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CASE FOR DIAGNOSIS

A patient with seizures, haemoptysis and dyspnoea

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Case history

A 27 year old woman was admitted to hospital because of seizures, haemoptysis and dyspnoea. She had been diagnosed as having tuberous sclerosis with mental retardation, epilepsy and secondary hydrocephalia due to a cerebral tuber obstructing the foramen of Monroe. Two years prior to admission, the hydrocephalia of the lateral cerebral ventricles was corrected by a ventriculo-cardial shunt. The patient was a nonsmoker and had no history of asthma. One month before admission, she developed progressively worsening exertional dyspnoea, without coughing. Her medication included carbamazepine, 400 mg daily, and clonazepam, 3 mg daily.

Physical examination showed a patient in moderate respiratory distress. Blood pressure was 130/90 mmHg, pulse rate 120 beats·min^{-1} and rectal temperature 36.5° C. Crackles were heard over both lungs. Neurological examination was normal. The patient had nodular lesions on her fingers and facial angiofibroma typical of tuberous sclerosis.

Haemoglobin was 6.7 mmol·L^{-1} with a mean corpuscular volume (MCV) of 79 fL. White blood cell count was 5,200×10^{12}·L^{-1}, with 0.61 neutrophils, 0.01 basophils, 0.03 eosinophils, 0.11 monocytes and 0.21 lymphocytes. Sedimentation rate was 10 mm·h^{-1}. Liver and renal function tests were normal. Carbamazepine and clonazepam serum levels were within therapeutic range. Blood, urine and sputum cultures were negative, as was viral and mycoplasmal serology.

Arterial blood gas analysis, whilst breathing room air, showed a pH of 7.34, arterial carbon dioxide tension (P_{a,CO_2}) of 4.8 kPa (36 mmHg), arterial oxygen tension (P_{a,O_2}) of 9.3 kPa (70 mmHg) with an oxygen saturation of 90%.

Pulmonary function tests showed: forced vital capacity (FVC) 3.0 L (86% predicted); forced expiratory volume in one second (FEV_1) 1.83 L (60% pred), FEV_1/FVC 61%; total lung capacity (TLC) 5.02 L (105% pred); functional residual capacity (FRC) 2.71 L (104% pred); residual volume (RV) 2.02 L (152% pred) and transfer factor of the lungs for carbon monoxide ($T_{L,CO}$) 3.2 mL·min^{-1}·mmHg^{-1} (12% pred).

Bronchoscopy revealed blood in the right bronchial tree, without any active bleeding lesion.

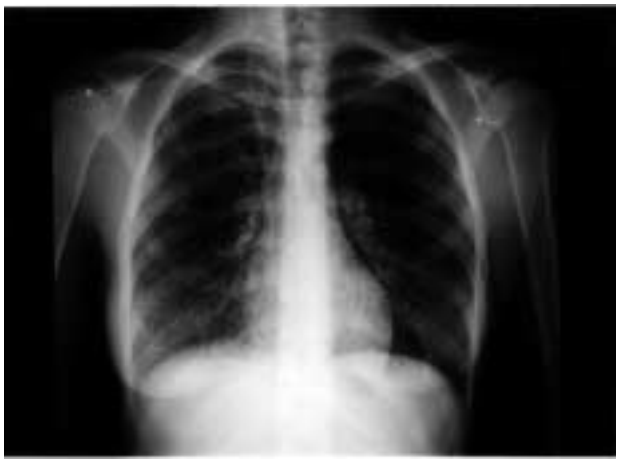

Fig. 1. – Chest roentgenogram.

