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Postobstructive Pneumonia: An Underdescribed Syndrome

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(See the Editorial Commentaries by Torres and Ferrer on pages 962–3.)

Background. Postobstructive community-acquired pneumonia (PO-CAP) is relatively common in clinical practice. The clinical syndrome is poorly defined, and the role of infection as a cause of the infiltrate is uncertain. We prospectively studied patients with PO-CAP and compared them to a cohort of patients with bacterial community-acquired pneumonia (B-CAP).

Methods. We prospectively studied patients hospitalized for CAP; 5.4% had PO-CAP, defined as a pulmonary infiltrate occurring distal to an obstructed bronchus. Sputum and blood cultures, viral polymerase chain reaction, urinary antigen tests, and serum procalcitonin (PCT) were done in nearly all cases. Clinical and laboratory characteristics of patients with PO-CAP were compared to those of patients with B-CAP.

Results. In a 2-year period, we identified 30 patients with PO-CAP. Compared to patients with B-CAP, patients with PO-CAP had longer duration of symptoms (median, 14 vs 5 days; $P < .001$). Weight loss and cavitary lesions were more common ($P < .01$ for both comparisons) and leukocytosis was less common ($P < .01$) in patients with PO-CAP. A bacterial pathogen was implicated in only 3 (10%) PO-CAP cases. PCT was <0.25 ng/mL in 19 (63.3%) patients. Although no differences were observed in disease severity or rates of intensive care unit admissions, 30-day mortality was significantly higher in PO-CAP vs B-CAP (40.0% vs 11.7%; $P < .01$).

Conclusions. Although there is substantial overlap, PO-CAP is a clinical entity distinct from B-CAP; a bacterial cause was identified in only 10% of patients. Our study has important implications for the clinical recognition of patients with PO-CAP, the role of microorganisms as etiologic agents, and the use of antibiotic therapy.

Keywords. community-acquired pneumonia; pneumonia; postobstructive pneumonia.

Postobstructive pneumonia, a pulmonary infiltrate distal to a bronchial obstruction that, in adults, is generally due to malignancy, has been reported in about 2% of patients hospitalized for community-acquired pneumonia (CAP) [1–4] . Our recent study in a veteran population [5] showed that 5.4% of patients hospitalized for CAP had postobstructive CAP (PO-CAP). Despite the prevalence of this condition, literature on the subject is surprisingly sparse [1, 6–12], and only Marrie [1] provides a complete clinical description of patients with this disease.

Opinion varies as to whether infection is responsible for PO-CAP. Some authors [6, 7] believe that infection is generally not involved, whereas others [8] regard bacterial infection as the usual cause. Because conventional practice is to treat all PO-CAP with antibiotics [13], we performed a prospective study to characterize the clinical and laboratory findings in patients with this disease, with particular attention to the role of bacterial infection.

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METHODS

Study Population

During a 1-year period, July 2011 through June 2012, we studied 259 consecutive patients hospitalized for CAP at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas [5]. CAP was defined as a newly recognized or worsening pulmonary infiltrate and ≥2 of the following: subjective fever or documented temperature >37.4°C (>99.4°F); increased cough; sputum production; shortness of breath; pleuritic chest pain; confusion; crackles; leukocytosis (white blood cell [WBC] count >12 000 cells/μL); or leukopenia (<6000 cells/μL). Patients who had been hospitalized in the preceding 4 weeks, who were bedbound in long-term-care facilities, or who had known aspiration were excluded [5]. Of the 259 patients, 14 (5.4%) had PO-CAP, defined as the radiographic appearance of a pulmonary infiltrate occurring distal to an obstructed bronchus. To increase the number of subjects under study, we continued to screen all CAP admissions for an additional year, enrolling only those patients with PO-CAP (n = 16). We then compared clinical and laboratory findings in PO-CAP patients (n = 30) with all cases of proven or presumptive bacterial pneumonia (B-CAP; n = 60) that had been identified during the initial 1-year study.

