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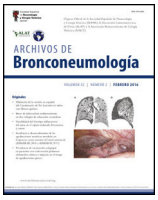

Scientific Letter

Association between idiopathic pulmonary fibrosis and lung cancer☆

Asociación entre fibrosis pulmonar idiopática y neoplasia pulmonar

To the Editor

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive form of fibrosing interstitial pneumonia, characterized by progressive symptomatic and functional worsening, with no clearly determined etiological profile. IPF is associated with passive smoking, gastroesophageal reflux, chronic viral infections, pulmonary emphysema, and lung cancer.[1,2] Lung cancer is more prevalent in these patients (as documented by clinical monitoring and postmortem reports), with a cumulative 3-year incidence of 82%. As such, IPF is considered an independent risk factor for the development of lung cancer (LC), correlating with time accumulated since diagnosis.[3–7]

We are therefore looking at a progressive disease with a poor prognosis and a higher incidence of LC, in which clinical management and therapeutic decision-making are a challenge.

We report a series of 13 cases from our hospital (Table 1), included between January 2014 and December 2018. In total, 93 % of the patients were male (n = 12), with a mean age of 67.9 years, and, interestingly, all participants had a history of smoking (current or former). Detailed anamnesis revealed a family history of LC in 30 % of cases, and one of the patients reported a family cluster of IPF. In total, 38 % (n = 5) met radiological criteria for combined pulmonary fibrosis and emphysema (CPFE).

In our series, the most common tumor lineage was squamous (n = 9), followed by adenocarcinoma (n = 3) at rates similar to those reported in the literature.[4,5,8] However, no statistical association was found between the higher incidence of peripheral lesions and their location in lower lobes, as previously described by Kwak et al.[9] ($p > 0.05$). IPF was diagnosed using clinical/radiological criteria[10] (n = 8) or lung histology showing a pattern of usual interstitial pneumonia (n = 7).

The diagnosis of LC was synchronous with IPF and incidental in 3 cases; this figure was much lower than that reported by Huddad and Massaro.[5] In the remaining patients (n = 10), the presence of lung cancer was detected after a mean follow-up of 18.2 months (SD: 78.56). Clinical disease staging in our series was as follows: IA (n = 2), IB (n = 1), IIA (n = 1), IIIA (n = 2), IIIB (n = 5), stage IV (n = 1), and 1 patient refused complete tumor staging. These findings diverge from the high incidence of early stage lung cancer described in other series.[4,8]

All patients were evaluated by the thoracic tumors committee of our hospital. Their final decision was surgical treatment in 3 cases, oncological treatment in 5 (4 chemotherapy and 1 chemotherapy and radiation therapy), and symptomatic treatment in 5 patients, in view of their functional status. At a second evaluation, patients undergoing surgical treatment (after a minimum disease-free period of 6 months) were assessed by the interstitial diseases committee, and treatment with antifibrotic drugs started in 66 % (pirfenidone in all cases). The other patients continued close clinical and functional monitoring, given their absence of symptoms. None of the patients who underwent surgical treatment presented IPF exacerbations and/or postoperative complications, despite thoracic surgery being one of the possible etiologies of acute exacerbation.[11] No statistically significant differences were found in the histological LC type or in the stage at diagnosis in the subgroup of CPFE patients.

Taking into account the limitations of the study, such as the differing follow-up times due to the low incidence of cases, 54 % of patients in the series have now died (n = 7). In the group of patients who died, the average survival from diagnosis of IPF was 9 months (SD: 80.54). This figure was higher in patients who received antifibrotics (mean survival 22 months). Mean survival from diagnosis of LC was 10.5 months (SD: 11.39), but 66 % (n = 2) of the subgroup of patients who underwent surgical treatment are still alive; the only patient from this group who died had a survival of 39 months. The subanalysis of the CPFE group revealed a similar overall mortality (60 %) with an average survival after LC diagnosis of 5.3 months (SD: 3.68).

In our series, as in other previously described cohorts, IPF appears to be the determining factor in life expectancy,[8,12] and the option of surgery must be considered in selected cases. An appropriate, detailed functional assessment of the patient is essential to optimize treatment on an individual basis. We firmly believe in the need for thoracic tumor and interstitial pathology committees to work together to design a joint approach.

Although these results must be interpreted with caution, they suggest that radiological monitoring required for diagnosing IPF could include the early detection of LC, and perhaps this previously anecdotal association will become an increasingly common finding in clinical practice. The need for specific

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Table 1
Detailed characteristics of patients with idiopathic pulmonary fibrosis and lung cancer.

	Age (years)	Date of diagnosis of interstitial pattern	Date antifibrotic treatment started	Combined pulmonary fibrosis syndrome-pulmonary emphysema	Histological strain	Clinical stage	Date of diagnosis of lung cancer	Treatment of lung cancer	Time to development of lung cancer (months)	Time from diagnosis of interstitial pattern to death (months)	Time from diagnosis of lung cancer to death (months)
Patient 1	65	October 1995		Present	Squamous	IIIB	November 2016	Chemotherapy	253	257	4
Patient 2	68	March 2007		Absent	Adenocarcinoma	–	May 2018	Symptomatic	134		
Patient 3	78	July 2011		Absent	Squamous	IA	January 2014	Left lower lobectomy	30		
Patient 4	48	April 2014	March 2015	Absent	Neuroendocrine	IIIB	June 2015	Chemotherapy	14	19	6
Patient 5	63	March 2015	December 2015	Absent	Squamous	IIA	November 2016	Symptomatic	20	25	5
Patient 6	85	September 2015		Present	Non-small cell	IIIA	March 2016	Symptomatic	6	16	10
Patient 7	61	September 2016		Absent	Squamous	IIIB	November 2016	Chemotherapy	2	16	14
Patient 8	68	October 2016		Present	Adenocarcinoma	IB	October 2016	Atypical excision	0		
Patient 9	63	July 2017	June 2018	Absent	Adenocarcinoma	IA	December 2017	Atypical excision	5		
Patient 10	67	August 2017		Absent	Squamous	IIIB	October 2017	Chemotherapy + radiation therapy	2	7	5
Patient 11	64	November 2017		Present	Squamous	IV	December 2017	Symptomatic	1	1	1
Patient 12	80	July 2018		Present	Not known	IIIB	July 2018	Symptomatic	0		
Patient 13	73	September 2018			Squamous	IIIA	September 2018	Chemotherapy	0		

