bronchiolitis might account for the increased risk of developing non-small-cell lung carcinoma in our patient, although this association requires further confirmation. In conclusion, constrictive bronchiolitis should be included as a differential diagnosis of DCLD and it is speculated that it may determine an increased risk of lung cancer.

Bibliografía

1. Baldi BG, Carvalho CRR, Dias OM, Marchiori E, Hochhegger B. Diffuse cystic lung diseases: differential diagnosis. J Bras Pneumol. 2017;43:140–9, http://dx.doi.org/10.1590/S1806-37562016000000341.
2. Raoof S, Bondalapati P, Vydyula R, Ryu JH, Gupta N, Raoof S, et al. Cystic lung diseases: algorithmic approach. Chest. 2016;150:945–65, http://dx.doi.org/10.1016/j.chest.2016.04.026. Epub 2016 May 13.
3. Kawano-Dourado L, Baldi BG, Dias OM, Bernardi FD, Carvalho CR, Dolhnikoff M, et al. Scattered lung cysts as the main radiographic finding of constrictive bronchiolitis. Am J Respir Crit Care Med. 2012;186:294–5, http://dx.doi.org/10.1164/ajrccm.186.3.294.
4. Herbst RS, Heymach JV, Lippman SM. Lung cancer. N Engl J Med. 2008;359:1367–80, http://dx.doi.org/10.1056/NEJMra0802714.

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Calcified Pulmonary Nodules in an Oncological Patient

Nódulos pulmonares calcificados en un paciente oncológico

Dear Director:

A 50-year-old female patient underwent thoracic and abdominal computed tomography examinations for oncological follow-up. The images showed multiple lung nodules, some of which were calcified (Fig. 1A and B), a calcified hepatic mass, and an expansile osteolytic lesion with internal foci of calcification on the ischiopubic ramus of the right hip (Fig. 1C). The patient had undergone colonoscopy 3 years previously due to rectal bleeding, which showed an exophytic and stenosing rectal lesion. The biopsy findings were compatible with well-differentiated tubular adenocarcinoma. Surgical resection confirmed the anatomopathological diagnosis and identified vascular and perineural invasion with metastasis to the peritumoral lymph nodes. The patient started chemotherapy at that time. Our main question was whether

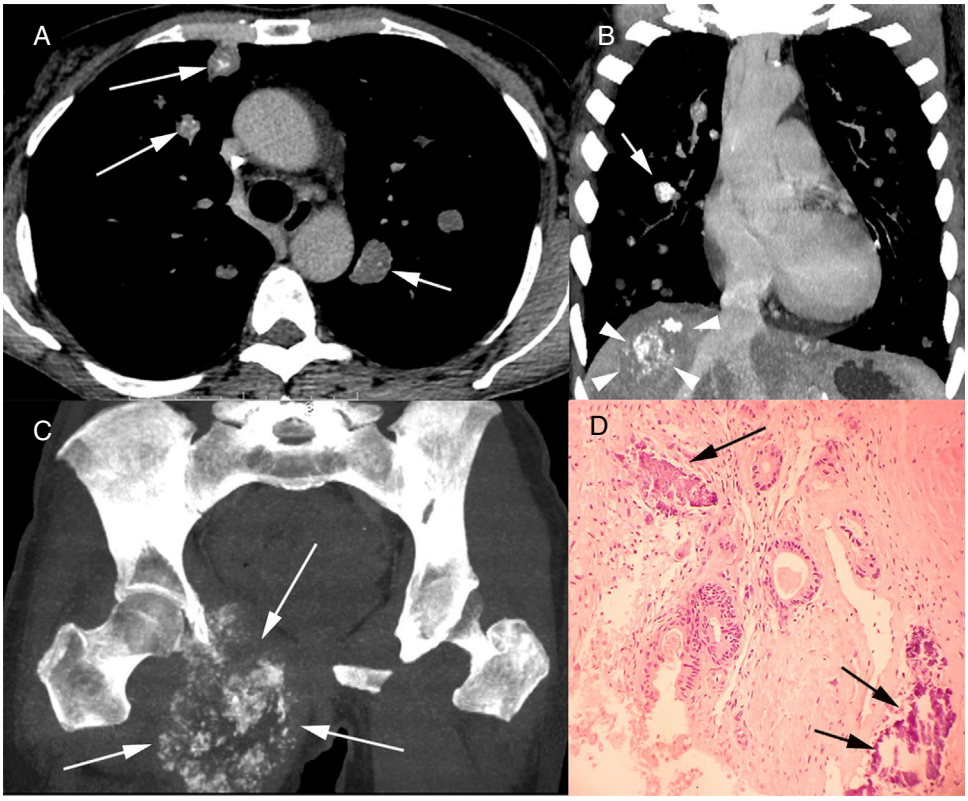

Fig. 1. Chest computed tomography with axial (A) and coronal (B) reconstruction showing multiple pulmonary nodules, some with calcification (arrows). Note also in B a calcified mass in the right lobe of the liver (arrowheads). In C, computed tomography of the pelvis with coronal acquisition MIP reconstruction, showing an osteolytic lesion with internal foci of calcification (arrows) and invasion of surrounding soft tissue. In D, histological section of the pulmonary nodule demonstrating atypical neoplastic glands infiltrating the connective tissue amid desmoplastic stroma. Note also the amorphous basophilic material, compatible with extracellular deposition of calcium adjacent to the neoplastic process (arrows; hematoxylin and eosin stain, ×100).

the new lesions were metastases of the rectal tumor or corresponded to a new tumor (e.g., bone sarcoma with pulmonary and hepatic metastases), which would imply the need to change the treatment strategy. Biopsies of the bone lesion and a pulmonary nodule were performed, and showed metastatic adenocarcinoma with a tubuloacinar pattern (Fig. 1D).

