Multifocal Micronodular Pneumocyte Hyperplasia in a Patient With Tuberous Sclerosis☆

Hiperplasia micronodular neumocitaria multifocal en una paciente con esclerosis tuberosa

Dear Editor,

Tuberous sclerosis complex (TSC) is an autosomal dominant syndrome characterized by mental deficiency, epilepsy and skin lesions (angiofibromas and subungual fibromas).[1] Lung affectation appears in 1%–2.3% of patients with TSC, mainly in the form of lymphangioleiomyomatosis (LAM),[1] although recent studies suggest that radiological findings may be seen in 26%–39% of patients.[2] Multifocal micronodular pneumocyte hyperplasia (MMPH) is the second lung manifestation and extremely rare. It may appear associated with LAM or, less frequently, as an isolated lung affectation in pre- or post-menopausal women with TSC, but it has also been reported in men with or without TSC.[3,4]

In reviewing the literature (Medline, 1991–2012), we have not found any publications in Spanish, and there are less than 50 cases reported with lung biopsy. We present the case of a 21-year-old woman diagnosed since childhood with TSC, with no known family history, and autoimmune hypothyroidism with substitutive treatment. Physical exploration was normal. Baseline arterial oxygen saturation was 98%. Basic analytical parameters were within normal limits, except for: urea 108 mg/dl; creatinine 3.7 mg/dl; urate 7.7 mg/dl, and pH in venous blood 7.29.

Cerebral magnetic resonance imaging showed subependymal nodules and lesions in the bilateral occipital and left parietal white matter, with persistence of astrocytomas. Chest radiography was done during the study prior to renal transplantation, which showed a bilateral nodular interstitial pattern, and the patient was therefore referred to the pulmonology department. The patient reported no occupational or leisure risks, nor did she present respiratory symptoms at that time.

Computed tomography (CT) demonstrated a bilateral nodular pattern of between 1 and 8 mm in diameter (Fig. 1), with no cystic lesions. In previous studies done during childhood, lung parenchyma was normal. Spirometry values were within normal limits, except for a slight reduction in carbon monoxide diffusion capacity.

Six months later, CT was repeated and the same pattern persisted, so we decided to perform lung biopsy with video-assisted thoracoscopy. In the lung biopsy, macroscopically there were whitish nodular areas observed, measuring 2–3 mm. Histology detected lung parenchyma with altered architecture where areas were observed with increased cell density with pseudo-nodular appearance, and among which there was normal lung parenchyma. The areas with pseudo-nodular appearance were located at the peripheral and central levels and constituted by lung parenchyma with thickening of septa that were often collapsed and covered with hyperplastic type II pneumocytes, with cubic morphology. There was no mitosis, necrosis, cystic lesions or proliferation of immature muscle cells suggestive of LAM (Fig. 1), all of which was compatible with the diagnosis of MMPH.

