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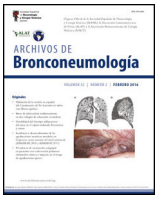

Scientific Letter

Transbronchial Cryobiopsy of Peripheral Pulmonary Lesions Guided With Real-Time Transthoracic Ultrasonography

Criobiopsia transbronquial de lesiones pulmonares periféricas guiada en tiempo real con ultrasonografía transtorácica

Dear Editor,

The diagnosis of peripheral pulmonary lesions (PPL) is important, especially when it is required to confirm or exclude malignancy. We present what we believe to be the first two cases of PPL diagnosed by transbronchial cryobiopsies guided by real-time transthoracic ultrasound and assisted by radial endobronchial ultrasound (r-EBUS).

The first patient was a 76-year-old male, a heavy ex-smoker with a peripheral left mass on chest X-ray. Thoracic computed tomography (CT) revealed a lingular solid mass with 38 mm larger diameter, based on pleura adjacent to the anterior thoracic wall (Fig. 1A) compatible with primary lung neoplasia. Chest ultrasound examination showed a nodule of 26 mm of maximum depth with pleural contact, mobile with respiratory movements and partially covered by the adjacent rib, leaving a narrow intercostal space for examination. Standard bronchoscopy with a thin bronchoscope, showed no endobronchial lesions so the endoscopic examination was carried out with r-EBUS. A 1.4 mm radial ultrasound probe (Olympus Co, Japan) was advanced through the lingula bronchi until the hypoechoic heterogeneous nodule was visualized and then we tried to reproduce the path with the 1.9 mm cryoprobe (ERBE CA, Germany) (Fig. 1B). Prior to transbronchial sampling, the transthoracic ultrasound (convex transducer, F2.5 MHz D9.9, MINDRAY Co, China) was applied on the anterior chest wall (Fig. 1C) and was able to visualize, in real time, the transbronchial cryoprobe going through the mass and avoiding the pleura (Fig. 1D and supplementary video 1A). Curiously, applying freezing decreased the ultrasound image of the probe, except for the tip (supplementary video 1B), and allowed for the visualization of the tissue freezing process. Biopsies (4 samples, $1.1 \times 0.9 \times 0.3$ cm) were positive for adenocarcinoma.

The second case was a 39-year-old female who presented with fever and unresolved pneumonia which had resisted antibiotic therapy for a period of two months. The patient had no history of smoking and her physical examination revealed only bilateral basal fine crepitations. Thoracic CT showed bilateral basal consolidation opacities with positive air bronchogram. Microbiological examination for sputum and bronchoalveolar lavage samples were negative, including the tuberculosis work-up. For the diagnosis of the underlying pathology, the patient was subjected to r-EBUS assisted transbronchial cryobiopsy guided with transthoracic ultrasound. During the procedure, the radial probe was advanced through the lateral segment of the left lower lobe until the lesion was visible. Then, the 1.9 mm flexible cryoprobe was advanced to the target location. Simultaneously, the transthoracic ultrasound was applied on the chest wall and was able to detect the lesion. The transthoracic ultrasound was helpful in confirming that the cryoprobe was located within the lesion and distant from the pleura to avoid pneumothorax. Four transbronchial cryobiopsies were obtained and the histopathological examination revealed cryptogenic organizing pneumonia.

Conventional bronchoscopy has a low diagnostic value for PPL which may be less than 20% for nodules smaller than 2 cm in diameter.[1] Also, it should be noted that not all PPL can be seen by fluoroscopy, in addition to the presence of radiation hazards for the patient and the operators. Although CT guided percutaneous biopsy is a reliable technique for the diagnosis of these lesions, it is associated with a high risk of pneumothorax[2] and is therefore usually indicated when transbronchial procedures have proved unsuccessful. Chest ultrasound guided percutaneous biopsy is an equally long-established method but requires appropriate case selection in advance.[3] The pleural contact length made by the mass or nodule, for example, influences diagnostic yield. Chest ultrasound and CT guided percutaneous biopsy were not considered a convenient alternative because of the ultrasound findings in our first case and because of diagnostic suspicion in the second one. Moreover, these techniques do not allow for the obtention of cryobiopsy samples.

