosis (LAM) is a rare disorder characterized by hamartomatous proliferation of smooth muscle within lung parenchyma. LAM occurs only in women and exacerbates with menstruation, estrogen use, and taking oral contraceptives. The effect of pulmonary LAM on recurrent pregnancy loss has not been reported previously. A 28-years-old (gravida 2 parity 0 abortion 2) woman was admitted to the gynecology outpatient clinic because of habitual abortion. The patient had a history of early (one 8-week and another 6-week) pregnancy losses. CT scan showed widespread and varied dimension thin edge cystic lesions extending to about 1 cm in diameter of the largest size observed in all segments of both lungs. All other recurrent pregnancy loss tests were within normal limits, except pulmonary LAM findings on CT scan. Clinicians should keep in mind the diagnosis of pulmonary LAM, in cases with progressive dyspnea (especially in luteal phase of menstruation) and recurrent pregnancy losses.

Key words: Fibronectin; Habitual abortion; Invasion; Pulmonary lymphangioleiomyomatosis.

Introduction

Lymphangioleimyomatosis (LAM) is a rare disorder characterized by hamartomatous proliferation of smooth muscle within lung parenchyma and/or extra pulmonary lymphatic structures above and below the diaphragm. The incidence and prevalence of pulmonary LAM are unknown. LAM occurs only in women, usually of childbearing age, and has been observed to be rapidly progressive during pregnancy [1]. Also exacerbations of LAM have been reported menstruation, with estrogen use, and while taking oral contraceptives. During the course of disease, the most common manifestations include dyspnea, pneumothorax, and cough. Less common clinical features include chest pain, hemoptysis, chylothorax, lymphedema, and ascites [2]. The effect of pulmonary LAM on recurrent pregnancy loss has not been reported previously. In this report, the authors present a case of LAM with habitual abortion.

Case Report

A 28-years-old (gravida 2 parity 0 abortion 2) woman was admitted to the gynecology outpatient clinic because of habitual abortion. The patient had the history of early (one 8-week and another 6-week) pregnancy losses. She had progressive symptoms such as cough and dyspnea since childhood. The woman did not have any symptoms and clinical signs, except increasing dyspnea especially during menstruation. CT scan showed widespread and varied dimension thin edge cystic lesions extending to about 1 cm in diameter of the largest size observed in all segments of both lungs (Figure 1). Opacities of frosted glass was monitored in the lung parenchyma between cystic lesions, this was monitored diffusely in the entire lung parenchyma.

The authors focused on pulmonary LAM because of CT scan reports and clinical signs. The pathologic evaluation of lung biopsy and pulmonary function tests confirmed the diagnosis. Muscle focus and a few muscle cells on the wall of vessel were determined in lung biopsy specimen. They appeared as leiomy-

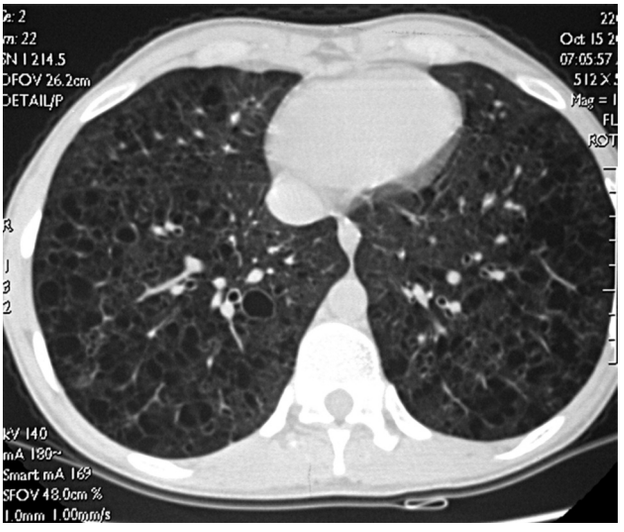

Figure 1. — Widespread varied dimension thin edge cystic lesions extending to about 1 cm in diameter of the largest size observed in all segments of both lungs.

Revised manuscript accepted for publication July 25, 2018

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLVI, n. 5, 2019
doi: 10.12891/ceog4808.2019

7847050 Canada Inc.
www.irog.net

Published: 10 October 2019

oma-like clusters.

Karyotypes on both partners, hysterosalpingogram, blood tests for PRL, TSH, fasting glucose, midluteal P, tests of lupus anticoagulant activity (dilute Russell viper venom test and partial thromboplastin time-Lupus anticoagulant (PTT-LA), IgG and IgM anticardiolipin and antiphosphatidyl serine antibodies, and cervical cultures for Chlamydia, Mycoplasma, and Ureaplasma, a thrombophilic workup (protein C activity, protein S activity, antithrombin activity, activated protein C resistance, factor V Leiden mutation, factor II mutation, and fasting homocysteine), and sperm analysis were within the normal limits.

