The Association between Pneumococcal Pneumonia and Acute Cardiac Events

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Background. Increased cardiac stress, hypoxemia, and inflammation may contribute to acute cardiac events, such as myocardial infarction (MI), arrhythmia, and/or congestive heart failure (CHF). We sought to determine the incidence of such events in patients who were hospitalized for community-acquired pneumococcal pneumonia.

Methods. We studied the medical records of all patients who were admitted for pneumococcal pneumonia during a 5-year period (2001–2005) to identify those who had MI, atrial fibrillation or ventricular tachycardia, or new-onset or worsening CHF at the time of hospital admission.

Results. Of 170 patients, 33 (19.4%) had ≥1 of these major cardiac events. Twelve had MI, of whom 2 also had arrhythmia and 5 had new-onset or worsening CHF. Eight had new-onset atrial fibrillation or ventricular tachycardia; 6 of these also had new CHF. Thirteen had newly diagnosed or worsening CHF, without MI or new arrhythmias. Hypoxemia and anemia were prominent. Importantly, patients with concurrent pneumococcal pneumonia and cardiac events had a significantly higher mortality than those with pneumococcal pneumonia alone (P < .008). The coexistence of pulmonary and cardiac disease was often overlooked by admitting physicians who, seeking a unifying diagnosis, emphasized one diagnosis to the exclusion of the other.

Conclusions. Patients with pneumococcal pneumonia are at substantial risk for a concurrent acute cardiac event, such as MI, serious arrhythmia, or new or worsening CHF. This concurrence significantly increases mortality due to pneumonia. Admitting physicians tend to seek a unifying diagnosis, but the frequent coexistence of pneumonia and cardiac events indicates the importance of considering multiple diagnoses.

Acute bacterial pneumonia stresses the heart by increasing myocardial oxygen demand at a time when oxygenation is compromised by ventilation-perfusion mismatch. Such circumstances increase the risk for disruption of a vulnerable atherosclerotic plaque [1, 2], a phenomenon that is observed with other kinds of stress [3–6]. Pneumonia also raises circulating levels of inflammatory cytokines, which promote thrombogenesis [7, 8] and suppress ventricular function [9, 10]. Taken together, these pathophysiologic events might be expected to lead to major, acute cardiac events, such as myocardial infarction (MI), arrhythmia, and/or congestive heart failure (CHF).

In adults, the incidence of pneumonia is greatest among middle-aged and elderly persons, populations that are also at the greatest risk for heart disease. Infection with Streptococcus pneumoniae (pneumococcus) is the most common cause of community-acquired pneumonia leading to hospitalization [11]. It would not be surprising, therefore, for pneumococcal pneumonia in hospitalized adults to be associated with MI, arrhythmia, or CHF. Such an association was a subject of modest interest in the first half of the 20th century; the final edition of Friedberg’s cardiology textbook [12] devoted 2 pages and 7 references to it. Although current textbooks do consider the general association between sepsis and CHF, and recent studies [13–16] address the association between hospitalization in an intensive care unit and troponin leak, remarkably little has been written about major cardiac events at the time of hospitalization for community-acquired pneumonia. We previously noted an association between MI or atrial fibrillation (AF) and pneumococcal pneumonia [17]. We now present the results of a systematic case series documenting a striking incidence of acute cardiac...
events in patients hospitalized for pneumococcal pneumonia.

METHODS

Site of study and medical records. The Michael E. DeBakey Veterans Affairs Medical Center (Houston, TX) provides medical care for veterans who live in and around Houston. Continuity of care is excellent, and fully computerized medical records document every encounter between a patient and the medical system, including all medical and nursing notes, laboratory data, and readings and images of electrocardiographic or radiological studies. This study was approved by the Institutional Review Board of Baylor College of Medicine (Houston, TX).

Pneumococcal pneumonia. We included all patients who were hospitalized from 1 January 2001 through 31 December 2005 and who received a diagnosis of pneumococcal pneumonia on the basis of (1) clinical and radiologic evidence for pneumonia and ≥1 blood culture yielding S. pneumoniae, or (2) a clinical syndrome of pneumonia, radiologic documentation of a new pulmonary infiltrate, a sputum sample showing >10 inflammatory cells per epithelial cell with clear predominance of gram-positive cocci in pairs and chains, and a culture yielding pneumococci with no other likely bacterial pathogens [17, 18].

