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Scientific letter

Idiopathic Nonspecific Interstitial Pneumonia. A Case Series and Literature Review

Neumonía intersticial inespecífica idiopática. Una serie de casos y revisión de la literatura

Dear Editor:

Idiopathic pulmonary fibrosis (IPF) and nonspecific interstitial pneumonia (NSIP) account for more than two-thirds of all idiopathic interstitial pneumonias (IIPs). In particular, the prevalence of NSIP varies between 1 and 9 cases per 100,000 population.[1,2] This disease has a heterogeneous clinical course and assigning a diagnosis to a patient is difficult because sometimes boundaries between IIPs are often blurred. The definitive diagnosis is established by lung biopsy,[1,4] histopathologic pattern of NSIP could be found in a wide variety of clinical contexts and the prognosis is less certain in the fibrotic forms.[2,3] The research in IIPs has tended to focus on IPF due to its worse prognosis[5,6] and the existence of a treatment with antifibrotic drugs (pirfenidone and nintedanib) that have shown to slow disease progression and, in some cases, improve disease-free survival.[7,8]

The purpose of this study was to analyze the clinical characteristics, lung function and survival in a consecutive case series with definitive diagnosis of idiopathic NSIP. In this retrospective cohort study, we included all patients in a single tertiary hospital with diagnosis of idiopathic NSIP by lung biopsy (transbronchial or surgical) from April 2010 to December 2018, with a minimum follow-up of 6 months, in which there was also a multidisciplinary discussion. We excluded: the cases associated with connective tissue disease (CTD) and undifferentiated CTD, the cases related to hypersensitivity pneumonitis and drug toxicity and the patients with familial pulmonary fibrosis. The following variables were included: age, sex, smoker, symptomatology, radiological findings, lung function, histologic findings, treatment received and survival. All data analysis was performed using SPSS 20.0.

Ten patients were analyzed, 6 (60%) were male. The mean age was 68 years (SD: 11) (55–82). The average follow-up was 50 months (SD: 30) (6–90). No active smoking patient, 5 ex-smokers (50%) and 5 never smokers (50%). The main symptoms were dry cough in 7 patients (70%) and exertional dyspnoea in 6 (60%), 2 patients (20%) were asymptomatic and were referred because of the radiological alteration in computed tomography (CT) performed for another reason. At the radiological level in high-resolution CT (HRCT), the most frequent was to find involvement of the lower lobes in 8 patients (80%), with predominantly peripheral extension in 9 (90%), bronchiectasis in 9 (90%) being in 4 cases (40%) by traction, reticular involvement in 7 patients (70%), ground-glass opacities in 5 (50%) and honeycomb only in 1 case (10%). In no case were pulmonary nodules, mediastinal lymph nodes or pleural effusion detected. At the functional level the average forced vital capacity (FVC) was 66% (SD: 27.35%), (34–117%), the average carbon monoxide (DLCO) diffusion was 81.50% (SD: 28, 50%), (41–147%), the average total lung capacity (TLC) was 70% (SD: 13.11%), (54–98%). The functional parameters being worse in patients with clinical manifestations. At pathology, the 70% of cases were classified as fibrotic pattern, with only the 30% deemed to be cellular. Regarding treatment, 8 patients (80%) received corticosteroids, 2 (20%) cases required azathioprine in addition to therapy. Of the total of patients, 4 (40%) died: all of them due to severe respiratory failure, these patients had worse pulmonary function, more traction bronchiectasis in the HRCT and fibrotic forms in lung biopsies.

Assigning a diagnosis to a patient with IIP is difficult and at times imprecise, a superposition of radiological and histological findings between IIPs is possible.[1,9] These situations place us in a context of uncertainty, and we must make decisions based on other supplementary tests and the behaviour of the disease, so a careful multidisciplinary discussion is essential.[10] The diagnosis of idiopathic NSIP can only be made when all known potential causes of this reaction pattern have been excluded: CTD, inhalational exposures, drugs and family history of interstitial lung disease.