Discussion

LAM is a rare disease of unknown etiology that affects women only and nearly presents before menopause. It mainly affects the lungs where smooth muscle proliferation surrounds the lymphatics, small airways, and blood vessels causing progressive dyspnea, hemoptysis, pneumothorax, and chylous pleural effusions [3].

LAM is under the influence of ovarian hormones such as uterine fibroids, but this subject is open to discussion. There is evidence that the course of LAM is influenced by estrogens and progesterone. Pregnancy, menstruation, and the use of oral contraceptives and gonadotrophins can cause progression of the disease, where as menopause often leads to stabilization and improves prognosis [4]. The presence of intermediate elements such as cytokines and growth hormone are on the agenda, and these control stimulating effect of fibroids growth by ovarian hormones [5]. As in the present case, clinical symptoms increased such as dyspnea when the rise levels of estrogen and progesterone (especially menstrual luteal phase). Basically, fibroids are composed of smooth muscle such as myometrium. Mitotic activity of fibroids is greater than mitotic activity of myometrium. Mitotic activity of fibroids increases in luteal phase and remains high until menstruation [6]. This case demonstrated the importance of progesterone in cellular proliferation of fibroids.

Leiomyomas contain dense connective tissue components and extracellular matrix (ECM). Collagen, fibronectin, and glycosaminoglycan clearly participated in the formation and growth of the tumor volume. Cytotrophoblast binds to receptors on the fibronectin via integrins and it can cause retardation of invasion in pregnancy [7]. Fibronection which was secreted by pulmonary LAM cells could lead to a reduction of invasion in trophoblast cells and recurrent abortion.

The present authors believe that pulmonary LAM may be accepted as a novel cause of recurrent early pregnancy losses. Pregnancy-induced high serum level of estrogen and progesterone may stimulate the activity of pulmonary LAM cells, just like uterine myoma. Stimulated pulmonary LAM cells may increase the levels of ECM components such as fibronectin, collagen, and integrins in systemic circulation. The high serum level of ECM components may interfere with trophoblast invasion. Finally this pathophysiologic process may lead to early pregnancy loss.

Clinicians should keep in mind the diagnosis of pulmonary LAM, in cases with progressive dyspnea (especially in luteal phase of menstruation) and recurrent pregnancy losses.

References

[1] Yockey C.C., Riepe R.E. Ryan K.: "Pulmonary lymphagioleiomyomatosis complicated by pregnancy". *Kans. Med.*, 1986, *87*, 277.

[2] Taylor J.R., Ryu J., Colby T.V., Raffin T.A.: "Lymphangioleiomyomatosis. Clinical course in 32 patients". *N. Engl. J. Med.*, 1990, *323*, 1254.

[3] Johnson S.: "Rare diseases. 1. Lymphangioleiomyomatosis: clinical features, management and basic mechanisms". *Thorax*, 1999, *54*, 254.

[4] Silverstein E.F., Ellis K., Wolff M., Jaretzki A., 3rd.: "Pulmonary lymphangiomyomatosis". *Am. J. Roentgenol. Radium. Ther. Nucl. Med.*, 1974, *120*, 832.

[5] Chen W., Yoshida S., Ohara N., Matsuo H., Morizane M., Maruo T.: "Gonadotropin-releasing hormone antagonist cetrorelix down-regulates proliferating cell nuclear antigen and epidermal growth factor expression and up-regulates apoptosis in association with enhanced poly(adenosine 5'-diphosphate-ribose) polymerase expression in cultured human leiomyoma cells". *J. Clin. Endocrinol. Metab.*, 2005, *90*, 884.

[6] Kawaguchi K., Fujii S., Konishi I., Nanbu Y., Nonogaki H., Mori T.: "Mitotic activity in uterine leiomyomas during the menstrual cycle". *Am. J. Obstet. Gynecol.*, 1989, *160*, 637.

[7] Damsky C.H., Librach C., Lim K.H., Fitzgerald M.L., Mcmaster M.T., Janatpour M., et al.: "Integrin switching regulates normal trophoblast invasion". *Development*, 1994, *120*, 3657.

Corresponding Author:
S. GUVEN, M.D.
Department of Obstetrics and Gynecology
School of Medicine, Karadeniz Technical University
61080, Trabzon (Turkey)
e-mail: drsuleymanguven@yahoo.com