

Hypermetabolic bone on ^{18}F -FDG-PET/CT in a patient with lung cancer: Is it always metastasis?*



Hipercaptación ósea en

To the Editor:

We report the case of 77-year-old man, former smoker with a cumulative index of 50 pack-years, history of dyslipidemia, IgG lambda monoclonal gammopathy of uncertain significance (MGUS) (monoclonal component [MC]: 4.8 g/l) diagnosed in 2014, stable, with no evidence of progression, monitored annually by hematology, and moderate COPD, non-frequent exacerbator phenotype, receiving bronchodilator therapy, with mMRC dyspnea grade 1, and no previous admission due to exacerbation, and no respiratory symptoms or accompanying constitutional syndrome. In November 2017, after a routine chest X-ray revealed a solitary pulmonary nodule, a computed tomography (CT) scan of the chest was performed that showed a spiculated nodule measuring 13 mm in the anterior segment of right upper lobe (Fig. 1), in contact with the pleura, and with retraction of the adjacent horizontal fissure. Laboratory blood tests (biochemistry, including total proteins, immunoglobulins, serum proteins, free light chain index, complete blood count, and coagulation) were normal. A positron emission tomography (^{18}F -FDG-PET/CT) showed a solid hypermetabolic nodule (spiculated SUVmax 7.5) measuring 14 mm in punctiform contact with the pleura and fissure, suggestive of primary neoplastic etiology (Fig. 1). Multiple hypermetabolic bone lesions of lytic component were observed at the distal end of the right clavicle (SUVmax 8.4) (Fig. 1) and in the D3 vertebral body, and lesions with a blastic appearance were seen in the left femoral head/neck union (SUVmax 12). These lesions were initially thought to have a metastatic origin. Moreover, an irregular tracer distribution was described in other bony structures that could not be attributed to morphological lesions, and discrete metabolic activity was detected in the sternal manubrium, so a secondary etiology

could not be ruled out. A CT-guided transthoracic biopsy of the lung lesion was then performed, which was positive for adenocarcinoma of pulmonary origin. To complete staging (T1BN0Mx), we decided to obtain a biopsy of the lytic lesion in the right clavicle. This was positive for plasma cell cancer, consistent with plasmacytoma/multiple myeloma (MM).

After receiving the results of the bone biopsy, the disease was reevaluated, showing stable MC (6.6 g/l), with no other laboratory abnormalities. A 24 h urine study was negative, and bone marrow aspirate showed 15 % infiltration of plasma cells with atypical morphology (anisocytosis with predominance of large, multinucleated cells, occasionally with visible nucleoli), irregularly distributed, with areas of abnormal phenotype of up to 25 %. The study was completed with a whole-body magnetic resonance imaging (MRI) scan that showed focal lesions in the T3 vertebral body and in the distal end of the right clavicle, highly suggestive of an infiltrative process, with a suspicion of diffuse spinal medullary infiltration in the T4-L4 segment.

The patient was diagnosed with concomitant lung adenocarcinoma T1BN0M0 (TNM 7th edition) and MGUS transformed to symptomatic IgG lambda-type oligosecretory multiple myeloma with bone involvement, ISS stage I.

The patient had IgG lambda MGUS, an entity that occurs at a prevalence of 1–3 %. It is defined as the incidental finding of a monoclonal component in serum in a patient without diagnostic criteria for multiple myeloma, Waldenström macroglobulinemia, amyloidosis, or other lymphoproliferative disorders, and must meet the following diagnostic criteria: serum MC < 30 g/l, plasma cells in bone marrow < 10 %, and absence of lesions in target organs (CRAB criteria: hypercalcemia, renal failure, anemia, bone lesions, amyloidosis). The risk of progression to multiple myeloma or amyloidosis is 1 % per year, with a real probability of malignant transformation at 20 years of 11 %. Factors associated with a greater risk of progression are the level of MC, IgA type, altered free light chain index (kappa/lambda), progressive type, and presence of aberrant phenotype in > 90 % of plasma cells in the bone marrow.^{1,2}

