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Farmer's lung disease: Analysis of 75 cases☆

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ABSTRACT

Introduction: Farmer's lung disease (FLD) is a common form of hypersensitivity pneumonitis possibly underdiagnosed in our midst. The aim of this study was to describe clinical characteristics, evolution and factors that influence the prognosis of patients with FLD.
Patients and methods: A retrospective study that included all patients diagnosed with FLD presenting an environmental exposure risk, a clinic, lung function and a compatible radiology, in which antigen sensitization was demonstrated and/or a concordant pathology.
Results: We selected 75 patients with FLD, 50 with acute or subacute form (ASF) and 25 with chronic form (CF). Forty-four percent of patients (n = 33) were diagnosed during the months of March and April, especially those with ASF compared to CF (52 vs. 28%; $p = 0.0018$). In the ASF group, DLco showed an improvement during follow-up ($p = 0.047$). The determination of specific IgG antibodies was positive in 39 patients (78%) with ASF (44% of them against *Aspergillus*) and CF 12 (48%). The realization of antigenic avoidance (OR 9.26, 95% CI 1.3–66.7, $p = 0.026$) and the administration of immunosuppressive therapy (OR 16.13, 95% CI 1.26–200, $p = 0.033$) were predictors of better disease progression.
Conclusions: FLD is predominantly seasonal in our environment. CF usually has a negative specific IgG antibodies unlike ASF, where antibodies against *Aspergillus* are the most common. The realization of antigenic avoidance and immunosuppressive treatment are possible predictors of better disease progression.

Enfermedad del pulmón del granjero: análisis de 75 casos

Palabras clave:
Enfermedad pulmonar intersticial difusa
Neumonitis por hipersensibilidad
Pulmón de granjero
Variables pronósticas

RESUMEN

Introducción: La enfermedad del pulmón de granjero (EPG) es una forma frecuente de neumonitis por hipersensibilidad, posiblemente infradiagnosticada. El objetivo de este estudio es describir las características clínicas, la evolución y los factores que influyen en el pronóstico de los pacientes con EPG.
Pacientes y métodos: Estudio retrospectivo que incluyó a todos los pacientes diagnosticados de EPG por haber presentado una exposición ambiental de riesgo, una clínica, una función pulmonar y una radiología compatible, en los que se demostró sensibilización antigénica y/o una anatomía patológica concordante.
Resultados: Se incluyeron 75 pacientes con EPG, 50 con forma aguda o subaguda (FAS) y 25 con forma crónica (FC). Un 44% de los pacientes (n = 33) fue diagnosticado durante los meses de marzo y abril, especialmente aquellos con FAS en comparación con las FC (52 vs. 28%; p = 0,0018). En las FAS la DLco presentó una mejoría durante el seguimiento (p = 0,047). La determinación de anticuerpos IgG específicos fue

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positiva en 39 pacientes (78%) con FAS (44% de ellos frente a *Aspergillus*) y en 12 con FC (48%). La realización de la evitación antigénica (OR 9,26, IC 95% 1,3-66,7, p = 0,026) y la administración de tratamiento inmunodepresor (OR 16,13, IC 95% 1,26-200, p = 0,033) fueron los factores predictores de mejor evolución de la enfermedad.

Conclusiones: La EPG presenta un inicio con predominio estacional en nuestro medio. Las FC presentan habitualmente determinación de anticuerpos IgG específicos negativos, a diferencia de las FAS, donde los anticuerpos frente *Aspergillus* son las más frecuentes. La evitación antigénica y el tratamiento inmunodepresor son posibles predictores de mejor evolución de la enfermedad.

Introduction

Farmer's lung disease (FLD) is one of the most prevailing forms of hypersensitivity pneumonitis (HP) caused by inhalation of allergens from microorganisms lying in hay or grain stored under high humidity conditions.[1,2] These microorganisms trigger lymphocyte inflammation of the peripheral airways and surrounding interstitial tissue. Although *Saccharopolyspora rectivirgula* (formerly known as *Micropolyspora faeni*) and *Thermoactinonyces vulgaris* have traditionally been associated with FLD, Reboux et al. proved that *Absidia corymbifera* was the most common in eastern France,[3] which shows that the antigens are different depending on the region evaluated. The most common causative microorganisms in our environment are unknown.