Data Collected

We collected clinical and demographic data as summarized in Table 1. Pneumonia Severity Index (PSI) [14] and CURB-65

Table 1. Demographic and Clinical Features at the Time of Admission in Patients With Postobstructive Pneumonia Compared to Those With Bacterial Pneumonia

Characteristic	Postobstructive (n = 30)	Bacterial (n = 60)	P Value
Demographics and comorbidities			
Age, y[a]	70 (64–79)	69 (62–78)	.53
Male sex	29 (96.7)	56 (93.3)	.91
Smoking (current or former)	28 (93.3)	48 (80.0)	.17
Chronic obstructive pulmonary disease	13 (43.3)	33 (55.0)	.30
Coronary artery disease	8 (26.7)	20 (33.3)	.52
Chronic kidney disease	6 (20.0)	15 (25.0)	.60
Diabetes mellitus	9 (30.0)	19 (31.7)	.87
Clinical features			
Duration of symptoms, d[a]	14 (5–30)	5 (3–8)	.001
>5% weight loss	19/28 (67.9)	16/49 (32.7)	.003
Cough	24 (80.0)	56 (93.3)	.13
Sputum	16 (53.3)	48 (80.0)	.009
Dyspnea	20 (66.7)	51 (85.0)	.045
Pleuritic chest pain	5 (16.7)	13 (21.7)	.58
Hemoptysis	5 (16.7)	1 (1.7)	.029
Altered mental status	9 (30.0)	16 (26.7)	.74
Upper respiratory symptoms	0 (0.0)	8 (13.3)	.066
Vital signs			
Temperature >37.4°C	10 (33.3)	34 (56.7)	.037
Systolic blood pressure, mm Hg[a]	130 (110–160)	117 (101–129)	.016
Pulse, beats/min[a]	99 (87–108)	102 (88–116)	.44
Respiratory rate, breaths/min[a]	20 (18–22)	20 (18–24)	.13
Blood oxygen saturation, %[a]	96 (91–98)	93 (90–97)	.45
Laboratory features			
WBC count >12 000 cells/μL	10 (33.3)	38 (63.3)	.007
Band forms ≥3%	1 (3.3)	13 (21.7)	.038
Platelet count, cells/μL[a]	323 500 (236 000–401 500)	236 000 (174 000–306 000)	.022
Serum procalcitonin, ng/mL[a]	0.17 (0.08–0.55)	0.99 (0.11–3.24)	.038
Radiographic features			
Unilateral infiltrate	26 (86.7)	44 (73.3)	.15
Cavity	5 (16.7)	0 (0.0)	.006
Pleural effusion	4 (13.3)	11 (18.3)	.55
Severity indices			
PSI category[a]	4 (3–4)	4 (3–4)	.98
CURB-65 score[a]	1 (1–2)	2 (1–2)	.27
Outcomes			
Defervescence by day 5 of antibiotics	6/10 (60.0)	32/34 (94.1)	.036
Resolution of leukocytosis by day 5 of antibiotics	3/10 (30.0)	22/38 (57.9)	.22
Duration of hospitalization, d[a]	8 (5–14)	7 (4–11)	.19
ICU admission	2 (6.7)	11 (18.3)	.24
30-d mortality	12 (40.0)	7 (11.7)	.002

Data are shown as No. (%) of patients and refer to values at the time of admission, unless stated otherwise.

Abbreviations: CURB-65, confusion, blood urea nitrogen, respiratory rate, blood pressure, age ≥65; ICU, intensive care unit; PSI, Pneumonia Severity Index; WBC, white blood cell.

[a] Median (interquartile range).

