

BENIGN METASTASIZING LEIOMYOMA. REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Abstract

Benign metastasizing leiomyoma (BML) is defined as a histologically benign uterine smooth muscle tumor that acts in a somewhat malignant fashion and produces benign metastases. Here we present a case of a 42 years old female who had a 730 gr. uterine leiomyoma at the age of 26. Six years later she underwent, again, myomectomy. Several leiomyomata, with the total weight of 230 gr. were excised. At the age of 39, multiple lung metastases were found, one large lymph node in the pelvis and a 2.5 cm diameter tumor in the right rectal fossa. All these tumors resulted as benign leiomyomata. At the age of 40 she underwent hysterectomy. Multiple leiomyomata were found. In 2009, one year after the hysterectomy a 5 mm nodule was found in her left breast along with another nodule in her left chest wall. Needle biopsy from the breast lesion showed benign leiomyoma, identical to those in the uterus. So we concluded that this is a case of BML with breast metastases and the 2nd

case reported in the medical literature. The patient was treated with hormone therapy. To day, she is alive and well with no new metastases to the best of our knowledge.

Introduction

Uterine smooth-muscle tumors with unusual growth patterns are rare and include a variety of neoplastic lesions characterized histologically by their similarity to adult smooth-muscle tissue. They include 3 primary neoplasms: intravenous leiomyomatosis (IVL), benign metastasizing leiomyoma (BML), and leiomyomatosis peritonealis disseminata (LPD) [1]. Benign metastasizing leiomyomatosis (BML) is a rare disease in which the lung is the most affected extra-uterine organ. It is a benign spindle cell lesion affecting women who have undergone hysterectomy for uterine leiomyomata in young adulthood, and subsequently present pulmonary metastases during the peri-menopausal period. The BML histology is compatible with benignity and similar to the

smooth muscle cells found in a uterine fibroid [2]. The nature of benign metastasizing leiomyoma has been debated since it was first reported in the English literature in 1939 [3]. The original hypothesis was that BML is a benign leiomyoma colonizing the lung [4] while others argued that it may represent primary pulmonary leiomyomatosis coexisting with a uterine leiomyoma.

We present a review of the recent literature along with the clinical and pathologic features of one case from Hasharon Hospital, Rabin Medical Center, Petah-Tikva, Israel.

Case report

41 years old, Caucasian female underwent left needle biopsy for a nodule in her left breast.

Her past medical history revealed myomectomy in 1995, at the age 26. The tumor

weighed 730 gr. and the histological diagnosis was leiomyoma, not otherwise specified (NOS). At the age of 32, in 2000 she underwent again myomectomy for multiple leiomyomata of the uterus. The histopathological diagnosis was leiomyomata with 1-2 mitoses/10 HPF. On CT scan (Fig. 1), at the age of 39 (2008), multiple metastases were found in the right lower lobe of the lung up to 0.7 cm in diameter.

Severe enlargement of lymph nodes in the pelvis was found and a 2.5 cm diameter tumor was found in the right ischio-rectal fossa. Needle biopsy of the pelvic nodules revealed leiomyoma with low mitotic count. At the age of 39, (2008) she was underwent total hysterectomy. Multiple leiomyomata were found with the total size of 11x11x4 cm. Histopathologically all were leiomyomata with 1 mitosis/10 HPF. Right groin



Figure 1. CT-lungs. Nodules in lung parenchyma (CT pulmonar. Noduli în parenchimul pulmonar)

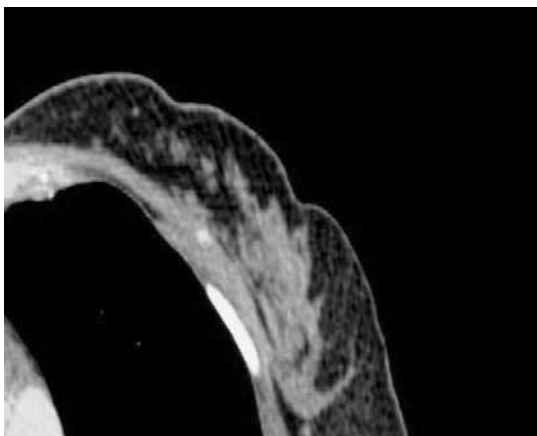


Figure 2. CT-Chest wall mass (CT-masă în peretele toracic)

Figure 3. US breast mass (ecografie-masă mamară)

myomectomy revealed tumors 15x9x7.5 cm in dimension. The histopathological diagnosis was leiomyomata with 1mitoses/10 HPF.

