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Metastasising leiomyoma of the uterus with pulmonary involvement — case report

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Abstract

Benign metastasising leiomyoma (BML) is characterised by extrauterine smooth muscle tumours in women after surgical treatment for uterine leiomyoma. Usually manifested as solitary or multiple focal lesions in various organs, it imposes a scrutinous diagnostic work-up to exclude a malignant disease and requires confirmation in microscopic examination of the extrauterine focus. The authors present a case of a 56-year-old woman with BML manifesting as bilateral multiple pulmonary nodules, with a tentative diagnosis of a disseminated malignant disease of mesenchymal origin.

The patient underwent multiple diagnostic tests, which excluded malignancy. The definite diagnosis was established after the microscopic reevaluation of an excised pulmonary nodule. The patient is monitored with chest magnetic resonance.

BML should be considered in the differential diagnosis of multiple pulmonary nodules in asymptomatic women. Patients with BML require long-term monitoring, therefore the selected imaging method should not carry the risk of cumulative side effects.

Key words: computed tomography, magnetic resonance, pulmonary nodules, uterine myoma

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Introduction

Uterine leiomyomas are one of the most common benign tumours in women affecting as many as 20–80% of females, depending on age and ethnicity [1, 2]. Besides benign leiomyomas and malignant leiomyosarcomas, uterine smooth muscle tumours include benign tumours with an unusual growth pattern, some of which may demonstrate metastatic potential [3, 4].

Benign metastasising leiomyoma (BML) is a rare entity characterised by the presence of smooth muscle tumours of uterine origin in various organs. Although benign, its biological behaviour mimics that of a malignant tumour, therefore BML is a diagnostic pitfall. As the disease has extrauterine manifestation, patients with BML are rarely referred to gynecologists, but are diagnosed by other specialists or by general practitioners.

The lungs are the most common site of BML involvement. Pulmonary BML lesions typically present as multiple nodules, which vary in size and usually show poor contrast enhancement in computed tomography. A broad spectrum of diagnostic tests in search of a disseminated malignant disease is usually applied, however,

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this diagnostic work-up is inconclusive and the definite diagnosis of BML is based on the microscopic examination of the extrauterine tumour.

Case report

A never-smoking 56-year-old nulligravida was admitted to our department due to multiple pulmonary nodules detected in a routine chest radiograph performed because of newly diagnosed arterial hypertension. The patient denied any respiratory symptoms, loss of weight, fever or sweating. Her past medical history included hysterectomy due to uterine leiomyomas 15 years ago and left-sided oophorectomy due to an ovarian cyst 2 years ago. Prior to admission, she underwent multiple diagnostic tests in search of a disseminated malignancy. Computed tomography of the chest revealed the presence of multiple well-circumscribed nodules varying in size with poor intravenous contrast enhancement in both lungs; no enlarged lymph nodes were detected. Positron emission tomography with fluorodeoxyglucose (^{18}FDG-PET/CT) was performed, however, no foci of increased metabolism were revealed in the chest or abdomen. Blood testing for cancer markers, including CA 19-9, CA-125, CA 15-3, was negative. No data on bronchoscopy or the cytological examination of bronchial washing or bronchoalveolar lavage were available. The patient was referred for a diagnostic right-sided thoracotomy. Histopathological examination of the excised lung nodule revealed a smooth muscle tumour with positive immunochemical reaction to vimentin, therefore a diagnosis of a disseminated malignant disease of mesenchymal origin was established. The patient was qualified for chemotherapy, however, she was referred to our department by her attending oncologist for reevaluation due to the discrepancy between the clinical presentation, results of the imaging studies and the histopathological diagnosis.