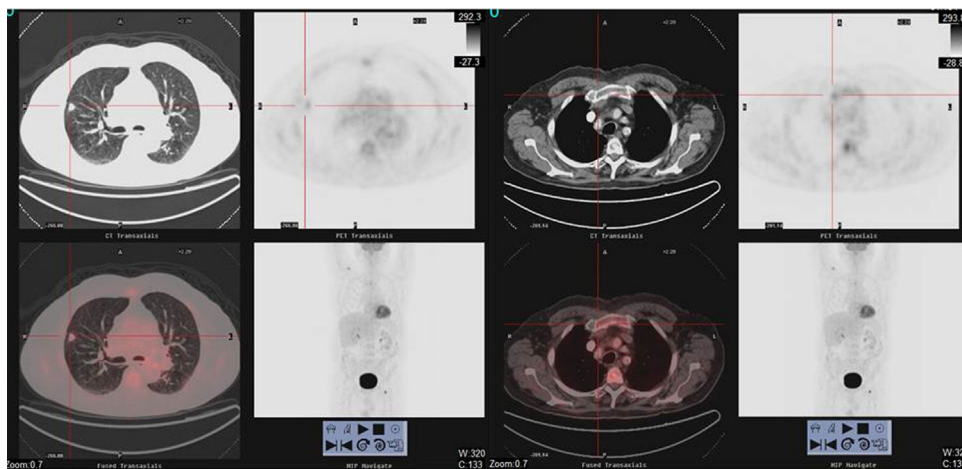


Fig. 1. ^{18}F -FDG PET/CT scan images showing (on the left) a solid spiculated hypermetabolic nodule (SUVmax 7.5), in punctiform contact with the pleura and the fissure, measuring about 14 mm, located in the anterior segment of the right upper lobe. Hypermetabolic bone lesion (on the right) with lytic component at the distal end of the right clavicle (SUVmax 8.4).

* Please cite this article as: Martín-Ontiyuelo C, Sánchez-Font A, Gimeno E, Suárez-Piñera M, Curull V. Hipercaptación ósea en ^{18}F -FDG-PET/TC en paciente con cáncer de pulmón, ¿es siempre una metástasis? Arch Bronconeumol. 2020;56:51–52.

Multiple myeloma is characterized by >10 % bone marrow infiltration by plasma cells that secrete MC in serum and/or urine, along with cytokines that can cause bone lesions. Incidence is 3–5 cases/100,000 inhabitants/year, and the average age of patients is 65 years. Symptomatic multiple myeloma is defined as the presence of MC in serum and/or urine, plasma cell infiltration of the bone marrow or plasmacytoma and evidence of organ damage (CRAB), while asymptomatic multiple myeloma is defined as the presence of MC in serum and/or urine and plasma cell infiltration in bone marrow/plasmacytoma with no organ damage (CRAB).^{1–4}

The patient received 5 sessions of stereotactic radiation therapy to the lung lesion (total dose: 55 Gy). He remained disease-free at 15 months, and subsequently initiated treatment with curative intent with lenalidomide and dexamethasone, achieving complete MM remission after 12 cycles of treatment.

In conclusion, patients with a history of MGUS who present bone lesions (although initially attributed to metastatic origin) and who remain asymptomatic should undergo guided bone biopsy, whenever possible, to rule out metastatic disease and/or progression to MM, since the therapeutic approach and the prognosis of the disease vary greatly, ranging from proposed palliative treatments to curative attempt. In these cases, multidisciplinary study and follow-up of patients is essential in order to optimize the diagnostic and therapeutic procedures.