On a routine, follow up CT in 2009, the lung nodules showed no change. A 0.3 cm nodule was found in her left chest wall (Fig. 2) and a 0.5 cm nodule in her left breast (Fig. 3).

The patient underwent tru-cut biopsy of the left breast. In the tru cut biopsy a fragment of breast tissue was seen and fragments of soft tissue (Fig. 4 H&E X40), which were composed of spindle cells with elongated nuclei, arranged in intersecting fascicles separated by hyalinized stroma. There was no nuclear pleomorphism, areas of necrosis or hemorrhage. Mitoses was only 1-2 per 10 high power fields (HPF).

On comparative examination of the breast biopsy (2009) and specimens from the

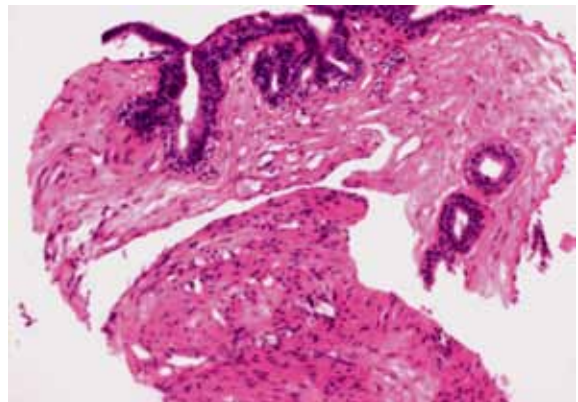


Figure 4. Breast Tru-cut biopsy H&E X40 (Biopsie mamară tru-cut H&E X40)

myomectomy (2000) similar elongated smooth muscle cells were seen without significant nuclear pleomorphism or coagulative necrosis in both of cases (Fig. 5, Fig. 6).

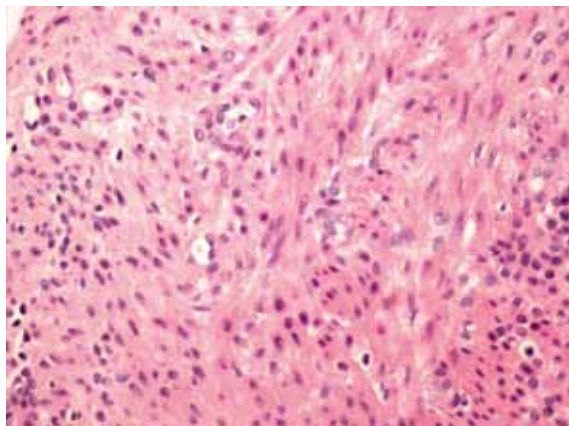


Figure 5A. Breast needle biopsy H&E X20 (2009) (Biopsie mamară cu ac)

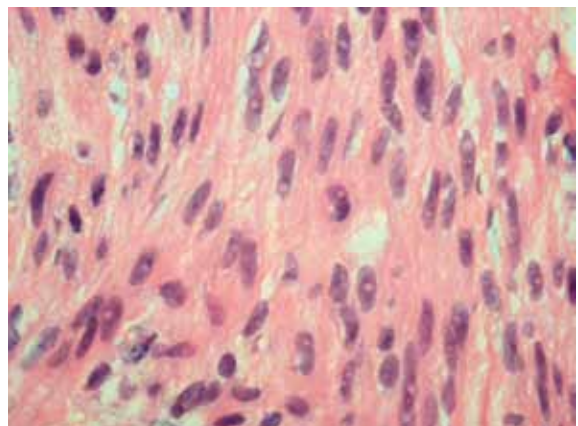


Figure 5B. Breast biopsy X40 (Biopsie mamară)