Acute cardiac disease at hospital admission. In accordance with American College of Cardiology guidelines [19], the diagnosis of acute MI was made on the basis of new electrocardiographic abnormalities (i.e., ST segment elevation or depression or Q waves) accompanied by troponin I serum levels of ≥0.5 ng/mL. Preexisting coronary artery disease (CAD) was said to be present when medical records documented a previous MI, abnormal coronary angiogram or stress test, or a distinctive electrocardiographic abnormality. Serious arrhythmias were defined as atrial flutter, AF, and ventricular tachycardia, but excluded terminal arrhythmias. We used Framingham criteria [20] to diagnose CHF. The development of new CHF or acute worsening of long-term CHF was determined after a careful examination of the medical records, wherein we compared physical findings, laboratory findings (such as increases in B-natriuretic peptide of >500 pg/mL), chest radiograph (for new or increased pulmonary vascular congestion), and echocardiograms. Only patients in whom CHF (as determined by a composite of the above) was new or had worsened on the basis of objective data were included in our final analysis.

Data collection. Many of these patients were examined and observed prospectively from admission by the senior investigator (D.M.M.). For this study, we carefully reviewed the complete electronic medical records made for each patient at hospital admission for pneumonia; a finding of MI, arrhythmia, or CHF, as defined above, prompted further review of prior records to determine whether the finding was a new one. Most patients had been examined as outpatients in the few months prior to admission, and all patients who survived the episode of pneumonia returned to the clinic for follow-up at least once after discharge from the hospital.

Literature search. We performed a Medline search for articles linking pneumonia, pulmonary infection, S. pneumoniae infection, pneumococcus, or sepsis to myocardial infarction, AF, atrial flutter, arrhythmia, myocardial damage, myocardial infarction, heart failure, or CHF that had been published from 1967 to the present. We searched Old Medline for articles published from 1962 to 1967 under the same subject headings and manually searched Index Medicus for articles published from 1953 to 1962. We also read the relevant references that had been cited in these articles.

RESULTS

Patients with pneumococcal pneumonia. During the 5-year study period (1 January 2001 through 31 December 2005), 170 patients met our inclusion criteria for pneumococcal pneumonia; 33 (19.4%) had ≥1 associated major cardiac event at hospital admission. Eleven of these 33 were in Pneumonia Severity Index risk class IV, and 20 were in risk class V [21]. For clarity of presentation, we stratified the 33 patients who had pneumonia and an acute myocardial event as follows (table 1): 12 (7.1%) of 170 had MI; 8 (4.7%) had new-onset or a new recurrence of arrhythmia without MI; and 13 (7.6%) had new-onset or worsening CHF without MI or a new arrhythmia. Of the 12 patients with MI, 2 had new-onset arrhythmia and 5 had new-onset or worsening CHF; of 8 patients with arrhythmia, 6 had new or worsening CHF. Thus, in total, among 33 patients who had acute pneumococcal pneumonia and a cardiac event, 12 (7.1%) had MI, 10 (5.8%) had new-onset arrhythmia, and 24 (14%) had new-onset or worsening CHF.

When considering all 170 patients who were admitted for pneumococcal pneumonia, 61 were bacteremic, 89 were nonbacteremic, and in 20, blood sample cultures were not performed or they had negative results but had only been performed after antibiotics had been administered. When

Table 1. Major cardiac events in 170 consecutive patients admitted to a hospital for pneumococcal pneumonia.

<table>
<thead>
<tr>
<th>Event</th>
<th>No. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>12 (7.1)</td>
</tr>
<tr>
<td>New arrhythmia</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>New or worsening CHF</td>
<td>5 (2.9)</td>
</tr>
<tr>
<td>New arrhythmia</td>
<td>8 (4.7)</td>
</tr>
<tr>
<td>New or worsening CHF</td>
<td>6 (3.5)</td>
</tr>
<tr>
<td>New or worsening CHF</td>
<td>13 (7.6)</td>
</tr>
<tr>
<td>Total patients with cardiac event</td>
<td>33 (19.4)</td>
</tr>
</tbody>
</table>