TSC is an autosomal dominant syndrome, but in up to one-third of cases there is no family history, as in the case we provide.[1] MMPH was described for the first time by Popper et al.[4]; it is generally associated with LAM, but it has also been described as a the only lung affectation in women and men with TSC, and more rarely without TSC.[3,4] Clinical manifestations include dry cough, moderate-exertion dyspnea, moderate or asymptomatic hypoxemia.[1,3,5] The radiological alterations of MMPH are not
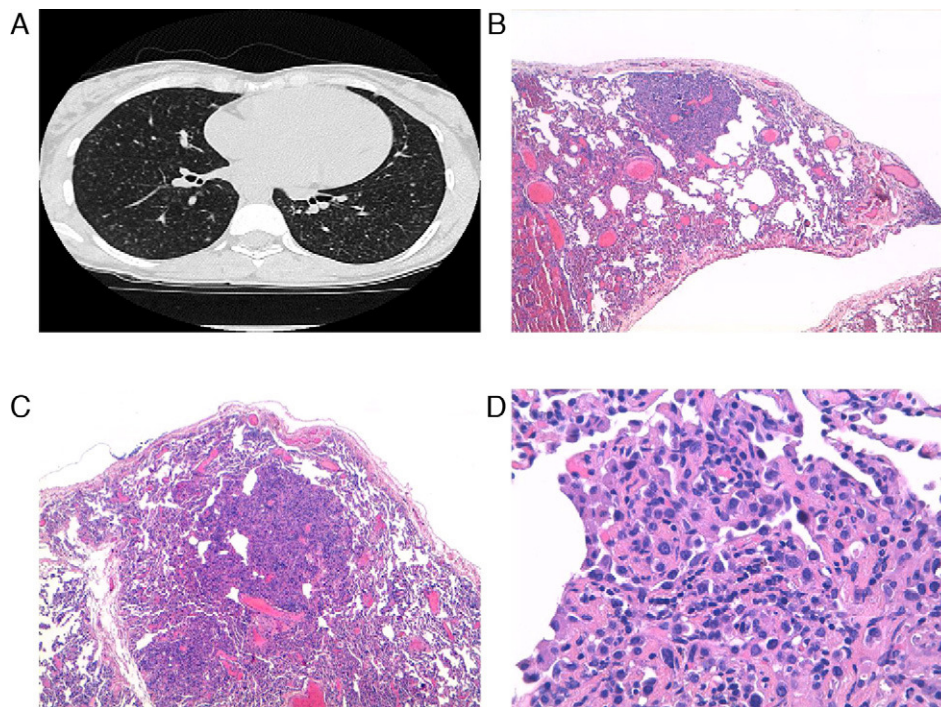

Fig. 1. (A) Micronodular pattern seen on computed tomography slice. (B and C) Parenchyma with altered architecture and areas of increased cell density and pseudo-nodular appearance (HE, ×40 and ×100). (D) Detailed view of the lesion, with increased septal thickness, pneumocyte hyperplasia and alveolar collapse (HE, ×200).

specific, and the differential diagnosis should include pulmonary tuberculosis, sarcoidosis, histiocytosis X, tumorlets and pulmonary metastases. The definitive diagnosis is established by lung biopsy. In small samples it is particularly difficult to differentiate it from papillary adenoma. The natural history is not clear, but it is unlikely for it to degenerate to malignancy, and the clinical evolution is good although there have been reported episodes of death due to respiratory failure.[3,5,6]

References

1. Umeoka S, Koyama T, Miki Y, Akai M, Tsutsui K, Togashi K. Pictorial review of tuberous sclerosis in various organs. Radiographics. 2008;28:e32.
2. Costello LC, Hartman TE, Ryu JH. High frequency of pulmonary lymphangioleiomyomatosis in women with tuberous sclerosis complex. Mayo Clin Proc. 2000;75:591–4.
3. Franz DN, Brody A, Meyer C, Leonard J, Chuck G, Dabora S, et al. Mutational and radiographic analysis of pulmonary disease consistent with lymphangioleiomyomatosis and micronodular pneumocyte hyperplasia in women with tuberous sclerosis. Am J Respir Crit Care Med. 2001;164:661–8.
4. Popper HH, Juettner-Smolle FM, Pongratz MG. Micronodular hyperplasia of type II pneumocytes: a new lung lesion associated with tuberous sclerosis. Histopathology. 1991;18:347–54.
5. Kobashi Y, Sugiu T, Mouri K, Irei T, Nakata M, Oka M. Clinicopathological analysis of multifocal micronodular pneumocyte hyperplasia associated with tuberous sclerosis in Japan. Respirology. 2008;13:1076–81.
6. Ristagmo R, Biddinger P, Pina E, Mever C. Multifocal micronodular pneumocyte hyperplasia in tuberous sclerosis. AJR Am J Roentgenol. 2005;184: S37–9.

