Occurrence of Pleural Masses in a Chronic Pleural Pyothorax

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A 74-year-old man, nonsmoker, presented with asthenia, inappetence, weight loss (about 10 kilograms in the last 6 months), right chest pain and some episodes of hemoptysis without fever.

Routine laboratory tests showed increased ESR (107 mm/h) and LDH (783 UI/L). Serum tumor markers (CEA, CA19.9) were negative. In 1958, the patient had undergone artificial right pneumothorax for tuberculosis with development of a chronic right pyothorax (Figure 1A).

A more recent chest CT confirmed the presence of a huge right pyothorax surrounded by a fibrous wall with calcifications and different nodular masses (up to 5 cm across) with soft-tissue enhancement determining external compression of the medium and lower lobar bronchi (Figure 1B). The patient underwent a transthoracic biopsy of the masses. At histology, biopsy showed a monotonous proliferation of medium-to-large cells with evident nucleoli in a necrotic and hemorrhagic background (Figure 1C). Tumor cells were positive for LCA, CD20, CD3, CD79a and PAX-5, but negative for cytokeratins, CD138, CD30, ALK, HHV-8, MPO, CD68. Labeling index by MIB-1 was very high (85%) and EBER probe by in situ hybridization showed numerous stained nuclei then confirming the presence EBV genome. A diagnosis of pyothorax-associated large B cell lymphoma was performed. The patient, alive with disease, appeared in a very poor performance status and denied any further therapy.

DISCUSSION

Pyothorax-associated lymphoma (PAL) is a rare distinct variant of diffuse large B-cell lymphoma first described in 1987 by Aozasa et al. It mainly occurs in 60–70 year-old Japanese people, and much more rarely in Caucasian patients, with marked male gender prevalence and a longstanding history (20–67 years) of pyothorax or chronic pleuritis due to artificial pneumothorax for pleuro-pulmonary tuberculosis.[2]

Patients clinically present with weight loss and chest pain, while imaging studies reveal pleural effusion and pleural thickening and/or masses. High level of serum NSE has been observed in some cases, then erroneously suggesting a small-cell carcinoma.[2]

At morphology, PAL appears as a monotonous proliferation of medium-to-large sized nucleolated cells with amphophilic cytoplasm and immunoblastic/plasmablastic appearance. These cells show a very high labeling index by Ki-67/MIB-1 (80–90%) and are positive for pan-B markers (CD20, CD79a, PAX-5) also variably co-expressing T-cell markers (CD2, CD3, CD7) and CD138, but not CD30 and ALK, then revealing a post/late germinal center B cell derivation.[3]

PAL seems to be driven by EBV infection or less frequently by HHV-8. So, EBV may be likely detected by LMP-1 or EBNA2 expression or EBER probe by in-situ hybridization.[2,4]

Differential diagnosis on clinical and imaging grounds is quite broad. Primary pleural solid (mesothelioma, solitary fibrous tumors, synovial sarcoma, angiosarcoma) or metastatic tumors may mimic PAL. Correct diagnosis always require knowledge of the patient past medical history (tuberculous pleuritis treated by pneumothorax), a good biopsy (even obtained by transthoracic needle biopsy as first reported in our case) and appropriate ancillary studies (immunohistochemistry and molecular analysis). Once lymphoma is suspected, differential diagnosis should mainly posed in regards with primary effusion lymphoma (PEL). This latter, by contrast, occurs in patients with HIV infection clinically presenting with massive effusions of the body cavities without evidence of neoplastic masses. PEL cells are negative for B-cell and T-cell markers, whereas they express HHV-8 but not EBV in virtually all cases.

