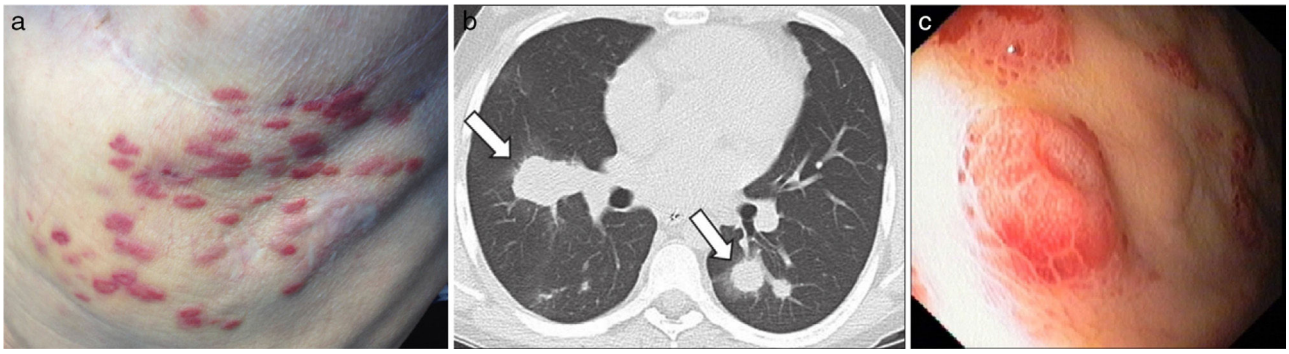

Fig. 1. (a) KS skin lesions, (b) pulmonary involvement by KS and (c) KS lesions dispersed in the patient's stomach.

patient presented severe anaemia (haemoglobin 6.8 g/dL) and he underwent endoscopic study which revealed multiple, vascular, round and elevated lesions dispersed in the stomach, suggestive of KS (Fig. 1c). The histological examination confirmed this suspicion after the identification of positive cells to HHV-8 and its serology was negative. Few days later, the patient died after the onset intra-abdominal sepsis.

KS in lung transplant patients has been rarely described in literature, contrary to other solid organ recipients.[2,4] Different clinical expressions and severity can occur, but usually they are aggressive, commonly involve skin and visceral organs[3,4] and time from transplantation to diagnosis can vary widely (3•124 months).[3] KS related to immunosuppression usually disappears with mTOR inhibitors[5] or with modification, reduction or cessation of immunosuppressive drugs, which in lung transplant patients is not recommendable due to loss of the graft,[3] making their therapeutic approach a challenge. Unfortunately, clinical deterioration in both patients did not allow us to start specific therapy for KS.

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Conflict of Interests

The authors declare that there is no conflict of interests directly or indirectly related to the contents of the manuscript.

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Richter Syndrome With Extensive Isolated Pleural Extranodal Involvement: The Importance of PET/CT Imaging☆

Síndrome de Richter con extensa afectación extranodal pleural aislada: importancia de la PET/TC

To the Editor,

Richter syndrome (RS) consists of the transformation of chronic lymphocytic leukemia (CLL) to diffuse large B-cell lymphoma (DLBCL), a rapidly growing variety of non-Hodgkin's lymphoma with poor prognosis. The disease course in 5%–10% of patients with CLL is complicated by RS, which generally presents clinically in the form of lymphadenopathies, splenomegaly, and worsening B symptoms (fever, night sweats, weight loss).[1] Positron emission tomography-computed tomography (PET–CT) is a powerful hybrid diagnostic tool that is useful in patients with RS because it helps plan and obtain histological biopsies of lesions with greater metabolism using other techniques.[2,3]

We report the case of a 74-year-old woman diagnosed with CLL in 2009, who attended the emergency department of our hospital with a 2-week history of progressive dyspnea, chest discomfort and low-grade fever. Chest radiograph revealed a large right pleural effusion causing mediastinal shift to the contralat-