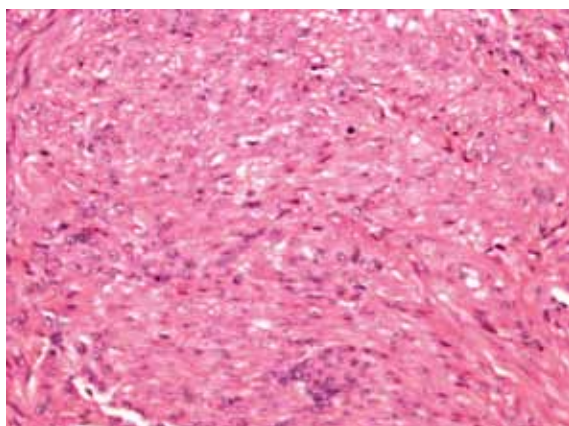


Figure 6A. Uterus-myomectomy H&E X20 (2000) (Miomectomie uterină)

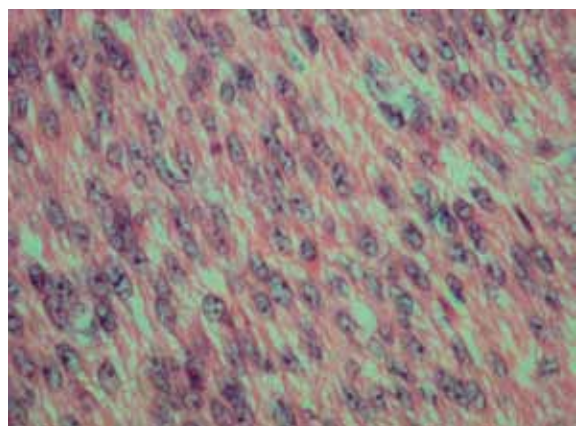


Figure 6 B. Uterus X40 (Uter)

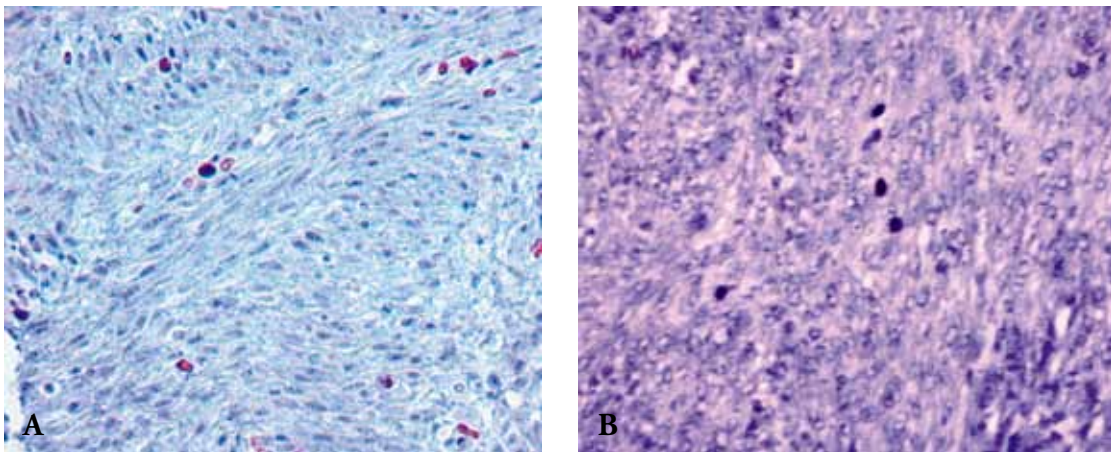


Figure 7. Immunohistochemical staining for Ki-67 X20, A. Breast biopsy (2009), B. Uterus Myomectomy (2000) [Colorație imunohistochimică pentru Ki-67 X20, A Biopsie mamară (2009), B. Uter. Miomectomie (2000)]