Although no well-established therapy exists and prognosis is very dismal (5-year survival accounts for 21.6% in the largest series),[5] PAL patients are generally treated by different combinations of chemotherapy and radiotherapy. Of note, local irradiation seems to control the disease.[2,5]

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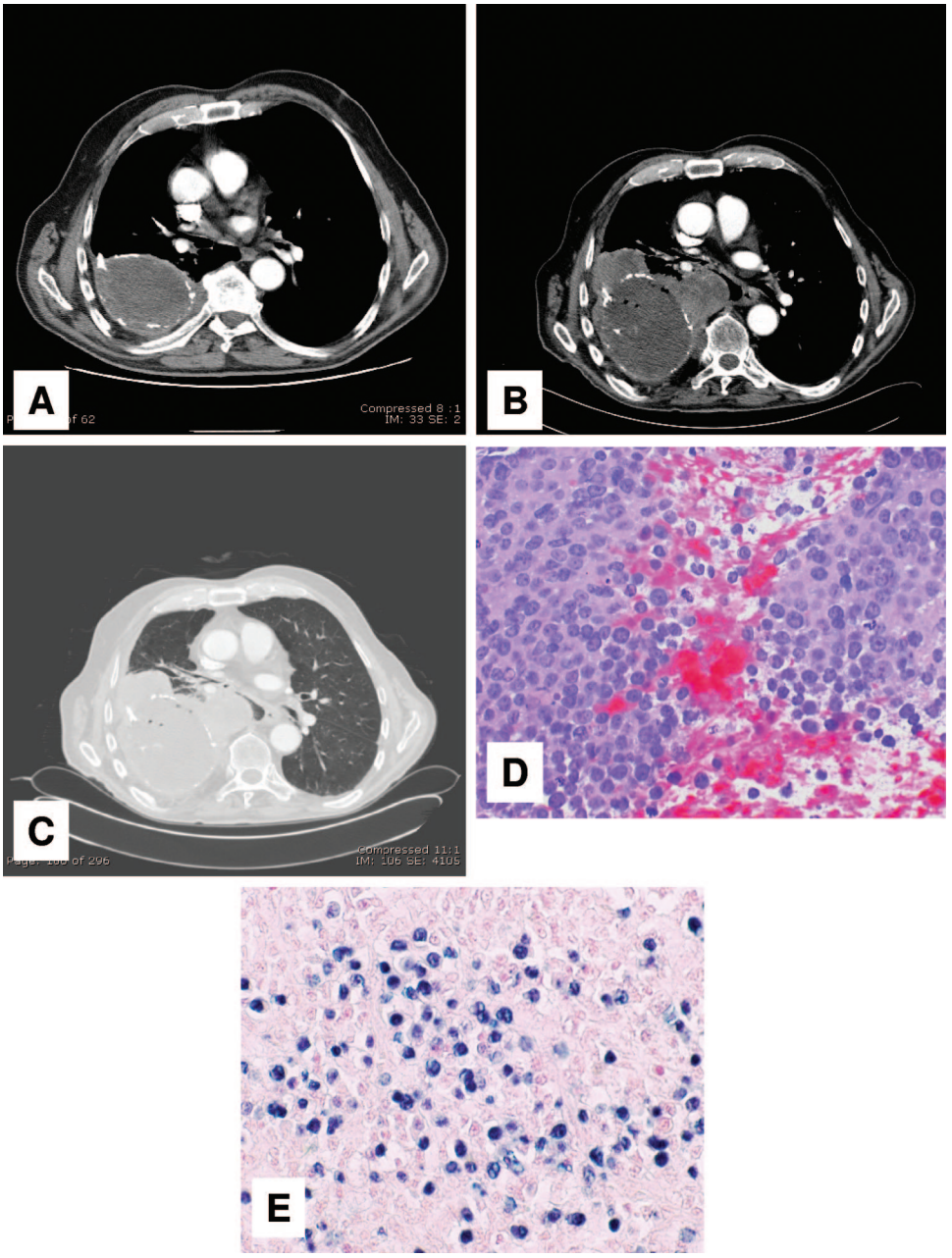

FIGURE 1. Chest CT (performed in 2003) showing a right pleural pyothorax with peripheral calcifications (**A**). A recent chest CT (in May 2007) revealing the presence of nodular masses with homogeneous nonenhancing soft tissue signal attenuation developed around the pyothorax and infiltrating the lung parenchyma (**B, C**). Histologic examination of the masses consisted of a monotonous proliferation of medium-to-large lymphoid cells (**D**, hematoxylin-eosin X200) showing positive nuclear staining for EBV (**E**, EBER probe, in-situ hybridization X200).

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