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Multiple Progressive Pulmonary Leiomyomatous Metastases Treated with Tamoxifen

A Case Report with a Review of the Literature

O. Säynäjäkangas, A. G. Maiche and K. A. Liakka

From the Departments of Pulmonary Diseases (O. Säynäjäkangas) and Oncology (A. G. Maiche) Lapland Central Hospital and the Department of Pathology, Oulu University, Finland

Correspondence to: Olli Säynäjäkangas, Luppotie 1, 96200 Rovaniemi, Finland. Tel: +358 16 3422 338. Fax: +358 16 3283 011. E-mail: Olli.saynajakangas@fimnet.fi

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Case report. A 47-year-old woman was admitted to Lapland Central Hospital in January 2002 for metacarpal pain and surgery. Routine x-rays of the thorax revealed multiple round shadows in both lungs suggestive of metastases. Computerized tomography (CT) of the lungs showed circular nodules, 5 to 10 mm in diameter, with some nodules as large as 20 and 30 mm (Fig. 1). The patient was in good condition and without symptoms. Intensive repeated examinations comprising whole-body CT, colonoscopy, gastroscopy and mammography revealed no extrapulmonary primary tumour. Bronchoscopy was normal. The previous medical history showed that she had undergone a hysterectomy in March 1988 for a uterine leiomyoma. Gynaecological examination revealed a normal post-hysterectomy status. The serum tumour markers carcinoembryonal antigen (CEA), Ca 15-3 and Ca 125 antigens were not elevated.

Thoracoscopy was performed and a firm, white nodule measuring 7 mm in diameter was resected from the left lung. Histological examination showed a lobulated tumour that was well circumscribed from the surrounding lung tissue and was composed of intersecting bundles of spindle cells and entrapped bronchiolar epithelial structures (Fig. 2). The spindle cells showed no nuclear atypia. Mitotic counts ranged from 0 to 1 mitose per 10 high-power fields and there was no tumour necrosis.

Immunohistochemical analysis showed a strong immunoreaction for vimentin and the smooth muscle antigens alpha-SMA, MSA and desmin. There was also a strong expression of oestrogen and progesterone receptors. Only the entrapped bronchiolar epithelium was positive for cytokeratin. Re-examination of the histological slides from the uterus resected in 1988 revealed a benign leiomyoma. These findings supported a diagnosis of benign metastasizing leiomyoma.

A control CT examination in March 2002 revealed progressive disease in both lungs. The nodules had increased in both number and size. Treatment with tamoxifen at 20 mg daily was started, and the patient was monitored by CT, which showed stable disease three months later and again in March 2003, one year after starting treatment with tamoxifen, at which point the patient was still without symptoms.

Discussion. Benign metastasizing leiomyoma (BML), also called leiomyomatous hamartoma or fibroleiomyomatous hamartoma, is a rare disease characterized by well-defined, histologically benign multiple tumours usually occurring in both lungs (1). Previously used synonyms for BML are pulmonary hamartoma or mesenchymoma and chondroid mesenchymoma (2). BML is usually encountered in women aged 30–50 years, who have undergone a hysterectomy for uterine myomas 0 to 24 years earlier (3).

The pathogenesis of the disease is unclear. Hormone-dependent tumour growth may be a possible mechanism, as spontaneous regression of the disease in pregnancy (4) and during the menopause (5) has been reported. Anti-oestrogen therapy has been found to be effective in individual cases (6). It has also been postulated that BML may be the result of vascular invasion of a uterine leiomyoma or may be related to intravenous leiomyomatosis

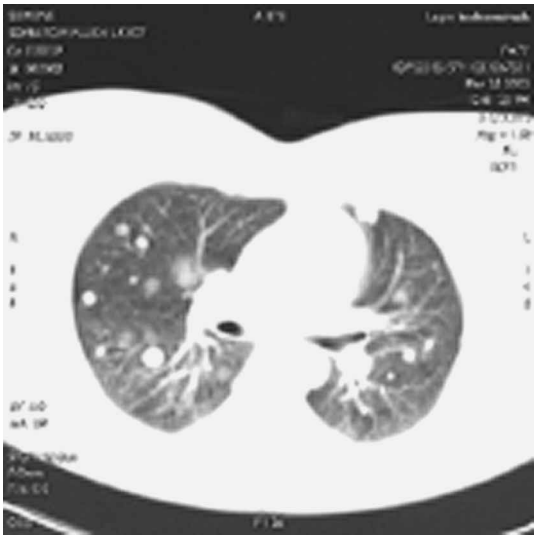

Fig. 1. CT scan of the chest demonstrating numerous well-circumscribed nodules in both lungs.

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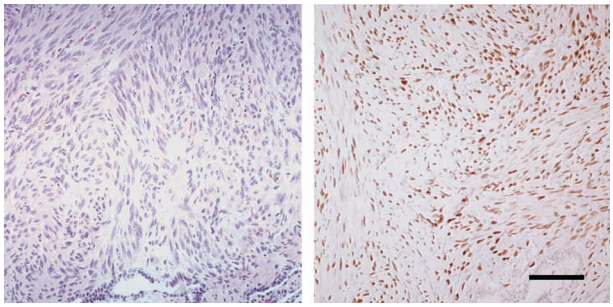

Fig. 2. Histological findings of the nodule resected from the left lung in a patient with benign metastasizing leiomyomatosis. Benign-appearing spindle-shaped cells arranged in intersecting fascicles are seen in haematoxylin and eosin stain (left). Strong immunoreaction shown for the oestrogen receptor (right). Bar 0.1 mm. Original magnification $\times 100$.

(7). On the other hand, Kayser et al. (1) regarded BML as a slow-growing variant of uterine leiomyosarcoma, with a more favourable prognosis. In a recent cytogenetic study (8) performed in a patient with BML a monoclonal origin was suggested for both uterine and pulmonary tumours and the pulmonary lesions were interpreted as metastatic. In contrast to most leiomyosarcomas, with complex and unbalanced karyotypic alterations (9), these tumours showed a balanced karyotype and an identical X-chromosome inactivation pattern (8).

In a previous study of tamoxifen medication for BML, there was no significant change in the size of the nodules despite the presence of positive oestrogen and progesterone receptors (10). In the present case, tamoxifen was found to be effective and well tolerated, and the disease was stable and the patient was without symptoms during the treatment. In this case there was strong expression of oestrogen and progesterone receptors, and it seems that the presence of these receptors determines the treatment results in BML.

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