Lymphangioleiomyomatosis of the lungs with staged bilateral chylothorax

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ABSTRACT. Lymphangioleiomyomatosis (LAM) is a slowly progressive, low-grade, metastasising neoplasm of women, characterised by infiltration of the lung parenchyma with abnormal smooth muscle-like cells, resulting in cystic lung destruction. The invading cell in LAM arises from an unknown source and harbours mutations in tuberous sclerosis complex (TSC) genes that result in constitutive activation of the mechanistic target of rapamycin (mTOR) pathway, dysregulated cellular proliferation, and a programme of frustrated lymphangiogenesis, culminating in disordered lung remodelling and respiratory failure.

Over the past two decades, all facets of LAM basic and clinical science have seen important advances, including improved understanding of molecular mechanisms, novel diagnostic and prognostic biomarkers, effective treatment strategies, and comprehensive clinical practice guidelines. Further research is needed to better understand the natural history of LAM; develop more powerful diagnostic, prognostic, and predictive biomarkers; optimise the use of inhibitors of mTOR complex 1 in the treatment of LAM; and explore novel approaches to the development of remission-inducing therapies.

LAM affects women of reproductive age (20-40 years old), is a hormone-dependent disease. Estrogen plays an important role, but sporadic forms or forms that are part of tuberous sclerosis are also observed, when LAM is combined with other manifestations of TSC. At the heart of LAM are mutations of the TSC1 or TSC2 genes, which lead to hyperactivation of the mTOR pathway, i. e., uncontrolled cell growth.

The main symptoms of LAM are shortness of breath (at first during physical exertion, then at rest), pneumothorax, cough (with hemorrhagic sputum), chylothorax, chest pain, and with aggressive progression, kidney damage in the form of angiomyolipoma. Diagnosis of LAM involves high-resolution computed tomography of the chest (a typical picture of multiple cysts in all lungs), a test for vascular endothelial growth factor D – VEGF-D (an elevated level is highly specific for LAM), lung biopsy (in doubtful cases), assessment of lung function (spirometry – reduction of DLCO, obstructive type of disorders), examination for tuberous sclerosis, renal angiomyolipomas, lymphatic lesions.

Key aspects of LAM treatment: sirolimus (rapamycin), a drug that inhibits mTOR and slows disease progression; bronchodilators, oxygen therapy, pleurodesis for repeated pneumothoraxes; lung transplantation at the terminal stage; exclusion of estrogen-containing drugs (oral contraceptives, hormone replacement therapy). Prognosis: the disease is slowly progressive. Thanks to sirolimus therapy, life expectancy can be 10-20 years or more after diagnosis.

In this article, we describe a case of pulmonary LAM complicated by staged bilateral chylothorax in a 43-year-old woman.

KEY WORDS: lymphangioleiomyomatosis, bilateral chylothorax, chemical pleurodesis, cystic lung destruction, pleurectomy, mTOR inhibitors, hormone-dependent disease.