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# Utility of high-resolution computed tomography and BAL in cryptogenic organizing pneumonia

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## Summary

**Background:** Cryptogenic organizing pneumonia (COP) is a rare disease, and its diagnosis requires histological confirmation. The objective of our study was to describe the findings of the thoracic high-resolution computed tomography (HR-CT) and bronchoalveolar lavage (BAL) in patients with confirmed COP and evaluate the complementary diagnostic use of BAL and thoracic HR-CT.

**Methods:** Patients recorded in the registry of interstitial pulmonary diseases between 1991 and 2008 were located and the COP patients selected.

**Results:** We identified 21 patients with histological confirmation of COP. The median age was  $58.0 \pm 15.9$  years, and 61.9% of patients were female. The most frequent thoracic HR-CT profile was patchy infiltrate (71.4%), followed by parenchymatous consolidation (42.9%). The most frequent BAL profile was mixed alveolitis (62%) with lymphocyte predominance, a CD4/CD8 index of 0.4 and foamy macrophages. The effectiveness of transbronchial biopsy was 66.6%. The diagnostic utility of Poletti's BAL criteria gives us a specificity of 88.8%, although the sensitivity obtained was low. The specificity of certain HR-CT profiles is 99%. In addition, we observed a complementary use of the HR-CT and the BAL.

**Conclusions:** The imaging findings and BAL could be useful for patients with appropriate clinical presentation and for those whose transbronchial biopsy is negative or for whom a confirmatory biopsy cannot be performed.

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## Introduction

The first descriptions of organizing pneumonia were given by Charcot<sup>1</sup> in the second half of the 19th century, although the concept of organizing pneumonia as a histopathological profile emerged under different names at the beginning of the 20th century<sup>2,3</sup> and acquired importance in the 1980s with specific clinical and radiological manifestations that had no apparent cause.<sup>4,5</sup>

Cryptogenic organizing pneumonia (COP) makes up between 1.8% and 13% of all interstitial lung diseases (ILDs) according to different studies.<sup>6–9</sup> A retrospective study showed that the incidence was 1.10/100,000 inhabitants<sup>10</sup> with increased incidence in the last 20 years.<sup>10,11</sup> It affects men and women equally, and is predominant during the sixth decade of life.<sup>4,5</sup> The patient tends to present a slow onset and a semi-acute clinical profile of coughing, fever, dyspnoea and crackles, the chest X-ray shows a unilateral or bilateral alveolar infiltrate<sup>11,12</sup> and it generally responds well to corticosteroids. The most frequent radiological pattern for thoracic CT shows patchy areas of consolidation (peripheral, bilateral, with an aerial bronchogram, and sometimes migratory).<sup>13</sup>

Although transbronchial lung biopsy (TBLB) is not considered to be very cost-effective for most ILDs,<sup>14</sup> for COP it has been described with a cost-effectiveness of up to 74%.<sup>15</sup> Video-assisted thoracoscopic lung biopsy is the gold standard for the diagnosis. However, the frequency of carrying out these surgical biopsy techniques to confirm these pathologies varies between 7.5%<sup>16</sup> and 30%.<sup>9,17</sup> This technique has its contraindications, and is associated with a varying morbidity and mortality that depends on the patient's functional state and the associated co-morbidity. Bronchoalveolar lavage (BAL) is indicated for all cases in which this pathology is suspected, since it helps to rule out other diagnoses and determines a cause of secondary organizing pneumonia.<sup>13</sup>

In many cases, the diagnosis of COP is based on clinical and radiological criteria, and especially HR-CT,<sup>18</sup> which in some studies has shown a reliability of up to 79%.<sup>19</sup> When we associate TBB and BAL, the diagnostic sensitivity reaches 86%.<sup>15</sup> BAL could be useful in cases in which clinical and radiological presentation suggests COP with non-diagnostic TBB, or when it is not possible to perform a confirmatory biopsy.<sup>15,20</sup>

The aim of our study was to describe radiological and BAL findings in patients with confirmed cases of COP.

## Methods

Patients were taken from the Interstitial Pulmonary Disease Unit, the Pulmonology Department's hospitalisation floor and the Collagenosis Unit of the Internal Medicine Department at the Virgen del Rocio Hospital in Seville from 1991 to 2008. Epidemiological data, personal history, clinical and radiological data, respiratory function, analytical data, microbiological studies with cellular and immune parameters in BAL fluid, TBB findings or pulmonary biopsy findings and the definitive diagnosis were all recorded. Patient consent was obtained to analyse data from proven cases.

## Exclusion criteria

Patients with a history of connective tissue disease, immune disorders, radiation treatment, aspiration pneumonia, transplants, cancer or lymphoma, or those with positive serology for certain pathogens and those with a history of taking potentially pneumotoxic drugs were excluded.

HR-CT was performed according to a previously established protocol. The radiological patterns used were as follows: 1) patchy infiltrate (two or more pathological dense areas in the lung, whether unilateral or bilateral); 2) parenchymatous consolidation; 3) ground-glass opacity; 4) adenopathies; 5) micronodules; 6) interlobulillar septal thickening; 7) pleural effusion; 8) honeycomb lung; 9) traction bronchiectasis.

In all cases, BAL was performed, and it was associated with TBB whenever a lack of contraindications allowed this to be carried out. BAL was performed according to the previously established protocol.<sup>21,22</sup> An immunological study was performed using the immunoperoxidase technique in cryopreserved samples, and it included the estimation of the percentage of cells expressing antigens associated with the T-cell count: CD3, CD4, CD8 and CD56. The percentage of CD3+ lymphocytes, as well as of the lack of expression of CD4 and CD8 (CD3+CD4-CD8- or double negatives), were also estimated.

## Diagnostic criteria

All cases included were histologically confirmed. To the effects of analysing the utility of HR-CT and the BAL, we also included all patients ( $n = 152$ ) with the most frequently occurring ILDs in our area with histological confirmation (idiopathic pulmonary fibrosis, sarcoidosis, hypersensitivity pneumonitis and chronic eosinophilic pneumonia). In this way, we calculated the sensitivity (S), specificity (Sp) and the positive and negative predictive values (PPV and NPV) for the radiological patterns and BAL Poletti's criteria. Poletti et al.<sup>14,20</sup> have studied the BAL of patients with COP. They described BAL criteria for defining NOC: > 25% lymphocyte count (with a CD4/CD8 count < 0.9) combined with at least two of the following criteria: foamy macrophages > 20%, >5% neutrophils and/or 2% and <25% eosinophils (moderate neutrophilia and/or eosinophilia).

## Statistical study

We used descriptive statistics expressing absolute and relative frequencies, the mean and standard deviation. For those variables with an asymmetrical distribution we calculated the median and interquartile range. Proportions were compared using the  $\chi^2$  test. To compare categorical and continuous variables we used the Fisher exact probability test and the Student *T*-test, respectively. In all analyses we considered the study to be statistically significant where  $p < 0.05$ . Statistical analysis was carried out using the SPSS computer program, version 13.0 (SPSS Inc. Headquarters, Chicago, Illinois, USA).

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