

Pulmonary involvement in tuberous sclerosis complex: presentation of a case

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Abstract. – A clinical case of a pulmonary involvement in Tuberous Sclerosis Complex is reported. This rare involvement (1%) is characterized by either interstitial disease or bullae; therefore, pneumothorax is likely to happen in lung parenchyma. Furthermore this complication induces a progressive serious respiratory failure untill the death of the patient.

Key Words:

Tuberous Sclerosis, Lymphangiomyomatosis, Lung fibrosis.

Introduction

Tuberous Sclerosis Complex (TSC) is an autosomal dominant disorder, strongly predominant in reproductive age women and characterized by hamartomas in one or many organs, particularly in the skin, central nervous system, retina and associated with mental retard. The most of patients with TSC hasn't sick parents with TSC because the mental retard of this disease generally avoids reproduction. Therefore a high rate of genetic mutations explains the great rate of sporadic cases¹.

Case History

A 42 years old woman, non smoker, mentally retarded, born in Ethiopia, was admitted to C. Forlanini Hospital in Rome (Italy) because of "chronic interstitial lung disease". Her father died at the age of 50 years for unknown causes, her mother is healthy, 4 sisters are healthy and 5 brothers died for unknown causes too.

At the age of 4 months the patient had the first TSC skin lesion under the right eyelid that gradually spread to the face and trounce; at the same time she had an episode of convulsive crisis with lost of consciousness, which didn't repeat till February 1994 when the patient had a new episode. In 1987 she underwent a diatermocoagulations for some skin lesions. In 1993 the patient had metrorrhagia; in March 1994 she underwent a brain MNR with evidence of tuberous sclerosis images with degenerate tuberous lesions. The EEG was normal; a neuropsychiatric examination showed mental retard, tetra hyper reflexes with right prevalence and negative Babinsky, normal muscles strength". A gynecological echography showed uterine myomatosis. An ocular echography showed right nodular retina detachment and left retina thickening. A thorax CT showed multiple diffuse emphysema bullae medium size of 2 cm diameter and with inter and intralobular thickening of lung septa. Abdomino-pelvic CT showed kidneys and uterus disomogeneous and larger than normally and with adenomyomatosis. A brain CT showed "subependimal periventricular calcifications in TSC".

Since January 1997 the patient was suffering for progressive dyspnoea with stable hypoxaemia (PaO₂: 58 mmHg) and in August 1997 started with a Long Term Oxygen Therapy (LTOT). In October the patient was hospitalized for right pneumothorax and she was treated by a surgical drainage.

In January 1998 the patient was hospitalized in our Hospital for improving of dyspnoea, dry cough and fever.

Physical examination: the patient was in serious respiratory distress, blood pressure was

140/80 mmHg, pulse rate 100 beats per minute and the rectal temperature 37.8° C .

Thorax examination showed 22 breathes per minute and diffuse expiratory wheezing in both lungs. Heart examination showed rhythmic beats (100 per minute) and olosystolic murmur on pulmonary focus.

Laboratory findings: hemoglobin was 9.4 g, Red cells Mean Corpuscular Volume (MCV) of 66.6 fl., Mean Corpuscular Hemoglobin (MCH) of 20.6 pg. and Mean Corpuscular Hemoglobin Concentration (MCHC) of 30.9%; white blood cell count was 20100/mm³ with 77.3% neutrophils, 1% basophils, 0.9%. eosinophils, 3.1% monocytes and 17.6% lymphocytes, sedimentation rate was 60 mm per hour, sideremia of 13 µg % and serum ferritin of 5 ng/ml. The levels of urea nitrogen, creatinine, electrolytes, prothrombine time and partial-thromboplastin time were normal. The T-helper lymphocytes (CD3+, CD4+) were 2260 cells/mm³, T-suppressor lymphocytes (CD3+, CD8+) were 1330 cells/mm³ and T-lymphocytes H/S ratio was 1.7.

The ECG showed sinus tachycardia and alterations of ventricular repolarization. Echocardiography was normal.

At the hospital admission the arterial blood gas analysis while breathing room air showed a pH of 7.41, arterial carbon dioxide tension (PaCO₂) of 50.6 mmHg, arterial oxygen tension (PaO₂) of 37.2 with an oxygen saturation of 64.9%. During 4 liters per minute LTOT with 28 % ventimask, we found pH of 7.44, PaCO₂ of 48.3 mmHg, PaO₂ of 65 mmHg, and oxygen saturation of 91.4%.

We didn't succeed in doing pulmonary function tests because of the absolute lack of patient's collaboration for the mental retardation.

Chest radiograph showed a bilateral basal interstitial pattern with no evidence of lymphadenopathy or pleural effusion. Chest High Resolution Computerized

Tomography (HRCT) scan revealed many wide emphysematous bullae placed in the entire bilateral pulmonary parenchyma and bronchiectasis placed in the middle lobe and lingula (Figure 1).



Figure 1. HRCT scan revealed many wide emphysematous bullae placed in the entire bilateral pulmonary parenchyma.

Bronchoscopy was normal; the bronchoalveolar lavage (BAL) revealed: cell count of 290/mm³ characterized by macrophages 29%, lymphocytes 59%, neutrophils 12%, eosinophils and basophils not found; CD3+ was 81%, CD4+ 34%, CD19 2%, CD8+ 46%, T-helper/T-suppressor 0.74.

Tumor markers showed CEA < 3 ng/ml (n.v. 3-15), Ca 19-9 of 4 U./ml (n.v. 37-90) and Ca 15-3 of 66 U./ml (n.v. 30-50).

Pelvic echography revealed multiple uterine myomatosis.

Discussion

We treated the patient with corticosteroids (methylprednisolone 1 mg pro/kg) and bronchodilators (theophylline and salmeterol). According to international medical literature, there is a hormone dependence of TSC demonstrated by the discovery of pulmonary receptors for progesterone², clinical remission after menopause³, slower diffuse progression after oophorectomy⁴, efficacy of medroxyprogesterone², worsening after use of estrogens⁵; we decided to treat our patient with tamoxifen 20 mg/die and medroxyprogesterone acetate 500 mg I.M. once monthly.

Pulmonary involvement is very rare during the course of TSC (1% of patients)⁶, and it is histologically similar to pulmonary lymphangiomyomatosis. The growth of smooth muscle causes multiple clinical manifestations depending on its location: airways obstruction, bullae and pneumothorax in lung parenchyma; venular congestion and vasal dilatation in pulmonary venules; pulmonary hypertension and cor pulmonale in lung arterioles⁷.

The chest roentgenogram shows symmetrically distributed interstitial disease, HRCT demonstrates thin-walled cysts, medium diameter of 20 mm, scattered in the whole lung⁸.

In the largest study about mortality of patients with TSC there was no difference in survival between male and female patients; mortality rate for TSC patients with pul-

monary involvement is not higher than in patients with TSC without lung involvement. In one study the average time between the onset of respiratory symptoms and death was five years and the diagnosis was cor pulmonale (59%) and spontaneous pneumothorax (41%)⁹. Our patient died for a multiple organ failure due to the serious respiratory failure in the intensive care ward after 18 months since the diagnosis.

As chronic interstitial lung disease recognizes a large amount of etiological causes (as well the "idiopathic" one), TSC must be mentioned among those uncommon but possible.

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