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Diagnosis of Pulmonary Adenocarcinoma Due to Hip Bone Metastasis☆

Diagnóstico de adenocarcinoma pulmonar por metástasis ósea en cadera

Dear Editor,

The fact that the first symptom of a primary tumor is bone metastasis is not uncommon and should be part of the differential diagnosis in patients with history of risk. Lung cancer has a predilection for bones, and metastases generally settle in the proximal femur.

We present the case report of a 56-year-old woman, with no personal history of interest other than being a pack-a-day smoker, who came to our consultation due to pain in the trochanteric region that had been evolving over the past 2 months. It was treated as trochanteric bursitis, with poor response to non-steroid anti-inflammatory medication. Given the lack of improvement and poor-quality radiographies, magnetic resonance imaging tests (MRI) were ordered, which revealed a central, expansive image with aggressive characteristics located at the major trochanter of the right hip (Fig. 1). With the suspicion of primary or metastatic malignant tumor, an extension study was done with thoraco-abdominal computed tomography, which revealed a left suprahilar lung mass measuring 20×23 mm that infiltrated the aortopulmonary window, with homolateral mediastinal lymphadenopathies and an osteolytic image in the right intertrochanteric femoral neck, measuring 45 mm with soft tissue mass. Bronchoscopy demonstrated inflammatory mucosa in the left upper lobe. Bronchial aspiration with no neoplastic cells. PET/CT: left perihilar mass 20×25 mm (SUV 16), lytic lesion with soft tissue mass in the trochanteric area of the right femur (SUV 8.7). Analysis: hemogram, 3750 leukocytes; hemoglobin, 8.5 g/dl; platelets, 164,000. Biochemistry: albumin, 3 g/dl; alkaline phosphatase, 113 U; lactate dehydrogenase, 130 U; the remainder was normal. Ions and coagulation, normal. Carcinoembryonic antigen, 127 ng/ml; Ca15.3, 37 U/ml; Ca 125 and Ca 19.9, normal. We carried out percutaneous biopsy of the trochanteric region, guided by

radioscopy, which was reported to be compatible with metastasis of lung adenocarcinoma.

With said diagnosis, and given the immobility of the patient, we opted for complete resection of the trochanteric metastasis and substitution of the defect by implanting a megaprosthesis. Post-op was adequate, and the patient was up and walking on the 5th day with a walker, and with the use of a cane one month later.

Evolution

Systemic chemotherapy was begun with cisplatin and vinorelbine, competing 6 cycles with no incidences and an acceptable quality of life for the patient. After 7 months, the patient was hospitalized due to a process of deterioration and disorientation, and cerebral MRI diagnosed cerebral metastases. Holocranial radiotherapy was begun, but one month later the patient started to have generalized bone pain, dysphagia and progressive dyspnea secondary to the progression of the disease in the lungs and mediastinum. The patient died 13 months after the diagnosis.

Discussion

It is important to include tumor pathology within the differential diagnoses of muscular-skeletal pain, especially in patients who have risk factors like smoking.[1] Clinically, it is difficult to diagnose
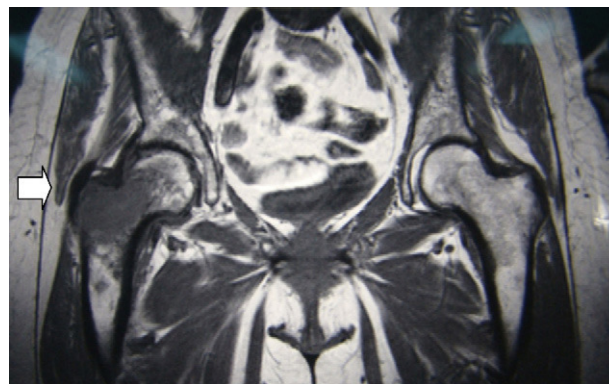

Fig. 1. Magnetic resonance imaging in T1 showing a central and expansive image with aggressive characteristics located at the major trochanter and neck of the right hip (arrow).