References

1. Swerdlow SH, Campo E, Lee Harris NL, Jaffe ES, Pileri SA, Stein H, et al. WHO classification of tumours of hematopoietic and lymphoid tissues, 2, 4th edition; 2017.
2. Baldini L, Guffanti A, Cesana BM, Colombi M, Chiorboli O, Damilano I, et al. Role of different hematologic variables in defining the risk of malignant transformation in monoclonal gammopathy. *Blood*. 1996;87:912–8.
3. Mateos MV, Bladé J, Lahuerta JJ, San Miguel J. Tratamiento del mieloma múltiple asintomático: recomendaciones del Grupo Español de Mieloma. *Med Clin (Barc)*. 2017;148:517–23.
4. Go R, Rajkumar S. How I manage monoclonal gammopathy of undetermined significance. *Blood*. 2018;131:163–73.

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<https://doi.org/10.1016/j.arbr.2019.06.010>

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Not Cancer After All: Two Rare Cases of IgG4-Related Lung Disease



Al final, no era cáncer: dos casos infrecuentes de enfermedad pulmonar relacionada con IgG4

Dear Editor,

IgG4-related disease (IgG4-RD) is an uncommon systemic disorder characterized by sclerosing lesions that can affect almost any anatomical site.¹ Pulmonary involvement has highly variable clinical and radiological presentations.² Although IgG4-related lung disease is usually preceded or accompanied by multi-organ involvement,³ rare cases of solely lung involving IgG4-RD have been described.^{4–6} Herein, we report two biopsy-proven cases of IgG4-RD with lung mass as the sole radiographic presentation.

64-Year-old man with a 27 mm spiculated mass in the right upper lobe on computed tomography (CT) in the setting of chronic cough with hemoptoic sputum. He was a previous smoker (100 pack-year of smoking). Bronchoscopy showed neither signs of bleeding nor morphological anomalies and bronchoalveolar lavage (BAL) was negative for malignant cells and acid-fast bacilli. Further investigation with positron emission tomography (PET) demonstrated a right upper lobe nodule with standardized uptake value (SUV) max of 2.6. Due to the high suspicion of primary lung malignancy, biopsy of the nodule was performed by transthoracic needle aspiration (TTNA), documenting a fibrocollagenous lesion with lymphoplasmacytic infiltration and wall thickening of venous-type vessels. On immunohistochemistry, the number of IgG4-positive plasma cells was >20 per high

power field (HPF) and immunostaining for CD20 and CD3 was positive. The serum concentrations of total IgG and IgG4 were normal.

71-Year-old man who presented with posterior upper thoracic pain for 2 years. He is an active smoker with 50 pack-year of smoking. Chest CT detected a 35 mm spiculated mass in the right upper lobe, which was biopsied by TTNA. Histological examination demonstrated a nodular lesion with total architectural distortion due to fibrosis and lymphoplasmacytic infiltration. On immunohistochemistry, the number of IgG4-positive plasma cells was >30 per HPF. Given the suspicion of IgG4-RD further workup was performed, showing elevated serum concentrations of IgG4 and normal concentrations of total IgG. PET demonstrated a right upper lobe nodule with SUV max of 3.1 and BAL pathological analysis was negative for malignant cells. Hence, in both cases the diagnosis of IgG4-RD was established based on clinico-pathological correlation.

Both patients started corticosteroid therapy with an initial prednisolone dosing of 0.6 mg/kg/d for 4 weeks. Patient 1 had a poor compliance to the treatment and presented no improvements after 2 months (Fig. 1). Patient 2 showed clinical improvement and a reduction of the mass' dimensions on CT imaging after 3 months of treatment (Fig. 2). The prednisolone dose was tapered by 10 mg/kg/d after the first and third month of therapy, maintaining 10 mg/d at the present time.

Although the epidemiology of IgG4-related lung disease (IgG4-RD) remains poorly described,⁷ it usually occurs in male adults with an average age of 69 years.⁸ Its clinical presentation depends on the location of the lesion, nonetheless half of patients present nonspecific respiratory symptoms, whereas the remaining present abnormalities on imaging studies in the absence of symptoms.^{2,8}