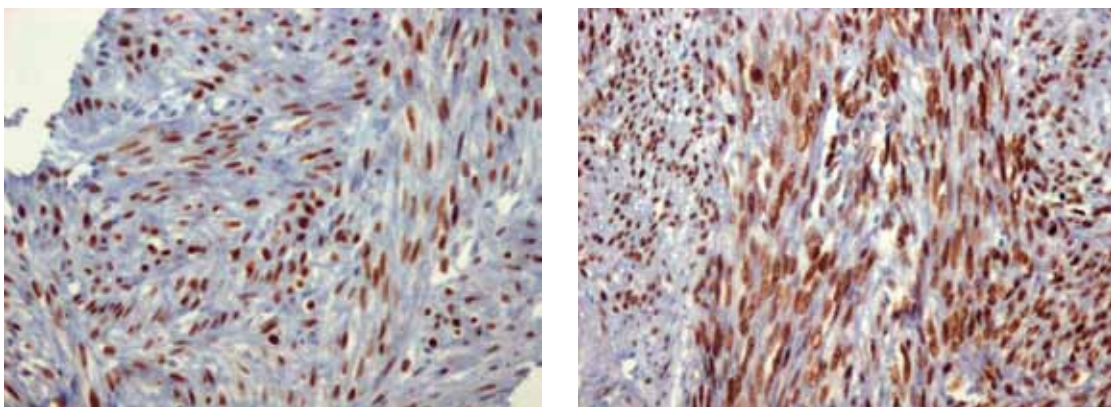


Figure 8. Immunohistochemical staining for Estrogen Receptor, A. Breast biopsy (2009) B. Uterus (2000) [Colorare imunohistochimică pentru receptori estrogenici, A. Biopsie mamară (2009) B. Uter (2000)]

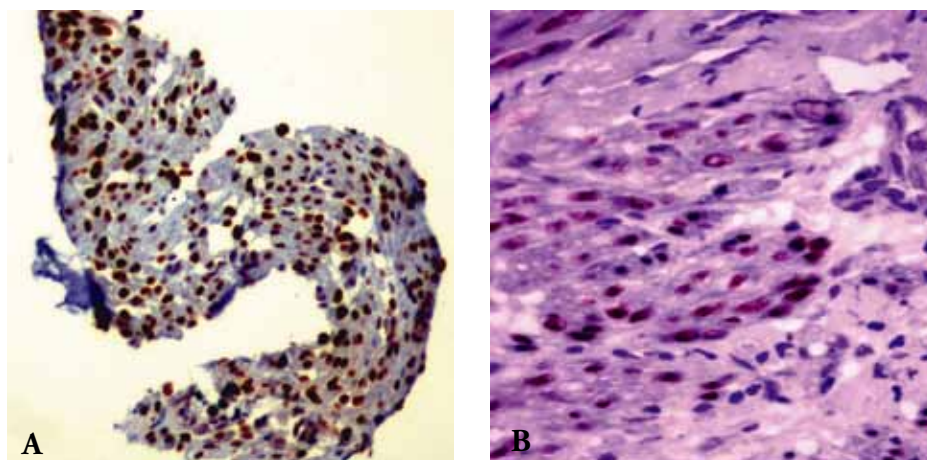


Figure 9. Immunohistochemical staining for Progesteron Receptor, A. Breast needle biopsy (2009) B. Uterus Myomectomy (2000) [Colorare imunohistochimică pentru receptori de progesteron, A. Biopsie mamară cu ac (2009) B. Miomectomie uterină (2000)]

Immunohistochemistry revealed that the tumor cells were diffusely positive for desmin and smooth muscle actin. Proliferative marker (Ki-67) was positive in 2% of the tumor cells in both breast and uterus.

Immunohistochemical staining for estrogen and progesterone receptors revealed strong positivity (80% of cells) in both of stains (Fig. 7, Fig. 8).

The histopathological diagnosis of the needle biopsy of the breast lump was benign metastasizing leiomyoma with 1-2 mitoses/10 HPF.

Discussion

Benign metastasizing leiomyoma is a rare phenomenon with approximately 117 well documented cases in the literature (Graph. 1) [5-84].

The first case reported was that of Krišche in 1889, in which fibromyomas of the uterus metastasized to many parts of the body [3]. The 2nd case of this type was reported by Langerhans in 1893 [3]. It was that of a 60 year old woman who had multiple nodules in the uterus and multiple pulmonary metastases. The 3rd case on record is that of Minkowski, in 1901 [3]. It was that of a 43 year old woman who had multiple nodules of smooth muscle, in the lungs and liver. 2 years before she underwent complete hysterectomy for a "fibromyoma" of the uterus.