Recent updates to bronchoscopic methods have aimed to increase the diagnostic value for PPL. Electromagnetic navigation bronchoscopy has achieved an accuracy of up to 81.7%, however, it is associated with high economic costs.[4] R-EBUS has emerged as a safer method in comparison to CT-guided biopsy but the yield of r-EBUS remains lower than that of CT-guided biopsy, due in part to the smaller sample size.[5,6]

The safety and feasibility of cryoprobes in combination with r-EBUS has also undergone a preliminary evaluation for the diagnosis of PPL and compared with forceps biopsies. Transbronchial cryobiopsy with r-EBUS assistance can obtain a better diagnostic yield and significantly larger samples.[7,8] Cryobiopsy could even increase the detection rate of epidermal growth factor receptor (EGFR) mutations in non-small-cell lung cancer in comparison to other tissue sampling techniques.[9] However, a meta-analysis[10] reported a pneumothorax average incidence of 10% after transbronchial biopsies with a cryoprobe in interstitial lung disease. Bleeding during cryobiopsy is common and the risk is greater than with conventional forceps biopsies. Moderate bleeding after cryo-biopsy was observed in 65 cases of 383 patients in 12 studies (16.9%).[10]

A main drawback regarding r-EBUS is the absence of real-time vision for biopsy. In this case report, we describe a novel technique for the biopsy of malignant and benign PPL near to pleura using transthoracic ultrasound guidance for cryobiopsies. The particular advantages of real-time guidance with external thoracic ultrasound are the ability to guide the biopsy tool directly to the lesion without C-arm fluoroscope, using echotexture to avoid necrotic areas, preventing injury to surrounding vascular structures and the pleura and to permit the exclusion of the pneumothorax.[11] For instance, in the diagnosis of interstitial lung diseases, distances of the cryoprobe to the pleura of less than 1 cm are associated with a significantly increased risk of pneumothorax,[12] while biopsies obtained too proximally to the middle third of the lung without ultrasound assistance increase the risk of severe bleeding.

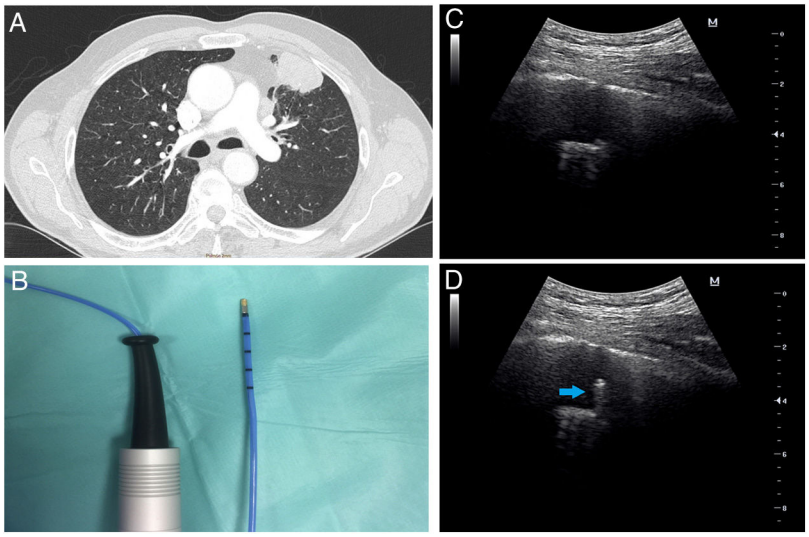

Fig. 1. (A) Chest CT image shows a lingular mass with pleural contact and bronchus sign. (B) Flexible cryoprobe indicated for transbronchial biopsy. Outer diameter 1.9 mm, length 900 mm. (C) Transthoracic ultrasound image before performing transbronchial biopsy of the mass. (D) Transthoracic ultrasound image during the performance of transbronchial biopsy, which locates the cryoprobe within the lung mass (arrow).