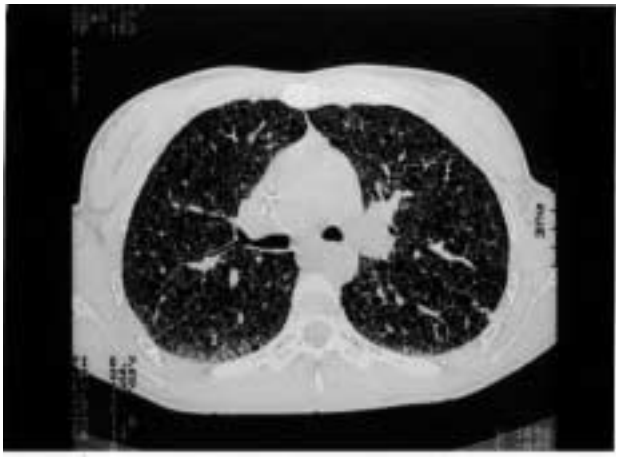

Fig. 2. – Chest computed tomographic scan at the subcarinal level.

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BEFORE TURNING THE PAGE; INTERPRET THE FIGURES AND SUGGEST DIAGNOSIS AND TREATMENT.

Interpretation of roentgenogram and computed tomographic (CT) scan

The roentgenogram shows a central venous line (the ventriculo-cardial shunt) and a diffuse interstitial pattern (fig. 1). The chest CT scan (fig. 2) reveals widespread, diffuse, small, thin-walled pulmonary cysts, less than 20 mm in diameter, present in all lung zones.

DIAGNOSIS: "Lymphangioleiomyomatosis in tuberous sclerosis"

The clinical, radiographic and functional findings are consistent with pulmonary manifestations, resembling lymphangioleiomyomatosis in a patient with tuberous sclerosis.

Treatment

Our patient was treated with 500 mg medroxyprogesterone acetate, intramuscularly once monthly, and there was no further deterioration after 3 months of treatment.

Discussion

Tuberous sclerosis (Bourneville's disease) is a clinical diagnosis made on the basis of fits, which may be focal or generalized, mental retardation, together with adenoma sebaceum, and shagreen patches and depigmented areas on the limbs and trunk, which characteristically fluoresce under Wood's light [1]. Computed tomography of the brain usually demonstrates calcified and uncalcified subependymal nodules and lesions in the cerebral parenchyma [2].

Pulmonary lymphangioleiomyomatosis (LAM) is caused by proliferation of smooth muscle cells in the walls of small airways, venules and lymphatics of the lung, as well as the mediastinal and retroperitoneal lymphatics [3]. LAM-like lesions occur in fewer than 1% of patients with tuberous sclerosis. The clinical, radiographic and pathological findings of pulmonary involvement in tuberous sclerosis are indistinguishable from LAM [4]. Some authors consider LAM to be a *forme fruste* of tuberous sclerosis [5, 6], others believe they are different entities [7].

Almost all patients with LAM are women with childbearing potential [8], although occasionally the disease is reported in post menopausal women [9]. LAM-like lesions in tuberous sclerosis may also occur in males. The typical clinical presentation of LAM includes: spontaneous pneumothorax due to cyst rupture in 40% of patients; chylothorax due to lymphatic obstruction in 80% of patients; haemoptysis, resulting from venular obstruction in 40% of patients; and slowly progressive dyspnoea caused by bronchial narrowing, leading to diffuse pulmonary cyst formation with normal or increased lung volumes and low transfer factor [3, 10].

Typically, the chest roentgenogram shows symmetrically distributed interstial disease. CT scan demonstrates thin-walled cysts, mostly less than 20 mm in diameter, scattered at random in all parts of the lungs [11]. Ground glass opacities may correspond to pulmonary haemosiderosis and/or relatively diffuse proliferation of immature smooth muscle cells [12].

The simultaneous findings of cerebral tubers, cutaneous lesions of tuberous sclerosis and the pulmonary manifestations allows the diagnosis of LAM-like lesions to be made without lung biopsy [4].

Although unequivocal data concerning results of ovariectomy, tamoxifen or progesterone treatment are missing, with such treatment clinical and radiological stabilization can be obtained [13]. A reduction of the FEV1/FVC ratio and an increase in % TLC at the first examination tend to be negative prognostic factors. At lung biopsy, a predominantly cystic type of LAM lesions and higher grades of abnormal areas and cystic lesions showed a tendency to poor prognosis [12].

Keywords: Lymphangioleiomyomatosis, pulmonary cysts, tuberous sclerosis.

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