Patient with diffuse idiopathic hyperplasia of neuroendocrine cells of the lung (DIPNECH) and bilateral nodules: Therapeutic dilemma☆

Paciente con hiperplasia difusa idiopática de células neuroendocrinas de pulmón (DIPNECH) y nódulos bilaterales: dilema terapéutico

Diffuse idiopathic hyperplasia of neuroendocrine lung cells (DIPNECH) is an uncommon premalignant entity, described by the histological presence of groups of at least five neuroendocrine cells without exceeding the basement membrane of the bronchial epithelium, in three bronchioles, and associated with a minimum of three extraluminal local proliferations (tumorlets or carcinoid tumours).[1]

There is controversy regarding the pathophysiology and management of this condition. Some aspects of the aforementioned definition have even been questioned more recently, and histopathological confirmation could be dispensed with, while adding respiratory clinical criteria and considering this condition as a primary entity or simply reactive to other pulmonary conditions.[2] In addition, its diagnosis is usually accidental (incidental radiological or pathological finding of resected surgical pieces), this being an underdiagnosed pathology with few published cases.[3]

The condition mainly affects adult females.[2] Clinically, it is characterised by coughing, dyspnoea, wheezing, and obstructive spirometric changes, due to hyperplastic obstruction of the bronchial lumen and the secretion of vasoactive amines. This fact is the one that most clearly indicates its prognosis. On the other hand, the possibility of progression to low- and medium-grade malignancies (classically typical and atypical carcinoid tumours, since progression to other histological lineages has not been demonstrated), may cast a shadow over their evolution.[4] Radiologically, this condition is characterised by the presence of a mosaic attenuation pattern (with or without bilateral nodules), although these findings lack great specificity.[5]

Given the scarce scientific evidence and the absence of unified criteria for the management of DIPNECH,[2] we present a clinical case, with the intention of opening up a debate on the best therapeutic approach.

This case was a 67-year-old female patient, allergic to Ibuprofen, with a history of pulmonary tuberculosis infection treated in childhood, recurrent pneumonia and occasional dry cough, The patient received treatment at our centre for severe thoracic trauma with multiple rib fractures, while detecting the presence of pulmonary nodules in emergency tomography (CT scan). After adequate evolution, the patient was discharged pending an outpatient-directed study to run the following additional tests for the correct characterisation of lung lesions:

- High-resolution thoracic CT scan: confirmed the presence of two polylobed solid central nodules, 14 mm in LID and another, 6 mm in LSI, both associated with areas with a ground glass pattern. No significant lymphadenopathy was detected.
- PET-CT: described identical CT findings. Nodules with a slight increase in FDG uptake (SUVmax 1.79), with infiltrative characteristics. Gallium PET-CT was suggested in order to achieve greater sensitivity to possible hidden neuroendocrine tumours.[6]
- Echobronchoscopy: the only finding was a 4.8 mm oval adenopathy in 4R location, which was punctured, finding no evidence of malignancy.
- Gallium PET-CT: showing overexpression of somatostatin receptors (SUVmax 2.99) in the major nodule.

As a result of all these findings, neuroendocrine origin of the pulmonary nodules was suspected.

Respiratory function tests were compatible with a non-reversible obstructive pattern (FVC 123%, FEV1 71%, DLCO 86%).

Presented to the multidisciplinary lung tumour committee, surgical resection of the larger lesion was indicated, performing an anatomical segmentectomy of the right segment 6 and robotic lymphadenectomy. The patient had good progression and was discharged on the third postoperative day.

The pathology report describes a typical 15 mm carcinoid tumour with free resection margins with no atypia, necrosis, or vascular invasion. The presence of foci of idiopathic diffuse hyperplasia of neuroendocrine cells in non-tumoral lung parenchyma (DIPNECH) was identified.

The committee ruled out adjuvant treatment for the resected nodule, and follow-up was indicated. The indication to resect or not the remaining nodule in the central location of the LSI was discussed. Located between the lingula and the culmen and measuring 6 mm, the nodule was of probable synchronous neuroendocrine origin but without histological confirmation.

Taking into account the size of the lesion, it should be remembered that the size limit for tumorlets is 5 mm, and therefore the treatment of this lesion must be based on surgical excision in the event of a carcinoid tumour.[2] However, the presence of DIPNECH demonstrated in the study of the specimen suggested the possibility of successive appearance

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of new lesions of neuroendocrine origin in revisions; subsidiary to other resections in the future. Possibly, the idea of having to perform a lobectomy in the end, to avoid a probable typical subcentimetre carcinoid (while the condition remained stable) was excessive in this case, in addition to the possibility of exacerbating the effects on respiratory functional changes typical of DIPNECH.

Other therapeutic options such as stereotactic radiotherapy or radiofrequency could be discussed, although its central location and probable neuroendocrine histology ruled out these techniques in practical terms. Systemic treatments were also ruled out due to the patient's scarce symptoms. The patient will continue with clinical and tomographic surveillance. Several series have indicated symptomatic improvement through treatment with somatostatin analogues, especially Octreotide,[6] which, in the case of coexistence with a neuroendocrine tumor, could decrease it in size. In the case of indolent progression, some recommend control by CT without contrast every 2 years, although in lesions larger than 1 cm, the possibility of closer control has been considered, given the greater possibility of malignancy.[7]

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