(confusion, blood urea nitrogen, respiratory rate, blood pressure, age ≥65) scores [15] were calculated at the time of admission. Blood cultures were obtained in nearly all patients. Sputum samples for Gram stain and culture were obtained from 68% of patients. The following studies were performed in >95% of patients: polymerase chain reaction (PCR) on nasopharyngeal swabs to detect 15 respiratory viruses (BioFire

Diagnostics, Salt Lake City, Utah); urine assay for *Legionella* and *Pneumococcus* antigens (BinaxNOW, Alere, San Diego, California); and serum procalcitonin (PCT) (Vidas, bioMérieux, Durham, North Carolina). PCT levels were interpreted in accord with published reports [16, 17], which suggest that a level <0.1 ng/mL strongly opposes the presence of bacterial infection, a level ≥0.1 to <0.25 ng/mL opposes bacterial infection,

a level ≥0.25 to <0.5 ng/mL suggests bacterial infection, and a level ≥0.5 favors bacterial infection. We also determined the time from initiation of antibiotics until defervescence (temperature ≤37.4°C for 2 consecutive days) or resolution of leukocytosis (first day in which WBC count was ≤12 000 cells/μL).

Literature Search
We searched Medline and Google Scholar for articles describing PO-CAP using the following search terms: "post-obstructive pneumonia," "post-obstructive," "obstructive pneumonia," "obstructive pneumonitis," and "pneumonitis." We also studied articles referenced by, as well as later articles that cited, these publications.

Statistical Analysis
Continuous variables were compared using the Mann–Whitney test. A χ^2 test was used to compare dichotomous variables; for expected observations in <5 patients, Fisher exact test was used. Statistical significance was set at $P < .05$.

RESULTS

Postobstructive Pneumonia
The demographics of 30 PO-CAP patients (Table 1) reflect the demographics of our medical center. Twenty-eight patients (93.3%) were former or current cigarette smokers, and 13 (43.3%) had chronic obstructive pulmonary disease. The median duration of symptoms preceding admission was 14 days (range, 2–60 days). Fourteen patients (46.7%) had subjective fever and/or chills, and 10 (33.3%) had a temperature >37.4°C during the first 24 hours of hospitalization. Cough, sputum production, and dyspnea were described by 80.0%, 53.3%, and 66.7% of patients, respectively. None (0%) reported symptoms of an upper respiratory infection. Hemoptysis and pleuritic chest pain each appeared in 5 patients (16.7%). The median weight loss during the 4–8 months prior to presentation was 5.1 kg. Leukocytosis was present in 12 (40.0%) patients; only 1 had ≥3% band forms. Cavitation was detected radiographically in 5 cases (16.7%). Sputum culture yielded *Streptococcus pneumoniae* and *Staphylococcus aureus* in 1 patient each. Another patient, whose sputum culture was negative, grew *S. aureus* in his blood. Urine pneumococcal and *Legionella* antigens were uniformly negative. Thus, by microbiological techniques, there was evidence for bacterial infection in 3 of 30 cases (10%) of PO-CAP. Viral PCR demonstrated rhinovirus in 2 cases and coronavirus in 3 cases. Median PCT in PO-CAP was 0.11 ng/mL; PCT was <0.25 ng/mL in 67.0% of cases and <0.1 ng/mL in 33.1% of cases.

The obstruction was caused by malignancy in all cases: small cell lung cancer in 15 (50.0%), adenocarcinoma in 8 (26.7%), and squamous cell carcinoma in 5 (16.7%). In 14 patients (46.7%), malignancy was first discovered at the time of presentation with pneumonia.

Comparison With Bacterial Pneumonia
Comorbid conditions and history of cigarette smoking were similar between PO-CAP and B-CAP patients (Table 1). Patients with PO-CAP had a longer duration of symptoms before admission ($P = .001$), and a greater proportion presented with weight loss ($P = .003$). PO-CAP patients were more likely to report hemoptysis ($P = .03$) and less likely to present with sputum production ($P = .009$) or signs of acute infection such as temperature >37.4°C ($P = .037$), leukocytosis ($P = .007$), or band forms ($P = .04$). Consistent with greater chronicity of disease, PO-CAP was more commonly associated with a platelet count >300 000 cells/μL (60.0% vs 26.7%; $P = .002$). Serum PCT levels were higher in B-CAP compared with PO-CAP (median PCT, 0.99 ng/mL vs 0.17 ng/mL; $P = .038$), and a serum PCT level ≥0.25 ng/mL was more common with B-CAP (73.3% vs 33.0%; $P < .001$). CAP severity, as assessed by PSI and CURB-65 or by the need for intensive care unit admission, was similar between groups. Defervescence by day 5 occurred more frequently in B-CAP than in PO-CAP ($P = .036$). The rate of resolution of leukocytosis did not differ between groups. Thirty-day mortality was greater in PO-CAP ($P = .002$).

