activation during transition to expiration may be a plausible interpretation that would explain the persistence of asynchrony and improvement with progressive depressurization.

References


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NUT Midline Carcinoma of the Lung, A Rare Form of Lung Cancer

Carcinoma NUT pulmonar, una forma poco frecuente de cáncer de pulmón

Dear Editor:

Nuclear carcinoma of the testis (NUT) is very rare tumors with specific genetic changes that progress very aggressively. They often affect children and young adults. They may occur in different organs, but they are characteristically located in the midline of the head and neck. Very few cases have been published that describe this entity in the lungs and mediastinum.

We report the case of a 23-year-old man, smoker of about 10 cigarettes/day, who presented in our hospital with a 2-week history of pain in the right hemithorax radiating to the shoulder, and asthenia. Computed tomography (CT) showed increased density without air bronchogram occupying the posterior and apical segments of the right upper lobe (RUL) with amputation of the corresponding segmentary bronchi, paratracheal mediastinal lymphadenopathies, and significant right pleural effusion (Fig. 1). Given these findings, a positron emission tomography (PET) was performed, revealing a metabolically positive mass in the RUL, with extensive pleural involvement in the same side, mediastinal lymph node involvement, and bilateral supra/infracavicular lytic bone lesions and metastasis. Fiberoptic bronchoscopy revealed complete stenosis of the posterior and apical segments of the RUL bronchi due to thickened, hypervascularized mucosa, possibly of a neoplastic origin. Diagnostic confirmation was obtained from a pleural biopsy obtained by thoracoscopy. The pathology report described a neoplasm formed of nests of undifferentiated cells, and, along with this cell population, abrupt areas of squamous differentiation. The

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undifferentiated tumor cells showed positive immunoreaction to NUT antibody and pancytokeratin (Fig. 1).

Given the definitive diagnosis of NUT carcinoma, the patient received 2 cycles of palliative chemotherapy with cisplatin and etoposide, and then started BET inhibitor therapy in a clinical trial setting. The oncological disease did not respond to treatment, and the pulmonary mass increased in size, with compression of the superior vena cava and pericardial effusion. The patient died 3 months after the initial diagnosis.

NUT carcinomas are poorly differentiated and genetically defined by the presence of a genetic rearrangement of the NUT gene, consisting of a chromosomal translocation between this gene (NUTM1) located in the chromosome 15q14 and other genes (BRD4 in chromosome 19p13.1 [70%], BRD3 in chromosome 9q34.2 [6%] or an unknown gene [24%]). The incidence is unknown, but this tumor is considered rare. It was originally thought to be a disease of children and young adults, but subsequent publications have shown that NUT carcinoma can equally affect individuals of any age and both sexes.

The tumor generally occurs in the midline structures, usually associated with the upper gastrointestinal tract, but it has been identified in other sites. According to reports in the literature, only 38 cases of primary intrathoracic NUT are known, of which 19 were of pulmonary origin.

In histopathological terms, it is very similar to squamous carcinoma, and therefore may be underdiagnosed. If NUT is suspected, diagnostic confirmation is obtained with immunohistochemical techniques, as in our patient, or by the detection of chromosomal rearrangement of the specific NUT variants.

To date, no specific treatment exists for NUT carcinoma. The rapid growth and aggressivity of this tumor rules out surgical treatment, and it does not appear to respond to most chemotherapeutic regimens and/or radiation therapy, although the best option appears to be a combination of gemcitabine, docetaxel and cisplatin. Some promising therapies, such as vorinostat and BET inhibitors, are currently under study and perhaps these will provide an effective treatment in the future. However, the current prognosis for this entity is death after a mean period of survival of around 7 months, as occurred in our case. To conclude, NUT carcinoma is extremely rare and very aggressive, so early clinical suspicion of this entity of utmost importance to avoid delays in establishing the most specific treatment possible in the shortest time.

References

Radiological Diagnosis of Pulmonary Tumor Thrombotic Microangiopathy: A Non-bronchial Cause of “Tree-in-Bud” Pattern on Computed Tomography

Diagnóstico radiológico de microangiopatía trombótica tumoral pulmonar: una causa no bronquial de patrón de árbol en brote en tomografía computarizada

Dear Editor,

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare and generally fatal form of pulmonary tumor embolism that generally presents with rapidly progressing dyspnea in patients with disseminated malignant disease. Clinical diagnosis is difficult, and unfortunately PTTM is generally only confirmed post mortem.¹ ²

We report the case of a 58-year-old man, former smoker (20 pack-years), who presented with a 2-week history of progressive dyspnea and dry cough. Significant clinical history included prostate adenocarcinoma (Gleason score 6), treated with radiation therapy with curative intent 6 years previously, with no biochemical evidence of tumor relapse. Clinical examination revealed tachypnea and fine crackles on auscultation. Basal oxygen saturation was 88% and laboratory test findings did not suggest infection, although D-dimer levels were elevated. A chest radiograph showed bilateral diffuse interstitial involvement and prominent lung hila. Chest CT angiogram ruled out embolism on the main pulmonary, lobar or segmentary arteries, although multiple mediastinal and hilar lymphadenopathies were detected, along with severe interstitial involvement consistent with thickening of the subpleural pulmonary interstitium (Fig. 1A) and the presence of numerous centrilobular nodules and “tree-in-bud” images (Fig. 1B and C).

Multiple focal bone lesions, predominantly sclerotic, were also observed in the vertebrae and sternum, consistent with metastasis (Fig. 1D). Given these radiological findings, PTTM secondary to prostate adenocarcinoma was suggested as an initial diagnosis, although other possibilities such as sarcoidosis or infection with an unusual pathogen were not ruled out. Four days after admission, the patient developed rapidly progressing respiratory failure that required urgent intubation. A few hours later, he suffered an episode of cardiorespiratory arrest with asystole and died despite prolonged attempts at cardiopulmonary resuscitation. The diagnosis of PTTM was confirmed on autopsy, which revealed an unsuspected undifferentiated occult gastric “signet ring” adenocarcinoma, with extensive metastases and multiple tumor embolisms in the small-caliber peripheral pulmonary arteries.

PTTM is a rare form of pulmonary arterial tumor embolism, in which small tumor cell embolisms cause fibrocellular proliferation in the intima of small-caliber pulmonary arteries. These changes lead to stenosis/occlusion of the pulmonary arteries and a subsequent rise in pulmonary vascular resistance, which in turn leads to rapidly progressing precapillary pulmonary hypertension.³ Clinically, patients tend to develop acute/subacute cor pulmonale and respiratory failure. Most patients who develop PTTM have

Fig. 1. (A) Axial image of chest CT (pulmonary parenchymal window) showing linear thickening of the subpleural lung interstitium (arrows). (B) Maximum intensity projection (MIP) axial reconstruction (pulmonary parenchymal window) of left lung, showing a peripheral “tree-in-bud” pattern consisting of linear opacities forming predominantly subpleural branches (circled). See also the presence of small centrilobular nodules (arrow). (C) MIP coronal reconstruction (pulmonary parenchymal window) of the left lung, also showing the “tree-in-bud” pattern (circled). (D) Chest CT sagittal image (bone window) revealing multiple focal bone lesions (arrows) in the sternum and several vertebrae, consistent with bone metastases.