The term of benign metastasizing fibroleiomyoma was introduced in 1939 by Steiner [3] in his report of a case of a 36 years old woman who died after massive pulmonary and hilar lymphatic metastases of a uterine leiomyoma. Despite the common belief that benign tumors typically lack metastatic potential, it has been shown that histologically benign typical leiomyomata may invade blood vessels.

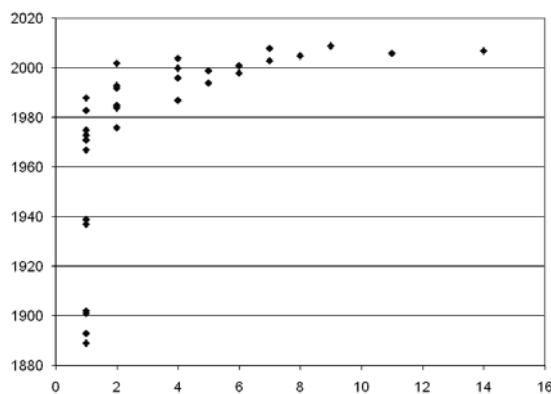
BML is uterine leiomyoma that histologically appears benign with a low mitotic rate and no quantitative differences between conventional leiomyoma, but is associated with the development of metastases in distant locations [68].

By geographic distribution, the majority of cases were observed in USA (31) and Europe (21 cases in Germany and 10 cases in Italy). There are a few cases in eastern countries and Israel (Graph. 2) [5-86].

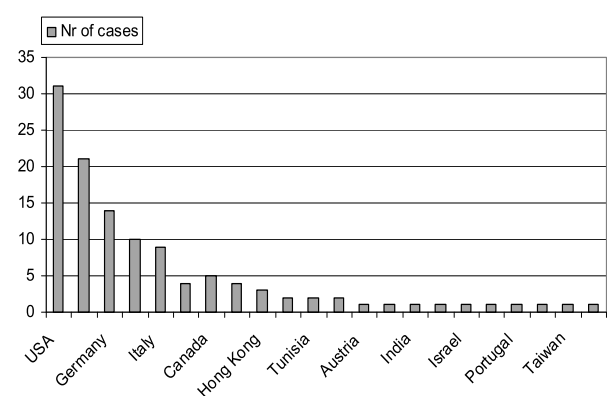
The disease is characterized by uterine leiomyoma in young adulthood, and pulmonary metastases occurring in the premenopausal period, and most common in middle-aged women [26].

The age distribution varies widely from the age of 19 to 77 years with a peak at age 40-49 years (Graph. 3).

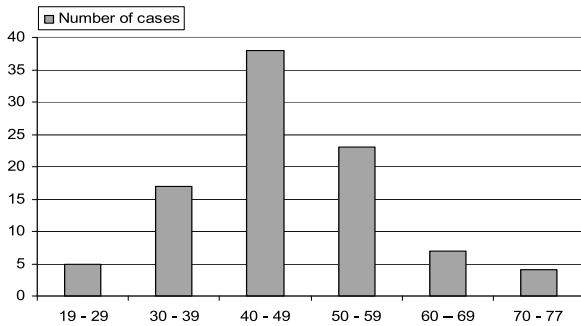
The majority of women with these tumors have a prior curettage, myomectomy, or hysterectomy [67] (Graph. 4). In a review of 99 cases was found, that 77 patients passed



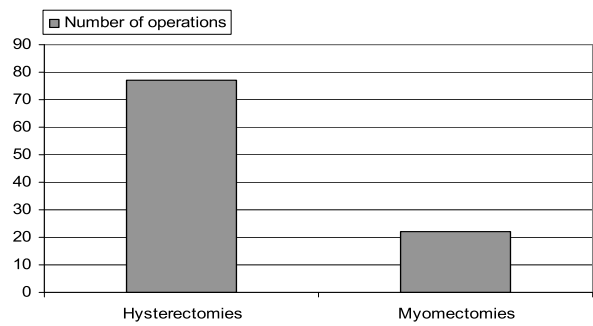
Graph (Grafic) 1. Number of BML according to year of publication (117 cases) [Numărul cazurilor de LBM în funcție de anul publicării (117 cazuri)]