One of the limitations of this study is the small sample size, due to the difficulty to performed lung biopsy and assign a definitive diagnosis of NSIP. In clinical practice, we have found that many patients, those who were asymptomatic, did not accept invasive procedures. In other patients their comorbidities contraindicated the diagnostic procedure. However, our demographic data shows that many patients with idiopathic NSIP are men with a mean age of 68 years, with almost half never smoking. Clinically, the disease develops with progressive dyspnoea and dry cough, although symptoms of systemic involvement may also occur: fatigue, weight loss and in some cases isolated febrile peaks.[1,2] In our study, 20% of the patients were referred by the casual radiological alterations, finding themselves asymptomatic. On HRCT, NSIP is characterized by thickening of inter and intralobular walls.[11,12] The location of the reticular involvement and the ground-glass opacities areas are findings with peripheral and basal predominance, with relative subpleural sparing in the dorsal regions of the lower lobes. There may be bronchiectasis and traction bronchiolectasis associated with loss of volume in the lower lobes. Honeycombing is uncommon and when it appears it tends to be mild, affecting less than 5% of the parenchyma and is associated with a poor prognosis.[12] Pulmonary function studies allow the assessment of the severity of the respiratory disturbance and are useful for monitoring the patient, being able to detect changes in the evolution of the disease.[13] The histologic features of NSIP include varying amounts of interstitial inflammation and fibrosis with a uniform appearance.[14] At pathology level, two patterns of NSIP are differentiated: the cellular and

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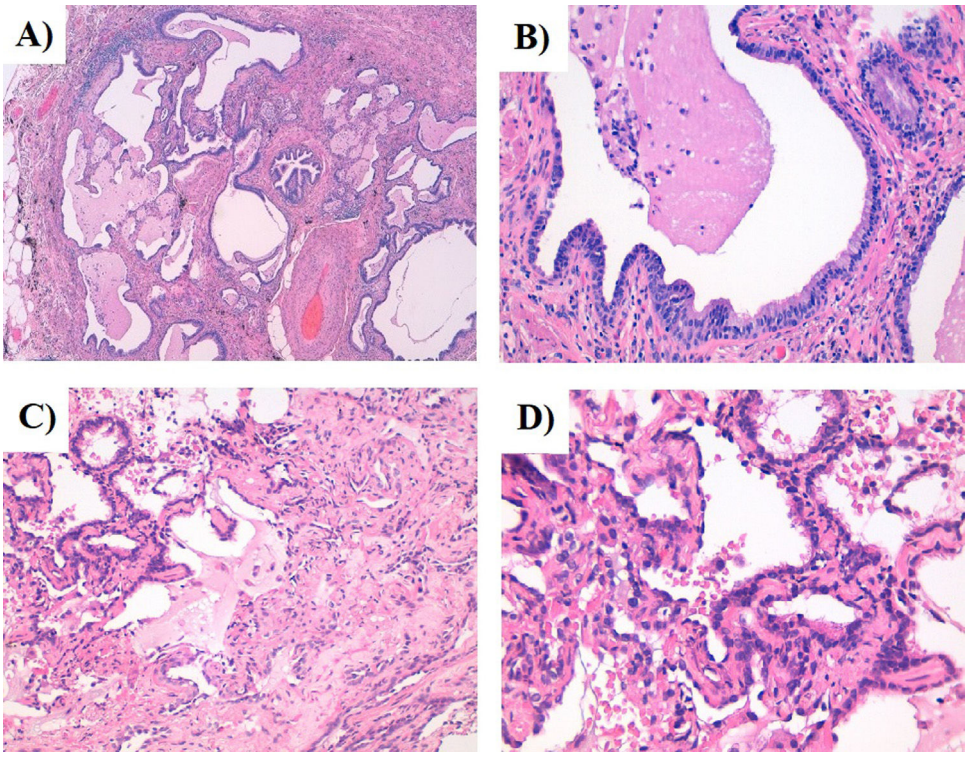