DISCUSSION
In 1949, McDonald et al [6] defined a radiographic opacity resulting from partial or complete obstruction of the bronchus by a neoplasm as obstructive pneumonitis (Table 2). Clinical and pathological review of 53 cases suggested that accumulation of secretions rather than infection was responsible; histologically, inflammatory cells without bacteria were present in the alveoli. The authors presented a case in which bronchoscopic resection of an endobronchial lesion eliminated the obstruction and resulted in resolution of the pulmonary infiltrate as well as the patient's cough and sputum production. These authors stated that, while generally not infectious, the pneumonitis occasionally progressed to bacterial lung abscess. Nearly all of their cases were accrued in the preantibiotic era, so bacterial infection, had it been responsible, would likely have progressed and become easily recognizable. In a later histopathologic study of 50 patients with obstructive pneumonitis, Burke and Fraser [7] reported that the infiltrate was not due to bacteria in 42 cases (84%). These investigators concluded that an opacification distal to an obstructing tumor is caused by retained epithelial secretions, although, in some proportion of cases, secondary infection may occur. The term "postobstructive pneumonia" began to replace "obstructive pneumonitis" in the 1970s [18]. In more recent studies [8, 9], ultrasound-guided aspiration of a cavity associated with a lung cancer yielded bacteria (generally mouth flora) in one-third of cases, but it is important to note that the aspiration was from a cavity, not from an infiltrate. Discordance between organisms identified by aspiration and those identified by sputum culture [8, 9, 19, 20] has led many

Table 2. Prior Studies That Addressed the Role of Infection in Postobstructive Pneumonia

First Author, Year	Criteria for Inclusion	No. of Patients	Methods to Detect Infection	Pathogenic Organisms Isolated	Clinical Information
McDonald, 1949 [6]	Resection of pulmonary neoplasm	53	Lung histopathology	Generally not considered infected, but infection may be superimposed	Only reported sputum production
Burke, 1988 [7]	Resection of pulmonary neoplasm	50	Lung histopathology and culture	No histologic signs of infection in 42 (84%); bacteria in 5 (10%).	No clinical data
Marrie, 1994 [1]	New infiltrate and clinical findings of pneumonia in patients with lung malignancy	23	Culture of sputum, blood, bronchial washings, pleural fluid, lung biopsy. *Legionella* antigen. Serologies for viruses and atypical bacteria	Bacteria in 5 (22%). Virus in 1 (4.3%).	Detailed clinical, laboratory, and radiologic characterization
Liaw, 1994 [8]	Obstructive pneumonitis; percutaneous biopsy	26	Culture of cavity aspirate	Febrile: bacteria in 5 of 8 (63%). Afebrile: bacteria in 0 of 3 (0%).	Only reported presence of fever
Liao, 2000 [9]	Cavitating lung tumor	22	Culture of cavity aspirate	Febrile: bacteria in 6 of 7 (86%). Afebrile: bacteria in 1 of 15 (7%).	Only reported presence of fever
Ferretti, 2008 [10]	Nonresolving focal pneumonia	20	Lung histopathology and culture	Bacteria in 2 (10%).	No clinical data
Present study	New infiltrate and clinical findings of pneumonia in patients with lung malignancy	30	Culture of sputum, BAL fluid, and blood. Pneumococcal and *Legionella* antigen, viral PCR, and serum PCT	Bacteria from sputum in 2 of 11 (18%). Bacteria from blood in 1 of 30 (3.3%). PCT opposes bacteria in 19 (63%). Virus in 5 (17%).	Detailed clinical, laboratory, and radiologic characterization

Abbreviations: BAL, bronchoalveolar lavage; PCR, polymerase chain reaction; PCT, procalcitonin.

investigators rightfully to question the value of sputum culture in PO-CAP.