Also, we hypothesize that guided real-time transthoracic ultrasound can increase the diagnostic yield of r-EBUS in a way that is similar to real-time convex EBUS transbronchial needle aspiration[13] when compared with non-real-time EBUS.[14] Nevertheless, in comparison with CT-guided biopsy, our technique may have the disadvantage of requiring two operators, one for bronchoscopy and the other for performing transthoracic ultrasound. Even though, thoracic ultrasound offers other advantages, including the lack of ionization radiation, low cost, flexibility, reproducibility of the examination and bedside availability.[15]

In conclusion, the combination of transthoracic ultrasound and flexible cryoprobe add to r-EBUS procedure the potentiality of vision-guided transbronchial cryobiopsies for PPL lesions with pleural contact. Using percutaneous chest ultrasound has enabled us to guide the cryoprobe to the target lesion to obtain accurate samples. Further benefits are visual confirmation that it is freezing the tissue, visualization of the distance to the pleura to prevent pneumothorax and the use of the color Doppler to avoid highly vascularized areas.

Our initial experience requires prospective validation in a larger patient cohort to confirm the reliability and reproducibility of these results combining transbronchial cryobiopsy with percutaneous chest ultrasound.

Funding

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Conflict of interest

The authors have reported to Archivos de Bronconeumología that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbres.2020.10.015.

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¿Debe incluirse la saturación basal de oxígeno en la estratificación de riesgo de la enfermedad pulmonar obstructiva crónica propuesta por GesEPOC?

Should Pulse Oximeter Saturations Be Included in the Risk Stratification for Chronic Obstructive Pulmonary Disease Proposed by GesEPOC?

Estimado Director:

La edición 2017 de la Guía española de la enfermedad pulmonar obstructiva crónica (GesEPOC), con intención de establecer un algoritmo de tratamiento, realiza una estratificación de riesgo de los pacientes en dos niveles: bajo riesgo (BR) y alto riesgo (AR), de acuerdo con tres criterios: función pulmonar, grado de disnea e historial de exacerbaciones[1]. Dicha estratificación se plantea inicialmente desde un marco teórico como la probabilidad de que el paciente pueda presentar una evolución clínica desfavorable. Tras su publicación, diversos estudios han evaluado su capacidad pronóstica refrendando su utilidad en este aspecto[2,3].

Por otro lado, la insuficiencia respiratoria crónica se asocia a una mayor tasa de mortalidad en los pacientes con enfermedad pulmonar obstructiva crónica (EPOC)[4]. La medición de la saturación de oxígeno periférico mediante oximetría de pulso (SpO_2) es fácil de realizar, y valores < 92% se correlacionan con la presencia de hipoxemia grave[5,6]. En base a ello, y con intención de analizar si añadir la medición de SpO_2 a los clásicos criterios de riesgo de GesEPOC mejoraría su capacidad pronóstica, realizamos un estudio retrospectivo de pacientes con EPOC estable seguidos en consulta monográfica de neumología. Fueron incluidos pacientes consecutivos diagnosticados de EPOC[7] y con historia de tabaquismo (consumo acumulado > 10 paquetes-año). Se registraron las siguientes variables obtenidas en la primera visita: función pulmonar, índice de masa corporal (IMC), grado de disnea según la escala mMRC, SpO_2 basal (realizada por el médico y recogida en situación de estabilidad clínica, respirando aire ambiente, en reposo y previa a la exploración física) e historial de exacerbaciones previo a la inclusión, considerando tanto las exacerbaciones moderadas (que requirieran tratamiento ambulatorio con antibióticos y/o esteroides) como las graves (que requirieran visita a urgencias o ingreso hospitalario). Se clasificó a los enfermos en AR y BR siguiendo los criterios actuales de la guía GesEPOC[1] (ante cualquiera de los siguientes criterios el paciente sería categorizado como de AR: FEV_1% < 50%, disnea ≥ 2 si está con tratamiento, 2 o más exacerbaciones moderadas o al menos una grave el año anterior), y se comparó con una clasificación en la que los pacientes de AR eran divididos en sujetos con SpO_2 < 92% (AR-SpO_2 < 92%) y SpO_2 ≥ 92% (AR-SpO_2 ≥ 92%). Se realizó un análisis de supervivencia mediante regresión de Cox para comparar ambas clasificaciones, obteniéndose el modelo 1 con la clasificación tradicional de GesEPOC y el modelo 2 incorporando a la clasificación la variable SpO_2. Los modelos fueron ajustados por edad y comorbilidad medida con el índice no ajustado de Charlson. Para la comparación de modelos se obtuvo el criterio de información Akaike (AIC). Se obtuvieron curvas de supervivencia ajustadas. La recogida de datos fue aprobada por el comité de ética de la investigación de Santiago-Lugo.