Fig. 1. Nonspecific interstitial pneumonia, fibrosing pattern. Lung tissue biopsies, *Hospital Clinico Universitario, Valencia.* (A and B) Patient with dilated and distorted alveolar spaces by dense fibrosis. The overlying pneumocytes show cuboidal hyperplasia. (C and D) Another patient with some relatively preserved alveolar walls, the collagen appears homogeneous temporally without fibroblastic foci.

the fibrotic patterns. The fibrotic pattern (Fig. 1) is most frequent and associates worse survival.[14]

Nowadays, when the disease progresses, immunosuppression remains the cornerstone of management. Corticosteroids are the predominant and often initial agent. This disease requires specialized follow-up; some patients may need long-term home oxygen therapy and even referral to lung transplantation. In other published studies the main predictors of mortality are: advanced age, decrease in FVC and DLCO, honeycombing at the HRCT and the finding of features of NIU pattern in pulmonary biopsy.[5,6,13,14]

In conclusion, idiopathic NSIP is a rare and difficult-to-diagnose disease that associates considerable morbidity and mortality. It is necessary to carry out specialized follow-up monitoring the disease behaviour and integrate a multidisciplinary teamwork.

References

1. Ancochea J, Gómez J, Vilar J, Xaubet A. Consenso para el diagnostico de las neumopatías intersticiales idiopáticas. Arch Bronconeumol. 2010;46:2–21.
2. Belloli EA, Beckford R, Hadley R, Flaherty KR. Idiopathic non-specific interstitial pneumonia. Respirology. 2016;21:259–68.
3. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. Am J Respir Crit Care Med. 2002;165:277–304.
4. Myers JL, Katzenstein AL. Beyond a consensus classification for idiopathic interstitial pneumonias: progress and controversies. Histopathology. 2009;54:90–103.
5. Flaherty KR, Thwaite EL, Kazerooni EA, Gross BH, Toews GB, Colby TV, et al. Radiological versus histological diagnosis in UIP and NSIP: survival implications. Thorax. 2003;58:143–8.
6. Ryerson CJ, Vittinghoff E, Ley B, Lee JS, Mooney JJ, Jones KD, et al. Predicting survival across chronic interstitial lung disease: the ILD-GAP model. Chest. 2014;145:723–8.
7. Noble PW, Albera C, Bradford WZ, Costabel U, Glassberg MK, Kardatzke D, et al. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomised trials. Lancet. 2011;377:1760–9.
8. Richeldi L, du Bois RM, Raghu G, Azuma A, Brown KK, Costabel U, et al. Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. N Engl J Med. 2014;370:2071–82.
9. Travis WD, Costabel U, Hansell DM, King TE Jr, Lynch DA, Nicholson AG, et al. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med. 2013;188:733–48.
10. Flaherty KR, King TE Jr, Raghu G, Lynch JP, Colby TV, Travis WD, et al. Idiopathic interstitial pneumonia: what is the effect of a multidisciplinary approach to diagnosis? Am J Respir Crit Care Med. 2004;170:904–10.
11. MacDonald SL, Rubens MB, Hansell DM, Copley SJ, Desai SR, du Bois RM, et al. Nonspecific interstitial pneumonia and usual interstitial pneumonia: comparative appearences at and diagnostic accuracy of thin section-CT. Radiology. 2001;221:600–5.
12. Webb WR, Müller NL, Naidich DP. The idiopathic interstitial pneumonias, Part I: Usual interstitial pneumonia/idiopathic pulmonary fibrosis and nonspecific interstitial pneumonia. In: High-resolution CT of the lung. 5th ed. Wolters Kluwer; 2015. p. 208–31.
13. Latsi PI, du Bois RM, Nicholson AG, Colby TV, Bisirtzoglou D, Nikolakopoulou A, et al. Fibrotic idiopathic interstitial pneumonia: the prognostic value of longitudinal functional trends. Am J Respir Crit Care Med. 2003;168:531–7.
14. Travis WD, Matsui K, Moss J, Ferrans VJ. Idiopathic nonspecific interstitial pneumonia: prognostic significance of cellular and fibrosing patterns: survival comparison with usual interstitial pneumonia and desquamative interstitial pneumonia. Am J Surg Pathol. 2000;24:19–33.

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