On admission, the patient was in a good general state, physical examination did not reveal any abnormalities. The results of blood and urine laboratory investigations were within the normal range. The chest radiograph did not reveal new focal lesions in comparison to the radiograph performed 12 months ago; multiple nodules were seen in the middle and lower areas of both lungs, with no evident hilar enlargement (Fig. 1). Chest computed tomography also failed to show any new lesions when compared with the CT scans previously performed, the detected pulmonary nodules were well-circumscribed, showed poor contrast enhancement and the largest nodule had the diameter of 25 mm. The endoscopic appearance of the bronchial tree was normal, bronchial washing was negative for atypical cells and bacteria. The histopathologic slides from the specimen obtained in the earlier performed thoracotomy were referred to a reference oncology centre for reassessment. The microscopic examination showed plump spindle cells with vesicular nuclei with no atypia and perivascular location, which showed vimentin, smooth muscle actin and desmin expression. No necrosis or abnormal mitotic figures were found (Fig. 2). A comparison with the microscopic appearance of the uterine leiomyoma was not possible as we did not have access to the material. Given the history of hysterectomy due to leiomyomas, the clinical course, the presence of the nodules in imaging studies, lack of evidence for malignancy, the final diagnosis of benign metastasising leiomyoma was established. As the patient was asymptomatic, no treatment was offered, she has been monitored every 12–18 months. Having demonstrated good agreement between the appearance of the BML lesions in chest CT and magnetic resonance (Fig. 3), the latter was selected as the imaging follow-up method to avoid excessive CT-related radiation exposure.

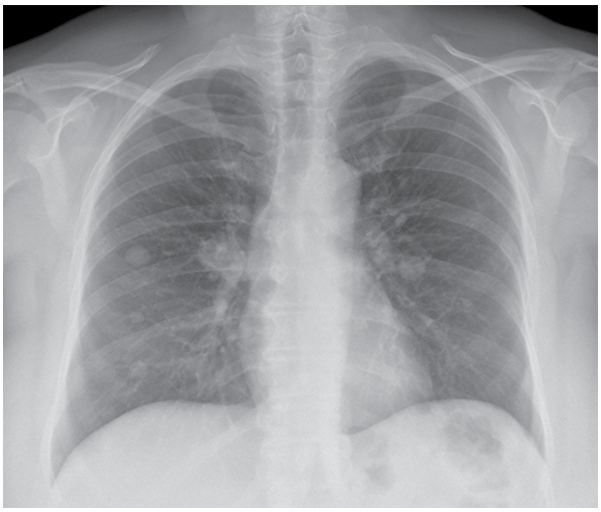

Figure 1. Posteroanterior chest radiograph showing multiple, round nodules in the middle and lower fields of both lungs

The patient has been under our observation for 45 months. She remains asymptomatic and there is no evident progression of the disease in MR of the chest.

Discussion

Benign metastasising leiomyoma is a rare entity with more than 150 cases reported in the

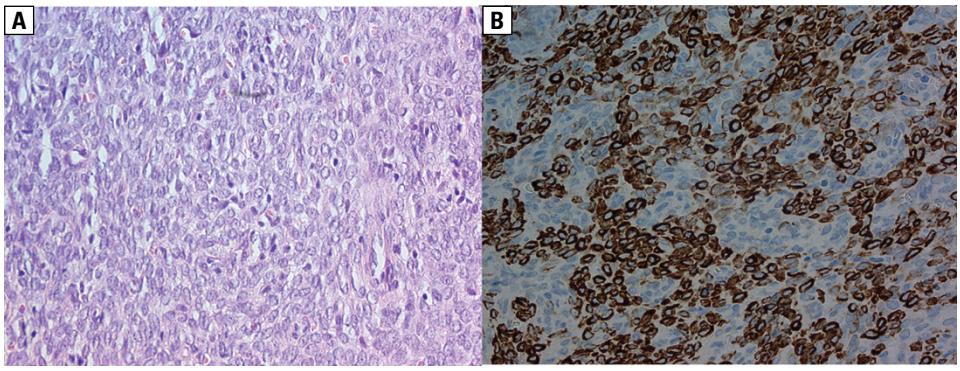

Figure 2. Metastasising leiomyoma — representative histopathology of the pulmonary lesion shows plump spindle cells with vesicular nuclei. There is no atypia and no mitotic figures are detected (**A** — H&E, 400 ×). Immunohistochemistry (**B** — IHC) shows strong cytoplasmic stain with antibody against desmin (400 ×)