In spite of being the first cause of HP in the rural environment, this disease has been rarely diagnosed in our country.[4–6] The diagnosis is based on clinical suspicion, performing a detailed clinical history of occupational and environmental exposures, with an indicative symptomatology and consistent lung function and radiological data on chest CT, cytological findings in bronchoalveolar lavage, and anatomopathological findings.[1,2]

Antigen exposure is already a risk factor, but not all exposed individuals develop an FLD. The positivity of specific IgG antibodies in plasma or the presence of a lymphocytic alveolitis, lacking other symptoms, has no clinical significance whatsoever.[6,7] The prevalence of the disease among exposed farmers is not well known because the studies evaluating it to date show methodological problems in their design. In addition, the definition of FLD, as in other forms of HP, has not been standardized and depends on the diagnostic methodology followed in every case. Despite these limitations, several studies offer similar results, where the FLD prevalence on exposed farmers range between 0.5 and 3%.[8,9] Lugo is a Spanish province located in the northwest of the country, with a significant primary sector (mainly agriculture and livestock), with 30,400 workers (8% of the total population).

The aim of this study is to describe the clinical manifestations, evolutionary course and factors that influence the prognosis of patients diagnosed with FLD at the University Lucus Augusti Hospital in the province of Lugo.

Material and methods

Study design

Retrospective observational study performed at the Hospital Universitario Lucus Augusti de Lugo, covering a health area of 221,441 people. We reviewed the medical records of all patients diagnosed with HP, extrinsic allergic alveolitis or FLD from 1997 to December 31, 2014. The study was approved by the Ethics Committee of Galicia (registration number 2015/416).

Inclusion and exclusion criteria

We included those patients who met the following criteria[10,11]:

- Reported exposure to the antigen (in this case, hay or silo).
- Clinical manifestations, physical findings and lung function compatible with the diagnosis of FLD.
- Radiology (chest X-ray and high resolution CT) consistent with the diagnosis of FLD.
- Specific IgG antibodies in plasma, positive against a disease-associated antigen and/or histology (transbronchial or surgical biopsy) that discards other processes and compatible with FLD (interstitial inflammatory infiltrates, non-caseating granulomas, and cell bronchiolitis, with or without fibrosis areas).

According to the criteria of Richerson[10] a biopsy is not initially deemed necessary, but we decided to include this requirement because it has been shown that many patients do not present specific IgG antibodies, positive against the antigens usually analyzed,[3] especially in chronic forms.

We excluded all patients who, even diagnosed with FLD, did not meet any of the criteria listed above or had other concomitant chronic pneumopathies.

Data collection

A data collection sheet was prepared with a detailed clinical history that included anthropometric data, clinical presentation, symptomatology and their duration, the month of the year of diagnosis, the initial value of PaO_2, biochemistry data, specific IgG antibody tests in plasma (*S. rectivirgula*, *Penicillium*, *Aspergillus*, *Trichosporon* and *Thermoactinomyces vulgaris*), lung function study (spirometry, determination of lung volumes and DLco), histological and radiological findings ("ground-glass", "Mosaic pattern", "micronodular pattern" or "reticular pattern/traction bronchiectasis/septal thickening"). For dyspnea, the scale used to evaluate this endpoint was MRC. In recurrent postexposure symptoms we excluded those episodes with an underlying and identified infectious cause.

The clinical manifestations were divided into acute, subacute and chronic depending on the time of clinical evolution (above or below 6 months) and, above all, on the radiological findings. In thoracic HRCT, in the acute phases, the presence of images in ground glass, hyperlucent lungs and, to a lesser extent, centrilobular nodules is characteristic. In chronic forms, the presence of honeycomb images is outstanding, occasionally emphysema and the inflammatory component is scarce or absent. For the analysis, they were grouped into acute-subacute forms (ASF) and chronic forms (CF)in accordance with the classification provided by Lacasse et al.[12]