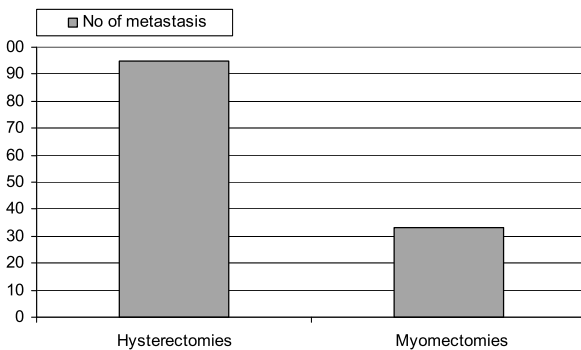
Graph (Grafic) 2. Number of cases BML by geographical distribution (117 cases) [Numărul cazurilor de LBM în funcție de distribuția geografică (117 cazuri)]



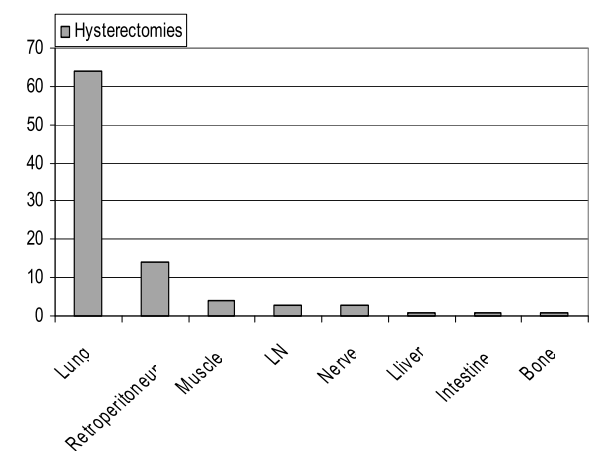
Graph (Grafic) 3. Age distribution of BML patients (94 cases) Range 19–77 years (mean 48) [Distribuția pe grupe de vârstă a pacienților cu LBM (94 de cazuri), între 19–77 de ani (media 48)]



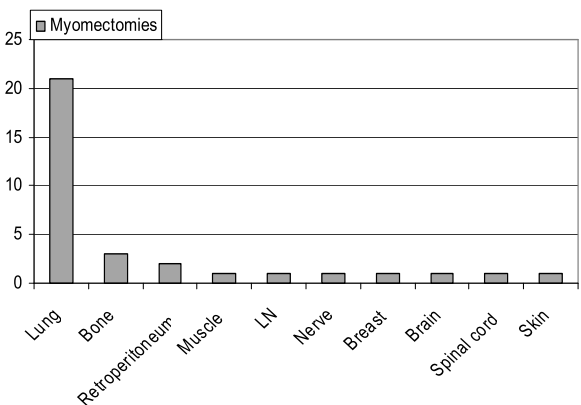
Graph (Grafic) 4. Number of operation in 99 cases of BML (Numărul intervențiilor chirurgicale în 99 cazuri de LBM)



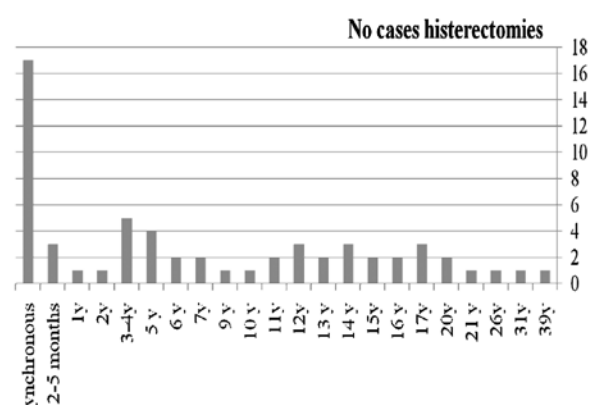
Graph (Grafic) 5. Number of metastasis 95 in 77 hysterectomies and 33 in 22 myomectomies for BML (Numărul metastazelor 95 în 77 hysterectomii și 33 metastaze în 22 miomectomii pentru LBM)