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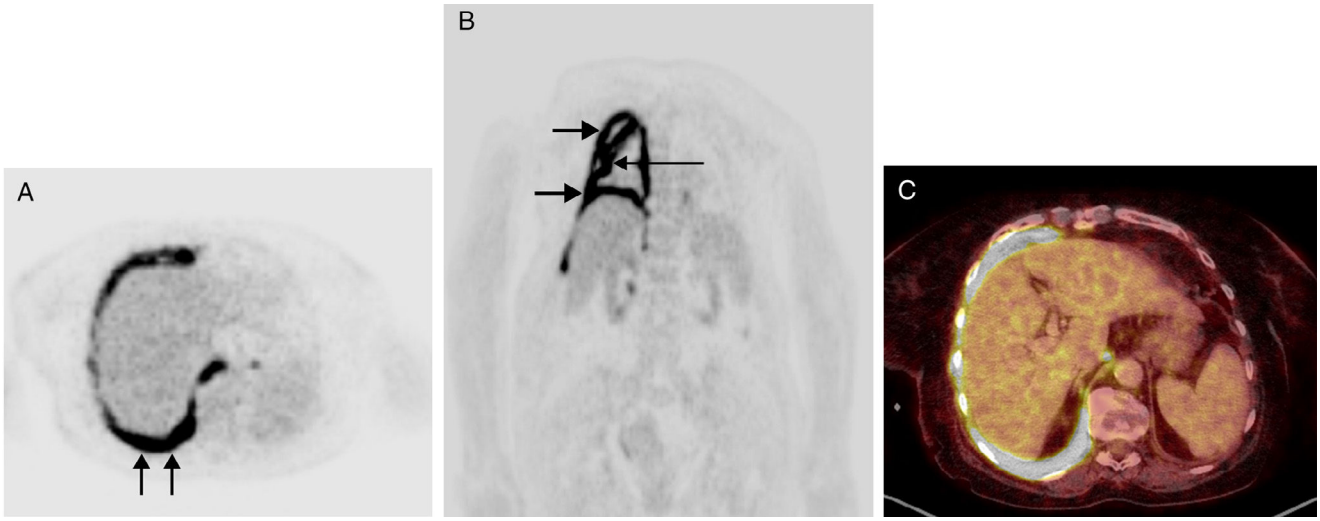

Fig. 1. (A) PET axial image of the chest revealing hypermetabolic circumferential thickening of the pleural surface of the right hemithorax. Note the increased thickening of the posterior pleural surface (arrows). (B) PET coronal image revealing hypermetabolic thickening of the pleural surface of the right hemithorax (short arrows). Note also the intense FDG uptake by the oblique fissure (long arrow). (C) PET–CT fusion axial image showing marked hypermetabolic thickening of the pleural surface of the right hemithorax at the level of the posterior costophrenic angle. On the basis of these images, this region was selected for biopsy.

eral side, and secondary atelectasis of a large part of the right lung. A pleural tube was placed in the emergency room, draining abundant serosanguineous fluid. A whole-body PET–CT scan with intravenous contrast and F18-fluordeoxyglucose (FDG) performed 3 days later showed marked diffuse hypermetabolic thickening of the pleural surface of the right hemithorax, with secondary compressive atelectasis of the ipsilateral lung, which did not show pathological FDG uptake (Fig. 1). No lymphadenopathies, signs of bone marrow infiltration, or other hypermetabolic lesions were observed in the abdominal viscera or the skeleton. In view of these findings, a core needle biopsy was performed in the thickest area of the pleura with the highest metabolism on PET–CT, confirming the diagnosis of an aggressive DLBCL. The patient initially improved with pleural drainage and chemotherapy (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), but died 4 months later due to systemic progressive disease.

Most RS present with nodal (lymph nodes) and bone marrow involvement, although atypical forms of extranodal involvement have been described in the digestive tract, the pulmonary parenchyma and the skin. Our case is exceptional because we could not find any reports in the literature of RS presenting with exclusively pleural extranodal involvement; we only found some isolated references to RS occurring with pleural effusion, but in general, it is always associated with the presence of lymphadenopathies in other sites, with no diffuse thickening of the pleural surface. Our patient, then, is a case of DLBCL with exclusively pleural extranodal involvement complicating the course of her CLL. Two forms of primary pleural lymphoma are described in the literature: body cavity lymphoma (lymphomatous pleural effusion), which usually affects patients with acquired immunodeficiency syndrome and is caused by the human herpes virus type 8; and lymphoma associated with pyothorax, recently renamed DLBCL associated with chronic inflammation, which often affects patients with fibrothorax caused by tuberculosis, although it has also been described in association with chronic osteomyelitis of the chest wall, thoracoplasty, or the presence of metal implants (this form of primary pleural lymphoma has also been associated with Epstein–Barr virus infection).[4] Our patient did not belong to either of these 2 groups of primary pleural lymphoma. In line with recent articles that highlight the importance of PET–CT in the diagnostic management of RS, performing this imaging study in our patient (as the only whole-body diagnostic imaging procedure) was very useful for demonstrating the intense hypermetabolism of the pleural surface of the right hemithorax and for ruling out hypermetabolic lesions in other sites.[2,3,5] The lack of FDG uptake in the right pulmonary parenchyma, which was confirmed by the CT component of the PET–CT, prompted us to obtain a radiological-guided percutaneous core needle biopsy in the area of hypermetabolic pleural thickening.

Our case illustrates an unusual form of extranodal, exclusively pleural RS in a patient with a history of CLL. It also illustrates the great potential of the PET–CT hybrid technique in the diagnostic management of RS as a guide for obtaining histological samples of lesions with increased metabolic activity, thus increasing the diagnostic yield of the biopsy.