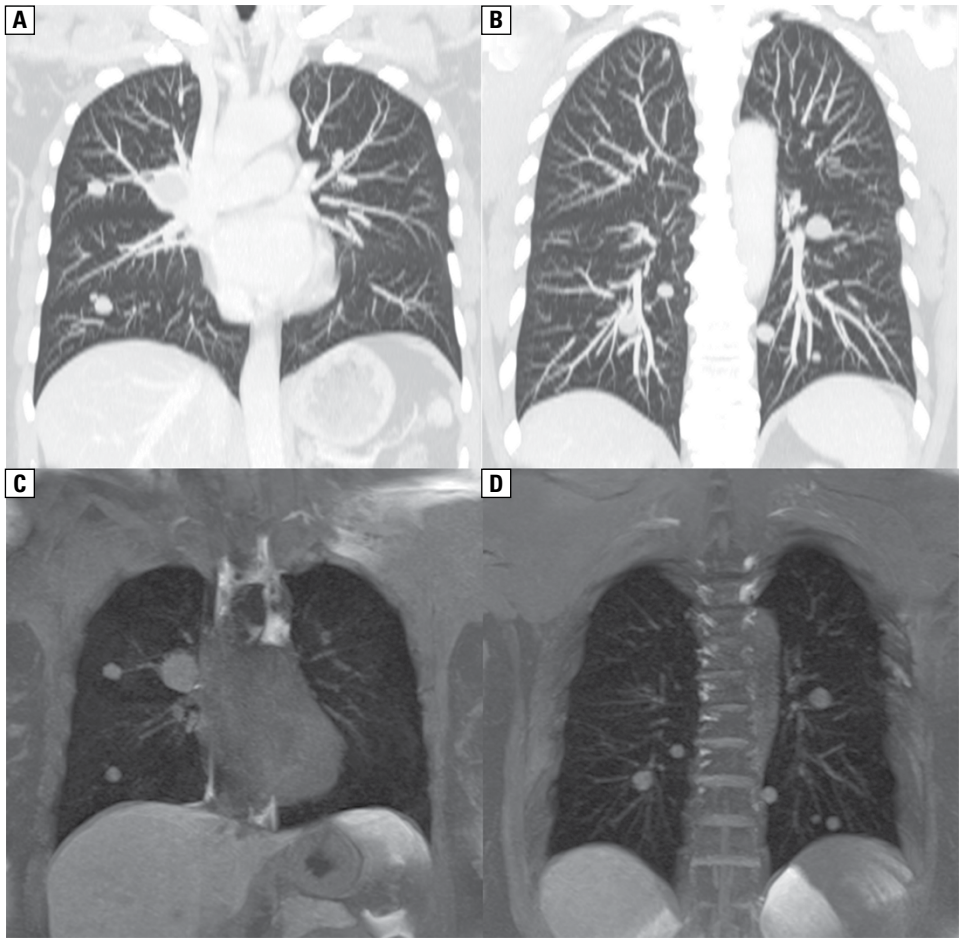

Figure 3. Corresponding sections (coronal plane) of chest computed tomography (**A**, **B**) and magneting resonance (**C**, **D**) showing good agreement in the imaging of the pulmonary nodules

literature [3, 5]. At least two cases have been also described in the Polish literature. Jęda *et al.* [6] reported a 72-year-old woman, in whom an extrauterine BML lesion was found in the small intestine. The second case described by Radzikowska *et al.* [7] presented with pulmonary BML metastases.

BML occurs mainly in women in reproductive age with a history of surgical treatment for uterine leiomyomas [2, 5]. BML foci may be detected from 3 months to even 30 years after hysterectomy or myomectomy [8, 9]. The lungs are the main site of involvement; BML is mostly manifested as multiple, well-circumscribed,

non-calcified nodules with poor contrast enhancement, but a miliary pattern has also been reported [10]. In some cases, BML pulmonary lesions were reported to show enhancement after contrast administration [7], which may further strengthen the suspicion of malignancy. In general, the pulmonary nodules do not demonstrate an elevated FDG uptake in PET/CT. Some authors postulated that in leiomyomas with higher concentration of growth factors, increased glycogen levels in the endometrium of the leiomyomatous uterus, and abundant vascularisation [11] an increased glucose metabolism may be seen. Therefore we may assume that FDG uptake may also be increased in BML foci, although, to the best of our knowledge, such a case has not been described to date. Although generally considered benign, some authors have suggested that BML should be classified as low grade leiomyosarcoma. There is a single report of a patient with BML, in whom a microscopic examination of an excised lung mass showed features of leiomyoma in the upper part of the lesion and leiomyosarcoma in the loweru. This was consistent with FDG uptake in PET/CT, which showed a polarised distribution within the mass, being much higher in its lower part [12]. The authors concluded that a malignant transformation of the pulmonary BML tumour could not be excluded.