Graph (Grafic) 6. Anatomical site of metastasis after hysterectomy (Localizarea anatomică a metastazelor după hysterectomie)



Graph (Grafic) 7. Anatomical site of metastasis after myomectomy (Localizarea anatomică a metastazelor după miomectomie)



Graph (Grafic) 8. Time interval from hysterectomy to diagnosis of metastasis (Intervalul de timp de la hysterectomie la diagnosticul metastazelor)

hysterectomy and 22 passed myomectomy (Graph. 4).

In 77 hysterectomies 95 metastases were found and in 22 myomectomies 33 metastases were found (Graph. 5).

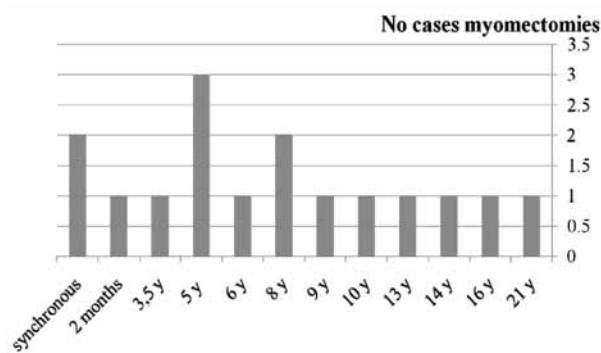
Anatomical site of metastases after hysterectomy were lung, retro peritoneum, muscle, lymph nodes, nerve, liver, intestine, bone. (Graph. 6) Anatomical site of metastases after myomectomy were lung, bone, retro peritoneum, muscle, lymph nodes, nerve, brain, spinal cord [36]. In one case breast metastasis was reported. (Graph. 7). Our case is the second reported case with breast metastasis.

Pulmonary nodules can be seen 1 month to 39 years after hysterectomy (Graph. 8) and 2 months to 21 years after myomectomies (Graph. 9). However, some cases have been described in which the uterine tumor was discovered simultaneously or even after the metastases were found [1-85].

The patients with pulmonary metastases are usually asymptomatic at presentation; the lesions are incidentally discovered on chest X-Ray, although symptoms such as cough, chest pain, and dyspnea have been described.

The clinical course is variable, the disease process is usually indolent, but may progress rapidly with resultant respiratory failure and death [51].

Usually the median survival after lung biopsy is long, more than 43 months. The patients did not die of this disease even though occurrence of new lesions or regrowth of nonresected lesions can occur, sometimes many years later [29].



Graph (Grafic) 9. Time interval from myomectomy to the diagnosis of metastases (Intervalul de timp de la miomectomie la diagnosticul metastazelor)

The pathogenesis of BMLs is object of controversy. Several hypotheses have been proposed. Several observations and animal experiments support the findings that BML may evolve from lymphatic and hematological spread, coelomic metaplasia and intraperitoneal seeding [1], but vascular dissemination is at present the most widely accepted.

The prognosis of BML depends upon the estrogen receptor status of the tumor.

The best management is combination of operation and hormonal therapy.

Our patient was treated with hormone therapy. To day, she is alive and well with no new metastases.

To the best of our knowledge this is the second case of BML with breast metastases described in the literature.

LEIOMIOM BENIGN METASTAZANT. PREZENTARE DE CAZ ȘI O REVISTĂ GENERALĂ A LITERATURII DE SPECIALITATE

Rezumat

Leiomiomul benign metastazant (LBM) este definit histologic ca o tumoră benignă a musculaturii netede uterine, cu o evoluție clinică într-un mod oarecum malign, producând

metastaze benigne. Vom prezenta un caz al unei femei de 42 ani, care a avut un leiomiom uterin de 730 g, la vârsta de 26 de ani. Șase ani mai târziu, a fost supusă, din nou, unei miomectomii. Au fost excizate mai multe leiomioame, cu