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Negative Endobronchial Ultrasound in Lung Cancer Staging☆

Ecobroncoscopia negativa en la estadificación del carcinoma broncogénico

To the Editor,

Endobronchia ultrasound-guided transbronchial aspiration (EBUS-TBNA) is the primary method of non-invasive staging in non-small cell lung cancer (NSCLC), due to its low morbidity, low cost, and similar sensitivity to mediastinoscopy.[1] However, in case of a negative EBUS-TBA, the need to obtain another sample by mediastinoscopy is controversial. The aim of this study was to determine the negative predictive value (NPV) of EBUS-TBNA in NSCLC lymph node staging.

A retrospective analysis was performed of data collected prospectively in a database that included all patients who underwent EBUS-TBNA for mediastinal lymph node staging and positron emission tomography-computed tomography (PET–CT). Two samples (if the pathologist was present in the examination room) or 3 samples (if the pathologist was absent) were obtained from lymph node stations measuring >5 mm in their smallest diameter or those measuring <5 mm with pathological uptake in PET–CT. The specimen was considered: *(1) representative* if more than 300 lymphocytes in total or more than 150 lymphocytes/field were observed on cytological examination; *(2) positive* if malignant cells were detected; and *(3) negative* in the absence of malignant cells and presence of a representative number of lymphocytes. The gold standard for demonstrating the presence or absence of nodal infiltration was the histological analysis of the mediastinal lymph node specimens obtained by thoracotomy or VATS. The following formula was used to calculate the NPV: true negatives (TN)/true negatives+false negatives (FN). TN was defined as negative EBUS-TBA confirmed by thoracotomy or VATS, and FN as negative EBUS-TNA with malignant cells observed on thoracotomy or VATS.

A total of 97 patients with NSCLC were identified, of whom 23 had undergone surgical resection with mediastinal lymph node dissection, and this group formed the final study cohort. Fifteen were men, and mean age was 65.49±9.8 years. Samples from 35 enlarged lymph nodes were obtained by EBUS-TBNA and thoracotomy/VATS, and results were concordant in 32: 11/12 in E7, 9/10 in 4R, 8/9 in 4L, 3/3 in 10R and 1/1 in 11L. Three false negatives were obtained, as shown in Table 1. The prevalence of mediastinal lymph node infiltration with negative EBUS-TBNA was 8.6%, with a NPV per lymph node of 91.4%. In total, 30 lymphadenopathies showed pathological uptake on PET–CT: 24 N2 (cN2) and 6 N3 (cN3), with a prevalence and NPV of 12% and 87.5%, and 0% and 100%, respectively.

Recent clinical guidelines[1,2] recommend mediastinoscopy after a negative EBUS when the mediastinum is abnormal, defined as the presence of enlarged lymph nodes with pathological uptake on PET–CT, according to the conclusions of a Bayesian analysis which determined that the post-test probability of malignancy in this group of patients would be high, at around 20%.[3] This estimate was made by taking into account the results of the ASTER study,[4] a trial comparing EBUS-TBNA with EBUS-TBNA plus mediastinoscopy, randomized at a ratio of 1:1, which showed that the combination of both techniques was more sensitive than each one separately.

However, this conclusion is rather controversial. In our series, in patients with a moderate to high risk of N2-N3, the NPV of EBUS-TBNA is high, in line with findings from various studies in which it ranged between 89% and 99%.[5–9] According with these results, the possibility has been raised that in resectable NSCLC, a negative EBUS-TBNA would not need further confirmation by mediastinoscopy, as suggested by recent guidelines from the Spanish Society of Pulmonology and Thoracic Surgery.[10] This recommendation is further strengthened by evidence that mediastinoscopy is not superior to EBUS-TBNA in nodal staging, and indeed its sensitivity is similar and sometimes lower.[11,12] This was also shown in the ASTER study,[4] which reported that to improve sensitivity, 11 mediastinoscopies would have to be performed to obtain 1 positive case. Therefore, as the authors themselves admit, confirming all cases with negative EBUS-TBNA by mediastinoscopy might not be necessary.

Nevertheless, it would be advisable to try to identify any features that could be associated with a greater likelihood of "unexpected" nodal involvement. In this respect, our study revealed that our 3 false negatives had the common factor of a centrally located tumor, predominantly in the upper lobes. This finding has already been recognized as a predictor of malignancy in patients with negative EBUS-TBNA: Ong et al.[13] showed that the presence of nodal metastases in patients with a normal mediastinum according to imaging techniques, of which 37% were detected by EBUS-TBNA, correlated significantly with central tumors, and of these, 67% were located in the upper lobes, a finding similar to that obtained in previous prospective studies.[14] Similarly, Talebian Yazdi et al.,[15] in a large series, found that central tumor location, along with enhanced uptake on PET, were factors predictive of false negatives in subjects with negative EBUS-TBNA.

This study has the limitations typical of a retrospective design and a small sample size, so definitive conclusions cannot be reached in certain aspects, such as the possible influence of PET uptake on EBUS-TBNA false negatives. However, the limitations of imaging studies in this regard are well known,[2] and if they are taken into account, we believe that our results could be of use for identifying patients in whom it may be appropriate to perform

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