Letters to the Editor

**Ralstonia Pickettii in Chronic Obstructive Pulmonary Disease Exacerbation**

**Ralstonia pickettii y exacerbación de EPOC**

*To the Editor:*

Chronic obstructive pulmonary disease (COPD) exacerbation accounts for 1.5% of emergencies treated in Spanish hospitals. Most exacerbations are caused by infections, which are associated with increased mortality in such cases and poorer quality of life. COPD-associated infections account for 13.7% of all infections treated in hospital and involve multiple microorganisms. We report a case of COPD exacerbation in which *Ralstonia pickettii*—a new microorganism with pathogenic potential in such patients—was isolated in respiratory samples. To our knowledge, this is the first report of such a case.

A 78-year-old man, an ex-smoker since 18 years ago with a smoking history of 40 pack-years, was diagnosed with COPD (stage IV disease according to the Global Initiative for Chronic Obstructive Lung Disease classification) and well monitored at an outpatient clinic. The patient also had sleep apnea-hypopnea syndrome treated with continuous positive airway pressure, chronic respiratory insufficiency with long-term home oxygen therapy, and rheumatoid arthritis with leflunomide. In the prior 3 months he had been admitted to hospital 3 times for COPD exacerbation, with isolation of Escherichia coli in sputum samples. After the results of an antibiogram, the patient received treatment with oral cefditoren (400 mg/12 h) for 21 days. He was admitted to hospital after 5 days of worsening dyspnea (first on exertion and then at rest), purulent sputum, and low-grade fever. Physical examination revealed coarse rhonchi. The laboratory workup showed a C-reactive protein level of 2.48 mg/dL. The chest x-ray (Figure) showed pulmonary air trapping and increased linear markings (tram trackings).**

Lung function tests gave the following results: forced expiratory volume in 1 second (FEV₁) of 670 mL (28%), forced vital capacity (FVC) of 1200 mL (35%), and a FEV₁/FVC ratio of 56%; with a negative bronchodilator test. Treatment included inhaled and systemic corticosteroids, inhaled bronchodilators, oxygen therapy, and empirical antibiotic therapy with intravenous ceftazidime (2 g/8 h). In view of the lack of response, despite prior antibiotic therapy, we decided to perform a fiberoptic bronchoscopy, which revealed mucopurulent secretions and diffuse thickening of the mucosa. Quantitative culture of the protected telescoping catheter tip showed 10⁷ colony-forming units (CFU)/mL of *E coli* that were sensitive to cefditoren and ceftazidime, and 10³ CFU/mL of *R pickettii* that were resistant to cefditoren and sensitive to ceftazidime. The clinical course was good, the antibiotic treatment was maintained for 21 days and the patient was discharged. Infection is responsible for 75% of COPD exacerbations. Fifty percent are caused by bacteria, particularly *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Chlamydia pneumoniae*, and *Pseudomonas aeruginosa*. The remaining causes include viruses and, exceptionally, other microorganisms.

Non-fermenting gram-negative bacilli are an emerging cause of infection. The main opportunistic pathogens in this group are *P aeruginosa*, *Acinetobacterbaumannii*, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia*. Another species belonging to this group is *R pickettii*, a microorganism present in soil, water, and plants. The genus *Ralstonia* includes former members of the *Burkholderia* species, separated because of their phenotypic characteristics, cellular lipid composition, DNA rRNA hybridization, and phylogenetic analysis of 16s rDNA nucleotide sequences.

Although the virulence of this pathogen was believed to be low, this affirmation is currently being questioned. In recent years, *R picketti* has emerged as an opportunistic community and nosocomial pathogen, involved in multiple infections such as bacteriemias, endocarditis, meningitis, osteomyelitis, septic arthritis, seminal infection, and peritonitis. Several outbreaks caused by foci of contamination associated with this bacterium in products used in laboratories and in the care of patients have been described. In most cases affecting adults, predisposing factors for infection include chronic renal failure, diabetes mellitus, liver cirrhosis, and hematopoietic progenitor cell transplant. This microorganism must therefore not be disregarded as a pathogen when isolated in theoretically germ-free secretions, particularly if there are predisposing factors.