NOTE. CHF, congestive heart failure.
Table 2. Myocardial infarction at the time of hospital admission for patients with pneumococcal pneumonia.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, years</th>
<th>Prior cardiac disease</th>
<th>Maximum temperature, °C</th>
<th>Pulse, beats/min</th>
<th>Pulse oximetry, % (inhaled oxygen)</th>
<th>Hb, gm%</th>
<th>New ECG changes</th>
<th>Troponin level, ng/mL</th>
<th>Cardiologic diagnosis</th>
<th>ECHO (wall motion abnormality)</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>83</td>
<td>...</td>
<td>36.7</td>
<td>124</td>
<td>92 (RA)</td>
<td>8.9</td>
<td>Elevated ST; Q waves II, III, aVF; RBBB</td>
<td>19.3</td>
<td>STEMI, CHF</td>
<td>EF-25% (global)</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>97</td>
<td>...</td>
<td>38.3</td>
<td>84</td>
<td>70 (2 L)</td>
<td>10.9</td>
<td>Diminished ST V4–V6</td>
<td>1.8</td>
<td>NSTEMI</td>
<td>ND</td>
<td>Died</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
<td>CAD</td>
<td>39.4</td>
<td>90</td>
<td>69 (100%)</td>
<td>9.4</td>
<td>Diminished ST I, aVL, V4–V6</td>
<td>4.0</td>
<td>NSTEMI</td>
<td>EF-25% (focal)</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>82</td>
<td>CAD, CHF</td>
<td>37.8</td>
<td>108</td>
<td>88 (2 L)</td>
<td>9.9</td>
<td>Diminished ST V3–V6</td>
<td>0.63</td>
<td>NSTEMI, AF, CHF</td>
<td>EF-47% (global)</td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>78</td>
<td>CAD</td>
<td>38.3</td>
<td>61</td>
<td>90 (3 L)</td>
<td>14.6</td>
<td>Elevated ST V2–V5</td>
<td>9.0</td>
<td>STEMI, CHF</td>
<td>EF-20% (global)</td>
<td>Died</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>...</td>
<td>35.6</td>
<td>110</td>
<td>91 (2 L)</td>
<td>8.9</td>
<td>ST, T wave diminished V2–V6</td>
<td>1.9</td>
<td>NSTEMI, CHF</td>
<td>EF-35% (global)</td>
<td>Survived</td>
</tr>
<tr>
<td>7</td>
<td>83</td>
<td>...</td>
<td>38.9</td>
<td>108</td>
<td>89 (RA)</td>
<td>9.8</td>
<td>3rd Degree AV block</td>
<td>2.6</td>
<td>NSTEMI</td>
<td>EF-55% Survived</td>
<td>Survived</td>
</tr>
<tr>
<td>8</td>
<td>64</td>
<td>...</td>
<td>37.2</td>
<td>124</td>
<td>73 (100%)</td>
<td>11.8</td>
<td>Elevated ST, diminished T wave II, III, aVF</td>
<td>1.9</td>
<td>STEMI</td>
<td>ND</td>
<td>Died</td>
</tr>
<tr>
<td>9</td>
<td>73</td>
<td>CAD</td>
<td>37.8</td>
<td>102</td>
<td>83 (100%)</td>
<td>9.1</td>
<td>Diminished ST I, aVL, V2–V6</td>
<td>2.2</td>
<td>NSTEMI, AF</td>
<td>ND</td>
<td>Died</td>
</tr>
<tr>
<td>10</td>
<td>77</td>
<td>...</td>
<td>36.1</td>
<td>109</td>
<td>91 (3 L)</td>
<td>9.0</td>
<td>Diminished ST, T wave I, aVL, V3–V6</td>
<td>1.5</td>
<td>NSTEMI, CHF</td>
<td>EF-50% Survived</td>
<td>Died</td>
</tr>
<tr>
<td>11</td>
<td>73</td>
<td>...</td>
<td>37.2</td>
<td>130</td>
<td>90 (2 L)</td>
<td>10.2</td>
<td>Diminished T wave I, aVL, V5–V6</td>
<td>0.6</td>
<td>NSTEMI</td>
<td>ND</td>
<td>Survived</td>
</tr>
<tr>
<td>12</td>
<td>73</td>
<td>...</td>
<td>37.8</td>
<td>85</td>
<td>99 (2 L)</td>
<td>11.0</td>
<td>Q waves in II, III, aVF</td>
<td>14.7</td>
<td>NSTEMI</td>
<td>EF-55% Survived</td>
<td>Survived</td>
</tr>
</tbody>
</table>

**NOTE.** AF, atrial fibrillation; CAD, coronary artery disease; CHF, congestive heart failure; EF, left ventricular ejection fraction; Hb, hemoglobin; ND, not done; NSTEMI, non-ST segment elevation myocardial infarction; RA, room air; RBBB, right bundle branch block; STEMI, ST segment elevation myocardial infarction.
considering only the patients with pneumococcal pneumonia who had concomitant cardiac events, 6 (50%) of the 12 patients in the MI group were bacteremic, 3 (37.5%) of 8 patients in the arrhythmia group were bacteremic, and 1 (7.7%) of 13 patients in the CHF group were bacteremic. Overall, of the 33 patients who experienced pneumococcal pneumonia and cardiac events, 30% were bacteremic.