Se incluyeron 710 pacientes, de los cuales 632 eran varones (89%), con una media de edad de 68,3 ± 9,6 años, un FEV_1% postBD de 50,5 ± 17,2 y un IMC de 28,3 ± 5,2 kg/m^2. El 25,9% eran fumadores activos y el índice paquetes-año fue de 59,3 ± 30,7. El índice de comorbilidad de Charlson fue de 1,98 ± 1,41. Eran clasificados de AR 522 pacientes (73,5%) y 188 (26,5%) de BR. La SpO_2 media fue de 93,1 ± 4,6%. Ciento sesenta y cuatro (23,1%) presentaban SpO_2 < 92%, de los cuales 155 eran de AR. El tiempo seguimiento medio fue de 53,9 ± 26,7 meses.

La mortalidad total durante el seguimiento fue del 25,8%, con diferencias significativas entre el grupo BR y el AR (10,1% vs 31,5%: p < 0,0001, respectivamente). El grupo AR-SpO_2 < 92% presentó una mortalidad del 54,2%, frente al 21,9% en el grupo AR-SpO_2 ≥ 92% (p < 0,0001). En el análisis de regresión de Cox, en relación con el grupo de BR, los pacientes de AR-SpO_2 < 92% tienen mayor probabilidad de muerte (HR: 4,79; IC 95%: 2,90-7,91; p < 0,001) que los de AR-SpO_2 ≥ 92 (HR: 1,7; IC 95%: 1,02-2,80; p < 0,001) (tabla 1; modelo 2) (fig. 1).

En nuestro estudio, al añadir la variable SpO_2 a los criterios tradicionales de GesEPOC mejoramos su capacidad pronóstica y permite clasificar a los pacientes de forma más precisa en relación con el riesgo de fallecimiento.

Aspectos como la alteración de la ventilación-perfusión, la desregulación del centro respiratorio o la disfunción de los músculos inspiratorios por la hiperinsuflación pulmonar son factores que contribuyen al desarrollo de hipoxemia en los pacientes con EPOC, lo cual ensombrecerá el pronóstico vital de estos enfermos[8-11]. Un punto de corte de SpO_2 ≥ 92% permite descartar insuficiencia respiratoria con una alta sensibilidad, y SpO_2 ≤ 88% tiene una alta especificidad para confirmar esta[5,6]. De forma pragmática y con intención de no excluir a ningún paciente en situación de insuficiencia respiratoria usamos el valor de SpO_2 < 92%[5]. En base a ello, no todos cumplirían criterios para iniciar oxigenoterapia crónica domiciliaria (OCD), por lo que una intensa terapia broncodilatadora, la abstención tabáquica mantenida y un precoz inicio de la rehabilitación respiratoria aportaría hipotéticamente una mejora en los valores de SpO_2 basal[12-15] y, por ende, en su pronóstico vital.