Open Forum Infectious Diseases
CORRESPONDENCE

The White Blood Cell Response in Sputum in Viral and Bacterial Pneumonias

Dear Editor,

Identification of a causative agent in patients hospitalized for pneumonia may play a critical role in understanding disease progression as well as in selecting appropriate antibiotic therapy [1, 2]. Utilizing quantitative bacteriologic and molecular techniques on high-quality sputum specimens has significantly improved diagnostic yields [3–5]. It is generally assumed that viral pneumonia causes a dry cough without sputum production, but this observation is largely based on observations in outpatients; we have shown that patients hospitalized for viral pneumonia may produce sputum that appears to be frankly purulent [4].

To our knowledge, the association between purulence, as defined by white blood cell (WBC) counts in sputum, and the etiology of pneumonia has not been reported. An investigation of this association must include consideration of coinfection by viruses and commensal organisms, so-called "normal respiratory flora" (NRF), which have recently been implicated as etiologic agents in 25%–35% of patients hospitalized for pneumonia [4]. We recently reported the results of an intensive study of the etiology of community-acquired pneumonia in patients who produced high-quality purulent sputum at the time of or soon after admission [4]. We now present data relating WBC counts in sputum to microbial etiology.

We studied a convenience sample of 139 patients hospitalized between September 1, 2017, and February 28, 2020, for community-acquired pneumonia, based on their ability to produce a high-quality sputum (≥20 WBCs per epithelial cell); 116 of these patients were included in our earlier study [4]. We included patients in whom an etiologic agent was detected. The methods have been described in detail elsewhere [4]. Polymerase chain reaction (PCR) for the respiratory viruses *Mycoplasma* and *Chlamydophila* was done on a nasopharyngeal swab in every case; results for *Mycoplasma* and *Chlamydophila* were uniformly negative. Pneumonia was attributed to recognized bacterial pathogens (RBPs) such as pneumococcus, *Haemophilus influenzae,* or *Staphylococcus aureus* if $\geq 10^5$ cfu/mL was detected and, using more stringent criteria, to NRF if $\geq 10^6$ cfu/mL was detected. The characteristics of these patients are summarized in Table 1.

We stratified these 139 patients with pneumonia into 1 of the following etiologic categories (Table 2): respiratory virus alone (n = 14 [10.0% of the 139 cases]), RBP (n = 54 [38.8%]), NRF (n = 22 [15.8%]), mixed RBP/NRF (n = 15 [10.8%]), RBP/viral co-infection (n = 18 [12.9%]), NRF/viral co-infection (n = 12 [8.6%]), and mixed RBP/NRF with viral co-infection (n = 4 [2.9%]). Mean sputum WBC counts were compared among etiologic categories using the Student *t* test after log transformation was fitted.

Table 1. Clinical Characteristics of 139 Patients Hospitalized for Community-Acquired Pneumonia

Characteristics	No. of Cases (%)
Age, mean ± SD, y	67.4 ± 11.6
Lung diseases	
COPD	35 (25.17)
Lung cancer	3 (2.15)
Pulmonary embolism	2 (1.4)
Interstitial lung disease	2 (1.4)
OSA	5 (3.6)
Tracheostomy	6 (4.3)
Pulmonary TB	1 (0.72)
Asthma	1 (0.72)
Comorbidities	
Diabetes mellitus	14 (10.1)
Inhaled corticosteroids	22 (15.8)
Immunosuppression	10 (7.2)
Malignancy	9 (6.5)
Smoking	
Current	24 (17.3)
Former	9 (20.1)
None	28 (20.1)

Abbreviations: COPD, chronic obstructive pulmonary disease; OSA, obstructive sleep apnea; TB, tuberculosis.

Table 2. WBC in Sputum of 139 Patients Hospitalized for Community-Acquired Pneumonia

Etiologic Group	No. of Cases (%)	WBC/mL in Sputum, Mean ± SD, $\times 10^6$	*P* Value vs Viral Pneumonia
Respiratory virus alone	14 (10.0)	3.2 ± 2.5	–
RBP	54 (38.8)	11.0 ± 6.3	.02
NRF	22 (15.8)	10.4 ± 6.3	.07
Mixed RBP/NRF	15 (10.8)	63.1 ± 12.6	.01
RBP + viral coinfection	18 (12.9)	15.8 ± 4.0	.01
NRF + viral coinfection	12 (8.6)	0.9 ± 15.8	.2
Mixed RBP/NRF + viral coinfection	4 (2.9)	125.0 ± 1.6	.01

Abbreviations: NRF, normal respiratory flora; RBP, recognized bacterial pathogen; WBC, white blood cell count.

In patients with viral pneumonia, the mean sputum WBC count (3.2×10^6/mL) was significantly lower than the mean sputum WBC count in pneumonias due to an RBP (11.0 ± 6.3; $P = .02$) (Table 2). The number of WBCs in sputum was nearly identical in pneumonia due to RBP and pneumonia due to NRF (11.0 ± 6.3 vs 10.4 ± 6.3; $P = 1.0$). Nonetheless, the comparison of WBC counts in patients with NRF pneumonia vs viral pneumonia did not reach statistical significance, probably because the numbers of cases were not as large as those for RBP. The greatest inflammatory responses in sputum were seen with mixed RBP and NRF, with or without viral co-infection, when compared with all other categories ($P = .007$).

These results show that (1) patients with pure viral pneumonia may produce purulent sputum in the absence of bacterial coinfection; (2) viral pneumonia stimulates lower numbers of sputum WBCs than bacterial pneumonia, even in patients who produce purulent sputum and are sick enough to require hospitalization; (3) sputum WBC counts are nearly identical for RBP and NRF, thereby supporting the role of NRF as a cause of pneumonia. To our knowledge, sputum WBCs have not been related to the etiology of pneumonia, although such studies have been done in patients with chronic obstructive pulmonary disease beginning as long ago as the 1960s [6] and continuing to the present time [7]. In a patient with pneumonia and purulent sputum, the absence of bacteria on gram stain and a positive viral PCR might allow immediate discontinuation of antibiotic therapy, thereby enhancing antibiotic stewardship efforts.

Our study is limited because it is confined to patients who were hospitalized and able to produce a high-quality sputum sample. It, therefore, cannot be generalized to all patients with pneumonia and does not address the clinical question of whether patients with viral pneumonia simply are less likely to produce purulent sputum. A further limitation is our inability to generalize our findings to an inflammatory response in sputum because we did not measure sputum cytokines such as interleukin (IL)-6, IL-10, or tumor necrosis factor alpha [8, 9]. Nevertheless, these data verify a long-held belief that WBC counts in sputum, as a surrogate for inflammatory response, are lower in viral than in bacterial pneumonia even in patients sick enough to require hospitalization.

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Patient consent. This study used previously collected data of patients who had been de-identified to be enrolled in analysis. The institutional review board of the Baylor College of Medicine has approved the study protocol and exempted us from obtaining informed consent due to the study's retrospective design.

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