**Myocardial infarction.** Twelve patients (table 2) had concurrent MI and pneumococcal pneumonia at admission. Three had ST-elevation MI, with subsequent evolution to Q waves. Nine had non–ST-elevation MI; in each case, electrocardiographic changes were observed in leads corresponding to myocardial regions supplied by defined coronary arteries. All 12 had elevated troponin I serum levels. Two underwent noninvasive stress testing, which revealed reversible ischemia in a defined coronary artery territory. Echocardiograms were available for 8 patients; 5 of these revealed depressed LV function (a new finding in 4 patients).

Although all patients with MI had ≥2 risk factors for CAD, in 8 patients it was documented for the first time during the admission for pneumonia. Symptoms of pneumonia preceded those attributable to cardiac disease in every case. In some cases, attention at hospital admission was focused exclusively on the myocardial event, with treatment for pneumonia being delayed up to 36 h, whereas in others, pneumonia was the admitting diagnosis, and the myocardial event received only perfunctory attention.

Factors likely to contribute to MI include inflammation, hypoxia, anemia, stress, and hypotension (figure 1). By virtue of having pneumonia, all patients had a major inflammatory illness. All were also hypoxic, and in 7 (58%) of the 12, oxygen delivery was further compromised by substantial anemia (hemoglobin, <10 g/dL). Four patients met criteria for shock (sepsis induced vs. cardiogenic), whereas the other 8 patients met criteria only for sepsis. Five patients (40%) who had MI and pneumonia died during the hospital admission, including 3 (75%) of 4 who developed shock.

**Arrhythmia.** Eight patients had new onset of an arrhythmia at or within the first 48 h of hospital admission for pneumococcal pneumonia; 7 had AF and 1 had ventricular tachycardia (table 3). None of these provided evidence of a new MI. In each case, the acute nature of the arrhythmia was suggested by the medical history and documented by the finding of normal rhythm on prior clinic visits. Of interest, 2 patients had a remote history of AF, but had been most recently documented as having a normal sinus rhythm. As with patients with MI, the history of pneumonia preceded that of the arrhythmia in every case. Pneumonia was initially overlooked in some patients, whereas in others, attention was focused on the pneumonia and the AF was assumed to be chronic. All were hypoxic