The diagnosis of BML must be confirmed in microscopic examination and therefore usually requires resection of an extrauterine tumour. In our patient, the pulmonary involvement was incidentally detected 15 years after hysterectomy. The radiological appearance of the detected lesion was similar to that described in earlier reports on BML, and the definite final diagnosis was based on the microscopic examination of a pulmonary nodule excised in right-sided thoracotomy. Interestingly, in the report by Radzikowska *et al*. [7], transbronchial lung biopsy was also feasible for the diagnosis of pulmonary BML involvement, what indicates that, in selected cases, open lung biopsy may be avoided. However, given the rarity of BML and the need to differentiate this condition with a disseminated neoplastic disease, it seems that invasive diagnostic procedures are fully justified.

The pathogenesis of BML has not been fully elucidated. As in the vast majority of cases extrauterine foci are seen in patients after surgical treatment of uterine leiomyomas, most authors believe that surgical injury promotes hematogenous spread of the tumour. The intravascular presence of the tumor cells may also be the result of necrosis or rupture within the primary focus in the uterus, which may explain the extrauterine expansion in patients who had not been operated [2]. Analogically, BML may spread by lymphatic circulation. Other hypotheses include the development of BML from circulating stem cells or from the metaplastic coelomic transformation, probably enhanced by estrogen replacement therapy in women after surgical castration [13].

Given the low incidence of BML, no treatment guidelines have been established to date. The prognosis is good, most of the patients remain asymptomatic, however, in some cases tumour growth may cause a significant deterioration of health status. Treatment should be offered when the extrauterine tumours tend to grow or cause organ-specific symptoms. In most of the reported cases, only monitoring or surgical resection have been applied, however, surgical treatment cannot be considered in patients with multiple lesions. The extrauterine tumours express estrogen and progesterone receptors (similarly to the primary uterine focus), therefore treatment with luteinizing-hormone releasing hormone agonists or oophorectomy has also been offered [14, 15]. Other treatment options include selective estrogen receptor modulators (tamoxifen, raloxifene) and aromatase inhibitors [13]. In our patient, the lung nodules were detected incidentally and the disease was clinically indolent, so only observation was offered. She has remained asymptomatic and neither the size nor the number of the lung nodules had increased over the 45 months of follow-up. We selected magnetic resonance as the imaging method for monitoring for several reasons. Firstly, computed tomography is related with a significant radiation exposure, which may increase cancer risk [16]. Secondly, MR has a relatively good sensitivity for pulmonary nodule detection — 80-90% for nodules with a diameter of 3–4 mm and 100% for nodules > 8 mm [17]. This was confirmed by a group of Polish authors, who reported an 80% overall MRI sensitivity for lung nodule detection; for nodules > 8 mm MRI sensitivity also reached 100% [18]. The same authors demonstrated a good agreement between CT and MRI in the estimation of nodule size. Therefore, it seems that MRI is an attractive option for long-term follow-up of pulmonary nodules with a high probability of benign character. In our opinion, the choice of MRI for further monitoring in our case was justified. As the monitoring methods were not mentioned in most of the previously published case reports, we believe that our report may be the first to

show the usefulness of chest MR in monitoring BML patients with lung involvement.

Conclusion

Benign metastasising leiomyoma is a benign disease with a metastatic potential. Extrauterine tumours usually occur in patients with a history of uterine leiomyomas treated with hysterectomy or myomectomy. The definite diagnosis is challenging and requires confirmation in histopathologic evaluation. Surgical treatment may be offered to patients with solitary tumours; treatment options include hormonal therapy, selective estrogen receptor modulators and oophorectomy. In asymptomatic patients, careful monitoring may be applied; in patients with pulmonary involvement, chest MR may be a better choice than CT owing to CT-related radiation exposure. Although some patients may require intervention due to tumour growth, the prognosis is good.

Conflict of interest

The authors declare no conflict of interest.

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