Calcification of a pulmonary nodule is usually suggestive of its benign nature – such nodules are most commonly granulomas and less commonly hamartomas – but calcification and ossification can also occur in malignant lesions. Multiple pulmonary nodules have numerous etiologies, but the diagnostic possibilities are considerably reduced when these lesions show calcification. The main diagnostic considerations are calcified pulmonary metastases, amyloidosis, hyalinizing granulomas, epithelioid hemangioendothelioma, necrobiotic nodules, and multiple chondromas. Amyloidosis, in its nodular form, is usually asymptomatic. The definitive diagnosis is made by histopathology, on the basis of the finding of deposition of amyloid, which stains with Congo red and shows apple-green birefringence under polarized light. Hyalinizing granulomas are rare fibrotic pulmonary lesions, usually associated with autoimmune phenomena related mainly to exposure to mycobacterial or fungal antigens. Epithelioid hemangioendothelioma is a rare multifocal pulmonary neoplasm of endothelial origin. It is considered to be a sarcoma of low aggressiveness. Necrobiotic nodules can develop in patients with pneumoconiosis associated with rheumatoid arthritis. Calcification in pulmonary chondromas is a common radiological finding. The association of these chondromas with gastrointestinal stromal tumors and extra-adrenal paragangliomas is known as the Carney triad.[1–3]

The calcification of pulmonary metastases is very uncommon. The tumors that most commonly give rise to calcified metastases are sarcomas (osteosarcoma, chondrosarcoma, synovial sarcoma, and giant cell tumor of the bone), carcinomas (particularly mucinous and papillary adenocarcinomas), and treated metastatic choriocarcinoma. Several mechanisms are responsible for the calcification of metastases: bone formation in tumor osteoid in osteosarcoma; calcification and ossification of tumor cartilage in chondrosarcoma; dystrophic calcification in papillary carcinoma of the thyroid, giant cell tumor of the bone, synovial sarcoma, and treated metastatic tumors; and mucoid calcification in mucinous adenocarcinoma of the gastrointestinal tract and breast. Calcification can develop in metastases of several other tumors after chemotherapy or radiotherapy, generally secondary to degeneration, hemorrhage, and necrosis.[1,4,5] Although tubular-type adenocarcinoma is not listed among the major causes of calcified metastases, the patient described here had undergone previous chemotherapy, which may have been the mechanism for calcification formation.

Bibliografía

1. Maile CW, Rodan BA, Godwin JD, Chen JTT, Ravin CE. Calcification in pulmonary metastases. Br J Radiol. 1982;55:108–13.
2. Marchiori E, Souza JRAS, Franquet T, Müller NL. Diffuse high attenuation pulmonary abnormalities: a pattern-oriented diagnostic approach on high resolution CT. AJR. 2005;184:273–82.
3. Marchiori E, Zanetti G, Hochhegger B. Multiple calcified nodules. J Bras Pneumol. 2016;42:1.
4. Seo JB, Im JG, Goo JM, Chung MJ, Kim MY. Atypical pulmonary metastases: spectrum of radiologic findings. Radiographics. 2001;21:403–17.
5. Chan ED, Morales DV, Welsh CH, McDermott MT, Swarz MI. Calcium deposition with or without bone formation in the lung. Am J Respir Crit Care Med. 2002;165:1654–69.

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Las alteraciones en el pico de fusión de las sondas de hibridación usadas para el genotipado en la deficiencia de alfa-1 antitripsina no siempre implican errores

Changes in the Melting Point of Hybridization Probes Used for Genotyping in Alpha-1 Antitrypsin Deficiency Do Not Always Imply Errors

Estimado Director:

El análisis molecular del gen que codifica la alfa-1 antitripsina (AAT; gen *SERPINA1*) es la aproximación de referencia para la identificación de las variantes alélicas[1]. Entre los diferentes métodos moleculares que pueden emplearse para este fin se encuentran las denominadas sondas de hibridación o *HybProbes*[2], las cuales permiten realizar un seguimiento de la PCR a tiempo real y, una vez terminado el proceso de amplificación, obtener información sobre las variantes genéticas presentes en una determinada región dentro del amplicón. Se trata de un ensayo de genotipado homogéneo, es decir, todo el proceso ocurre en un solo tubo sin manipulaciones adicionales entre el inicio del ensayo y la observación de los resultados. Sin embargo, aunque es una técnica muy segura, en ocasiones podemos encontrarnos con errores sobre todo en la interpretación de los resultados[3].

En el transcurso de un análisis centrado en la prevalencia de las variantes *no-S/S* y *no-Z/Z* del gen *SERPINA1* en una población clínica de La Palma (Islas Canarias, España), con una muestra de 1.510 pacientes reclutados para este estudio independientemente del motivo que les llevó a la consulta de neumología, se detectaron 7 sujetos en los que las sondas *HybProbe* diseñadas para identificar las variantes *no-S/S* producían un pico de fusión desplazado con respecto a los picos normalmente registrados (fig. 1). En estos 7 pacientes se habían diagnosticado diversas patologías respiratorias, como enfermedad pulmonar intersticial difusa, síndrome de apnea-hipopnea del sueño o enfermedad pulmonar obstructiva crónica.

Para descartar un error en el proceso de genotipado debido a diferencias en la concentración salina de las 7 muestras de ADN afectadas, estas se volvieron a preparar y analizar, pero el software de genotipado de la plataforma de PCR a tiempo real (*LightCycler* 480) seguía asignando estas muestras a un grupo de genotipo diferente a los definidos por los estándares, utilizando los valores umbrales de similitud y resolución por defecto de la aplicación informática. El examen de las temperaturas de fusión indicaba una clara diferenciación entre los picos de fusión de