Our study systematically applied newly available techniques to search for a microbial cause, including PCR for viruses and enzyme immunoassay for detection of bacterial antigens in urine and PCT levels in serum. Several findings argue against a bacterial cause for most cases of PO-CAP. First, despite substantial overlap, the clinical presentation and laboratory findings in PO-CAP differ from those in B-CAP. PO-CAP is a more chronic condition with a substantially longer median duration of symptoms and a greater proportion with weight loss. Findings that are usually associated with a bacterial infection, such as a preceding upper respiratory infection, hyperacute presentation, fever, leukocytosis, leukopenia, or increased band forms [5], are less prevalent in PO-CAP. All patients in our study received antibiotics, but fever was more likely to persist in patients with PO-CAP. Second, ours is the first systematic study of PCT levels in patients with PO-CAP. Despite problems with sensitivity and specificity [5, 21], this test has been widely recommended to distinguish bacterial from nonbacterial infections [22–25]. In nearly two-thirds of PO-CAP cases, PCT was ≤0.25 ng/mL, which is thought to oppose the diagnosis of bacterial infection, and in 33% PCT was ≤0.1 ng/mL. Third, despite an intensive and systematic search for bacterial infection, only 3 (10%) PO-CAP patients had evidence of bacterial infection. No previous study has examined the role of viruses in PO-CAP. A respiratory virus was identified by PCR in 16.7% of patients with PO-CAP, similar to 18.4% in those without obstruction. Finally, the 30-day mortality was greater in patients with PO-CAP than in those with B-CAP (*P* = .002).

We did not present data on time from hospital admission to suspicion for the specific diagnosis of PO-CAP, because (1) it is difficult to ascertain this information, as one member of the team may consider the diagnosis but the others do not; (2) computed tomographic (CT) scans are increasingly used routinely in our middle-aged and elderly patients who present with pneumonia, and the diagnosis was often made by CT without PO-CAP having been suspected; and (3) time to CT scan in our medical center is often dependent upon logistics (eg, weekend vs weekday admission) rather than medical considerations, as is the time to definitive (histologic) diagnosis of malignancy.

The present study had some limitations. Data were collected at a single institution that treats predominately male patients; in addition, despite an intense search for an infectious cause, the possibility remains that patients in whom a bacterial etiology was not identified still had a bacterial infection. Strengths include prospective identification of PO-CAP among all CAP patients; comparison with documented B-CAP; and nearly uniform use of newer diagnostic studies, such as urinary antigens, viral PCR, and serum PCT.

In conclusion, this study provides evidence that PO-CAP is a clinical entity distinct from B-CAP. Patients with PO-CAP have greater chronicity of disease, manifested by a longer duration of symptoms, greater weight loss, absence of symptoms of upper respiratory infection, lower WBC counts with fewer band forms, and higher platelet counts. They are less likely to have sputum production but more likely to have hemoptysis, fever, and a cavitary lesion on chest radiograph. Serum PCT at admission is lower than in bacterial pneumonia. PO-CAP patients defervesce more slowly in the hospital and have substantially higher 30-day mortality. Overlap with B-CAP, however, limits the possibility of

making a clinical distinction at the time of admission in an individual case. Given the strong evidence against a role for bacterial pathogens, results of the present study should encourage more limited antibiotic use in patients with PO-CAP. Our experience has been that when patients fail to respond to a first course of antibiotics, physicians repeat sputum cultures, which now are contaminated with newly acquired gram-negative colonizing organisms, and then give additional antibiotics to "cover" these newly recognized bacteria. The results of our study strongly oppose this kind of medical management. If a patient fails to defervesce with a first course of antibiotics, full attention should be focused on treating the obstructing lesion.

Notes

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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