

## Benign metastasizing leiomyomas in the lungs: a case study

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### Abstract

Benign metastasizing leiomyoma (BML) is a rare disease that occurs in middle-aged women with a history of uterine myomas. The most common location of BML is the lungs.

We report the case of a 44-year-old obese woman (BMI 45.5) who underwent surgery to remove uterine leiomyomata and then continued to take a drug containing the hormone estradiol for a period of 15 years. Computed tomography chest examinations revealed multiple size nodules of varying size in both lungs. Videothoracoscopy and right thoracotomy was performed, and a few nodules were enucleated from each lobe of the right lung. Postoperative histopathological examination revealed benign metastasizing leiomyoma staining positive for estrogen and progesterone receptors (ER+, PR+). Because of the hormonally dependent cell proliferation, the previously used hormonal drug was discontinued. Treatment with a gonadotropin-releasing hormone analog was included, yielding radiological stabilization of the lung lesions.

**Key words:** BML, benign metastasizing leiomyoma, uterine myomas.

### Introduction

Benign metastasizing leiomyomas develop in middle-aged women with a history of uterine myomas. This rare condition was first described by Steiner in 1939 [1-5] despite the universal belief of the time that benign neoplastic tumors do not metastasize.

Lungs are the most common location of uterine myoma metastasis, but other locations have also been described in this context, including the mediastinum, heart, trachea, esophagus, skin, skeletal muscles, deep soft tissue, breasts, liver, urinary bladder, retroperitoneal space, nervous system, and bones [1, 4-6].

### Case report

The patient, a 44-year-old non-smoking woman with obesity (weight: 115 kg, BMI: 45.5) was admitted to the hos-

### Streszczenie

*Benign metastasizing leiomyoma* (BML) to rzadka choroba występująca u kobiet w wieku średnim, które chorowały lub chorują na mięśniaki macicy. Najczęstszą lokalizacją łagodnych przerzutowych mięśniaków (BML) są płuca.

W pracy zaprezentowano przypadek 44-letniej otyłej kobiety (BMI 45,5), która przeżyła operację usunięcia mięśniaków macicy, a następnie przez 15 lat stosowała lek hormonalny zawierający estradiol. W badaniu tomografii komputerowej klatki piersiowej rozpoznano bardzo liczne guzki różnej wielkości w obu płucach. Wykonano wideotorakoskopię, a następnie torakotomię prawą i wyłuszczone po kilka guzków z każdego płata płuca prawego. W badaniu histologicznym rozpoznano łagodne przerzutowe mięśniaki z dodatnią ekspresją receptorów ER(+) i PR(+). Z uwagi na ich hormonalnie zależny rozrost odstawiono dotychczas stosowany lek hormonalny i włączono leczenie analogiem naturalnego hormonu – gonadoliberyny, uzyskując stabilizację radiologiczną zmian w płucach.

**Słowa kluczowe:** BML, łagodne przerzutowe mięśniaki, mięśniaki macicy.

pital due to numerous round shadows in both lungs, revealed incidentally during a control radiological examination. The patient did not report any ailments.

Her medical history included gynecological surgery to remove uterine myomas 13 years earlier. At that time, her gynecologist recommended to her the contraceptive Cilest (0.25 mg norgestimate and 0.035 mg ethinylestradiol), which she continued to take without interruption. Her medical history also featured an appendectomy, a bilateral procedure for carpal tunnel syndrome, and arterial hypertension treated with Ramipril (1 x 5 mg) and Metoprolol (1 x 50 mg).

The patient was the mother of 3 healthy children. Her first period occurred at the age of 11. The periods were regular: every 28 days for 4 days. Before the uterine myoma surgery, the periods had been very profuse.

Physical examination revealed bradycardia (approx. 52 bpm), arterial pressure: 140/90, onychomycosis affect-

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ing the toenails (during topical treatment), and postoperative scars on the hypogastrium.

Laboratory tests demonstrated that the level of alanine aminotransferase (ALAT) was increased to 89.5 IU/l.

Chest X-ray and computed tomography (CT) visualized numerous (several dozen) well-defined round shadows of varying diameter (2-32 mm) in both lung fields, enhanced after the addition of contrast (Fig. 1). No comparisons could be made with previous X-ray photographs, as the patient had not been examined radiologically for the previous 26 years.

The results of respiratory function tests (arterial blood gas, spirometry) were normal. The patient did not consent to bronchofiberscopy.

She was qualified for right-sided videothoracoscopy; during the procedure, a marginal resection of a fragment of the right lung's lower lobe with a grey-white nodule (7 mm in diameter) was performed.

The ensuing pathomorphological investigation identified the tumor as an adenomyoma, which was confirmed by immunohistochemical tests. Proliferation index Ki-67 was positive in approx. 1% of cells. Actin (+), desmin (+), S-100 (-), and TTF-1 (+) were also labelled. Furthermore, positive expression of estrogen and progesterone receptors was detected: ER (+), PR (+).

The patient did not report for a control examination scheduled at the Thoracic Surgery Clinic; after 2 years, she was referred to the hospital by a pulmonologist in order to undergo invasive diagnostics and possibly treatment of suspected metastatic lesions in the lungs.