In the respiratory tract, *R picketti* has been found to colonize the oral cavity and the upper respiratory tract in healthy individuals. Cases of respiratory infection have been described in patients with the aforementioned predisposing factors or in association with cystic fibrosis. *R picketti* has also been identified in pneumonia, usually in immunocompromised patients, although a case has been described in an immunocompetent person. To our knowledge, *R picketti* has not been previously reported as responsible for COPD exacerbation. In the case outlined here, no potentially harmful environmental agents were identified. Although the *E coli* infection had been correctly treated based on the results of the antibiogram, our patient worsened. For this reason, the exacerbation was attributed to *R picketti*. Moreover, there were no other isolations at the hospital that suggested a possible outbreak. Predisposing factors might have been treatment with leflunomide or previous courses of antibiotics or corticosteroids as these could have caused immune system dysfunction and favored the growth of this rare pathogen.

We conclude that *R picketti* can cause COPD exacerbation, particularly in the presence of circumstances that might predispose to immunosuppression. Although such an association has not been reported to date, it should be taken into consideration in future.

**References**

Factors That Modify C-Reactive Protein Production in Patients With Community-Acquired Pneumonia

Factors que modifican la Producción de Proteína C Reactiva en Pacientes con Neumonía Adquirida en la Comunidad

To the Editor:

Although a number of studies have assessed the value of C-reactive protein in managing patients with community-acquired pneumonia, their results have been inconsistent. Furthermore, to differentiate between community-acquired pneumonia and other diseases, different C-reactive protein values have been proposed as the best cutoff point: 50 mg/L, 100 mg/L, and 125 mg/L. Some studies, moreover, have linked high admission levels of C-reactive protein with the etiology or prognosis in patients with community-acquired pneumonia, whereas others have failed to confirm this association. Although most guidelines currently used in managing community-acquired pneumonia do not include C-reactive protein assessment as a tool to assist clinical decision making, some guidelines, including those of the British Thoracic Society, recommend that further prospective studies be conducted in order to further investigate the potential value of C-reactive protein levels in the management of patients with community-acquired pneumonia.

Given this background, we conducted a study designed to determine whether C-reactive protein admission values might be affected by specific patient characteristics. Accordingly, we analyzed the influence of age, sex, comorbidity, the number of days since onset, and previous treatment with antibiotics on C-reactive protein levels in a cohort of 161 patients attended to consecutively in the emergency department of our hospital. The sample, which consisted of 112 men (69.6%), had a mean (SD) age of 63.1 (18.5) years and included 84 patients (52.2%) with chronic diseases. Disease severity was measured using the Pneumonia Severity Index, with patients categorized as follows: 31 patients (19.2%) in class I, 72 patients (44.7%) in classes II and III, 45 patients (27.9%) in class IV, and 13 patients (8.0%) in class V. Hospitalization was necessary for 78 patients (48.4%), and 17 patients (10.5%) died while in hospital. The cause of the pneumonia was identified in 65 cases (40.3%). The most frequently encountered microorganisms were Streptococcus pneumoniae (42 patients, 26%), Chlamydia pneumoniae (8 patients, 4.9%), Legionella pneumophila (6 patients, 3.7%), and Mycoplasma pneumoniae (3 patients, 1.8%). Serum samples were analyzed for C-reactive protein in a turbidimetric assay (Tinaquant; Roche Diagnostics, Mannheim, Germany) following the manufacturer’s instructions and for a C-reactive protein detection range of 1 mg/L to 560 mg/L.

The assay revealed that 155 patients (96.2%) had C-reactive protein levels above 100 mg/L on admission. The Table summarizes the associations between patient C-reactive protein values and the variables analyzed. Sex, the presence of comorbidities, the number of days since onset, and previous treatment with antibiotics had no bearing on C-reactive protein levels on admission. C-reactive protein levels were, however, lower in elderly patients. No relationship was found between C-reactive protein levels and either death during hospitalization (217.6 [159.4] mg/L) or recovery (286.4 [159.8] mg/L) (P not significant).

The results of our study indicate that age may have a bearing on C-reactive protein levels. Our results are, furthermore, consistent with previous sepsis model analyses that found that the production of tumor necrosis factor-α and interleukin 1β—both considered to be stimulants of C-reactive protein production—was lower in elderly patients. For this reason we are of the opinion that future research into the value of C-reactive protein in respiratory infections should take into account patient age, and should assess the usefulness replicated C-reactive protein measurement.

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