personalized radiological monitoring by tomography aimed at detecting early stage LC in this selected population must be evaluated.

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Bilateral pulmonary involvement. Non-Surgical options for inflammatory pseudotumor - A case report[☆]

Afectación pulmonar bilateral. Opciones no quirúrgicas del pseudotumor inflamatorio, a propósito de un caso

To the Editor:

Inflammatory pseudotumor is a rare entity that represents less than 1 % of all tumors of the lung.[1] Its radiological characteristics when viewed with standard tomographic techniques overlap with those of other entities,[2] complicating differential diagnosis, especially in lung cancer.

We report the case of a 49-year-old woman, former smoker with a pack-year index of 2, and a history of hypothyroidism. Her regular treatment was levothyroxine 75 mcg, 1 tablet a day. She attended the emergency department due to headache following an episode of sinusitis, with no associated respiratory symptoms. The baseline study included a standard chest X-ray, which revealed an incidental finding of a right apical lesion of irregular contours. An initial CT scan was requested that revealed a "rounded tumor mass in the right lung vertex, irregular contours, lobulated and spiculated towards the surrounding parenchyma. Lesion with heterogeneous enhancement with contrast, in extended contact with the posterior and superior apical pleura, measuring about 45 × 42 mm, with no evidence of pleural or extrapleural infiltration or extension; at the apex of the left lung, a small, nodular subpleural, lesion measuring less than 1 cm of dubious significance is observed". In light of these findings, positron emission tomography was performed. This highlighted the presence of this lesion, which was metabolically active with a maximum standardized value (standarized SUVmax) of 27.5, and the lesion in the left upper lobe, which had an SUVmax of 7.5. Bilateral hilar adenopathies were seen in the mediastinum, in

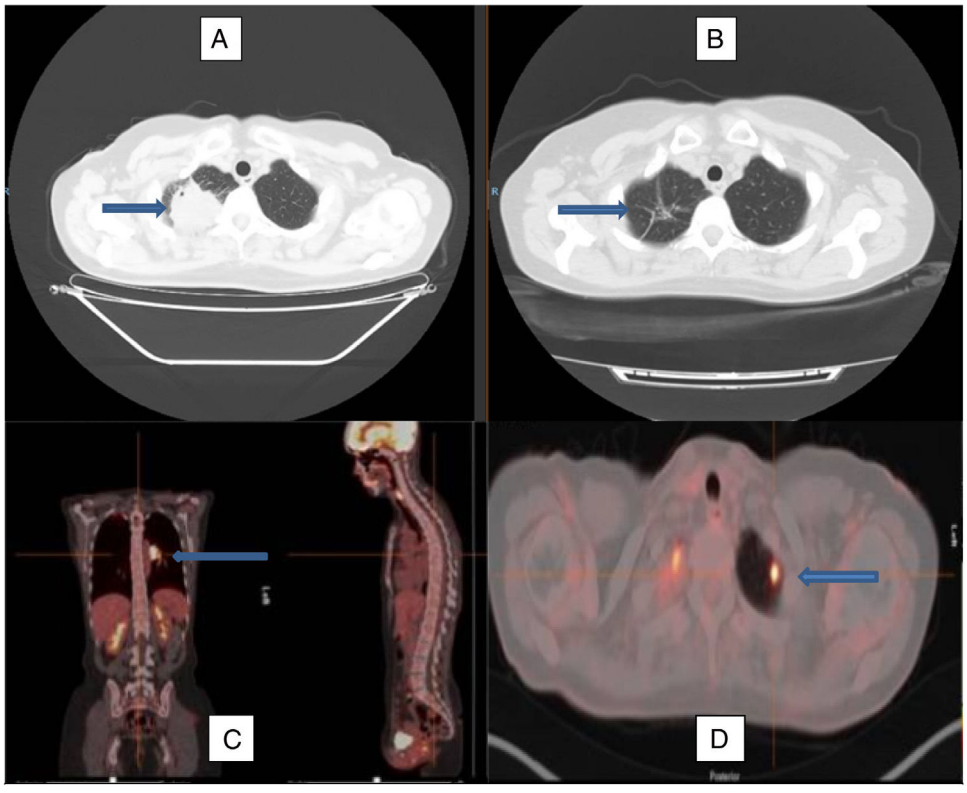

Fig. 1. Computed axial tomography image at diagnosis (A) and after treatment with corticosteroids (B), showing remission of the lesion in the right upper lobe, with some remnants of residual fibrous tracts (arrows). PET-CT image with enhanced uptake in the left pulmonary hilum (C) and in the left upper lobe (D), marked by arrows, reflecting the multilocular involvement of this case.

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