Right-sided thoracotomy was performed, and several solid nodules (8-25 mm in diameter) were enucleated from each lobe of the right lung. The postoperative course was uneventful. The result of pathomorphological investigation, benign metastasizing leiomyoma, was supplemented with a repeated analysis of samples from the uterine myomas

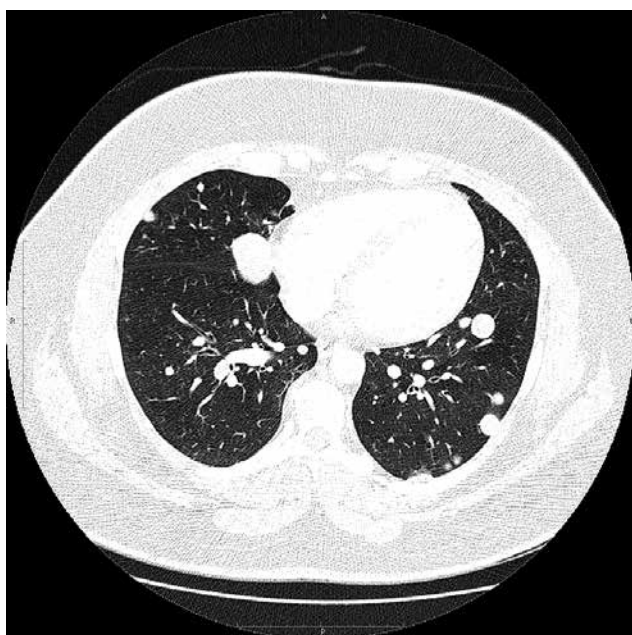


Fig. 1. Tomography of the chest (axial view). Tumors in both lungs

removed 15 years earlier. The control pathomorphological analysis confirmed the previous diagnosis: *leiomyoma cellulare*, mitotic index: MI 3/10 HPF, positive Ki-67 proliferation index in approx. 1% of cells, presence of estrogen receptors (+) and progesterone receptors (+++).

After a gynecological consultation, the contraceptive Cilest, which the patient had been taking for the past 15 years, was discontinued; the patient had her last period during the next month.

She was qualified by an oncologist for treatment with a gonadotropin-releasing hormone (GnRH) analog – Diphereline (Triptorelin). Chest CT images obtained after 3 and 6 months showed that the nodular lesions remained stable. The patient was offered hysterectomy and adnexectomy, but she is yet to make a final decision.

## Discussion

Benign metastasizing leiomyomas are most often diagnosed in women between the ages of 34 and 55 years; the mean age of diagnosis is approx. 47 years [1, 2, 4-6].

The disease may be asymptomatic and diagnosed by chance during an imaging examination. It may also cause symptoms such as cough, dyspnea, and pain. Benign metastasizing leiomyomas most often manifest after hysterectomy with myomectomy or myomectomy alone. According to different reports, the time between the gynecological procedure and BML manifestation may vary from 3 months to 26 years [1, 4-7]. Cases of concurrent manifestation of lesions in the uterus and the lungs have been described, as well as cases in which lung metastases were diagnosed before the uterine tumors [2, 6].

In the case of our 44-year-old patient, the lung lesions were found 13 years after uterine myomectomy. The actual time at which the lung lesions developed is unknown, as no radiograms of the patient's chest had been made for 26 years.

The morphological and histochemical properties of the patient's uterine myomas were similar to those of the lung tumors (Ki-67 approx. 1%, ER+, PR+). According to the literature, the low Ki-67 proliferation index in the removed lung tumors and uterine myomas confirmed the benign character of the lesions [1, 3, 8].

The pathogenesis of the disease is uncertain, but several hypotheses can be postulated. Benign metastasizing leiomyomas are believed to develop when smooth muscle cells are transported through the circulation system from benign uterine myomas to the lungs. This process may be induced by tissue trauma sustained during myomectomy or hysterectomy [1, 3, 6, 7]. Some authors believe that these are cases of leiomyosarcomas of low malignancy grade [3, 6, 8, 9], while others maintain that BMLs represent primary lung lesions that are concomitant with, but independent of uterine myomas, resulting from hormone action [3, 8, 9].

Detailed cytogenetic and molecular studies on BML have demonstrated that telomere length is not a decisive factor in the development of the disease [3]. The studies also revealed specific anomalies regarding both the num-

ber of chromosomes (trisomy 12) and their structure (translocation, aberration 19q, deletion 22q) [5, 8].

Currently, BMLs are considered to develop as a result of monoclonal spread of uterine myomas through the circulatory system [1, 3, 5, 7, 8]. Detecting the miR-221 marker may be helpful in differentiating myomas from sarcomas [5, 8].

Benign metastatic myomas usually exhibit a positive expression of estrogen and progesterone receptors, which is associated with their hormonally dependent growth and spontaneous regression during pregnancy or menopause [1, 6, 7, 9]. Independent growth of peripheral myomas may be stimulated by high levels of estrogens, as is the case with lymphangiomyomatosis (LAM) [6, 10]. An additional factor influencing the levels of sex hormones in the described patient was her uninterrupted 15-year use of Cilest, a contraceptive agent containing estradiol. The numerous contraindications for estrogen therapy include the presence of uterine myomas, as their further growth can be attributed to the pathogenic action of estrogens.

Another factor influencing the levels of sex hormones in our patient was her obesity, as fat tissue is one of the locations where extra-ovarian conversion of androstenedione to estrone (E1) occurs with the participation of the aromatase enzyme system [2, 10].

Treatment methods for BML include pharmacological or surgical oophorectomy and anti-estrogen therapy with estrogen receptor blockers or aromatase inhibitors [1, 2, 4, 7, 10]. Another pharmacological treatment consists in the use of a GnRH analog in order to inhibit the secretion of gonadotropic hormones, reduce the sensitivity of peripheral receptors to GnRH, and, consequently, inhibit gonadal function and reduce the level of estrogens [1, 2, 4, 7, 9]. Such was the treatment that was employed in the discussed patient.

## Conclusions

Uterine myomas may result in peripheral metastases despite their benign character. Like LAM, BML may be stimulated by high estrogen levels. The increased risk factors include premenopausal age, previous gynecological surgery due to uterine myomas, obesity, and hormone therapy.

## Disclosure

Authors report no conflict of interest.

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