![Figure 1. Postulated pathogenesis of cardiac events in pneumococcal pneumonia. CHF, congestive heart failure.](https://academic.oup.com/cid/article-abstract/45/2/158/420980)
Table 4. New onset CHF at the time of hospital admission for pneumococcal pneumonia.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, years</th>
<th>Prior cardiac disease</th>
<th>Maximum temperature, °C</th>
<th>Pulse, beats/min</th>
<th>Pulse oximetry, % (inhaled oxygen)</th>
<th>Hb, gm%</th>
<th>BNP level, pg/mL</th>
<th>CXR</th>
<th>Cardiologic diagnoses</th>
<th>ECHO</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>86</td>
<td>AF</td>
<td>36.7</td>
<td>130</td>
<td>60 (RA)</td>
<td>10</td>
<td>460</td>
<td>CMG, congestion</td>
<td>CHF, AF</td>
<td>EF-50%</td>
<td>Survived</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>None</td>
<td>36.7</td>
<td>61</td>
<td>75 (RA)</td>
<td>9.4</td>
<td>3840</td>
<td>CMG, congestion</td>
<td>CHF, 1st degree AV block</td>
<td>...</td>
<td>Survived</td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>Nonischemic CMP, AF</td>
<td>39.4</td>
<td>103</td>
<td>100 (RA)</td>
<td>7.2</td>
<td>...</td>
<td>Vascular congestion</td>
<td>CHF, ST, LBBB</td>
<td>...</td>
<td>Survived</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>CAD</td>
<td>37.8</td>
<td>114</td>
<td>96 (2 L)</td>
<td>13.3</td>
<td>1300</td>
<td>CMG</td>
<td>CHF, ST, LBBB</td>
<td>...</td>
<td>Survived</td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>Diastolic dysfunction</td>
<td>37.2</td>
<td>110</td>
<td>60 (RA)</td>
<td>15.4</td>
<td>...</td>
<td>Bilateral effusions</td>
<td>CHF, ST</td>
<td>EF-30%, LVH</td>
<td>Survived</td>
</tr>
<tr>
<td>6</td>
<td>64</td>
<td>CAD, CHF, AF</td>
<td>38.4</td>
<td>102</td>
<td>95 (3 L)</td>
<td>11.3</td>
<td>&gt;1300</td>
<td>CMG, congestion</td>
<td>CHF, MAT</td>
<td>EF-10%</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>Nonischemic CMP, CHF</td>
<td>35.6</td>
<td>102</td>
<td>70 (RA)</td>
<td>9.3</td>
<td>1830</td>
<td>CMG, effusions.</td>
<td>CHF, NSVT</td>
<td>...</td>
<td>Survived</td>
</tr>
<tr>
<td>8</td>
<td>73</td>
<td>Nonischemic CMP, CHF, AF</td>
<td>37.2</td>
<td>82</td>
<td>95 (5 L)</td>
<td>9.6</td>
<td>...</td>
<td>Left pleural effusion</td>
<td>CHF, AF</td>
<td>...</td>
<td>Died</td>
</tr>
<tr>
<td>9</td>
<td>79</td>
<td>CAD</td>
<td>37.8</td>
<td>110</td>
<td>97 (RA)</td>
<td>13.4</td>
<td>542</td>
<td>None</td>
<td>CHF</td>
<td>...</td>
<td>Died</td>
</tr>
<tr>
<td>10</td>
<td>78</td>
<td>AF</td>
<td>38.4</td>
<td>62</td>
<td>88 (RA)</td>
<td>10.4</td>
<td>1760</td>
<td>None</td>
<td>CHF, AF</td>
<td>EF-35%</td>
<td>Survived</td>
</tr>
<tr>
<td>11</td>
<td>62</td>
<td>CAD, CHF</td>
<td>37.2</td>
<td>100</td>
<td>96 (RA)</td>
<td>7.4</td>
<td>...</td>
<td>CMG, congestion</td>
<td>CHF, ST</td>
<td>...</td>
<td>Survived</td>
</tr>
<tr>
<td>12</td>
<td>58</td>
<td>None</td>
<td>36.1</td>
<td>101</td>
<td>97 (RA)</td>
<td>13.3</td>
<td>...</td>
<td>Bilateral effusions</td>
<td>CHF, ST</td>
<td>EF-30%</td>
<td>Died</td>
</tr>
<tr>
<td>13</td>
<td>76</td>
<td>CHF, AF, CAD</td>
<td>35.6</td>
<td>58</td>
<td>60 (40%)</td>
<td>11.9</td>
<td>1300</td>
<td>CMG</td>
<td>CHF, AF</td>
<td>...</td>
<td>Survived</td>
</tr>
</tbody>
</table>

**NOTE.** AF, atrial fibrillation; BNP, brain natriuretic peptide; CAD, coronary artery disease; CHF, congestive heart failure; CMG, cardiomegaly; CMP, cardiomyopathy; EF, left ventricular ejection fraction; Hb, hemoglobin; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; RA, room air; ST, sinus tachycardia.
at admission, although, in at least 1 patient, hypoxia had been corrected by nasal delivery of oxygen before the AF occurred. Six of these patients had coexisting, uncontrolled CHF that also appeared to be new. Nevertheless, none of these 8 patients died during the hospitalization for pneumonia.

The patient who had ventricular tachycardia was treated with electrical cardioversion, but patients with AF were treated medically; all 7 eventually reverted to a normal sinus rhythm. In 3 patients, this return occurred during the hospitalization; in the others, the time to resolution was uncertain, because follow-up electrocardiography showing normal sinus rhythm was performed weeks to months after the initial episode. The transient nature of the episodes of AF further supports the association between arrhythmia and pneumonia.

CHF. Thirteen patients had concomitant pneumonia and new or worsening CHF in the absence of MI or new arrhythmia (table 4). The patients in this category included 6 in whom pneumonia appeared to precipitate CHF (patients 1–6); 2 in whom preexisting, relatively well-controlled CHF predisposed the patient to pneumonia and was associated with worsening CHF (patients 7 and 8); and 5 in whom the overlap of pneumonia and CHF was so complete that no conclusion could be reached (patients 9–13). Eleven (85%) of these 13 patients had previously documented CAD, nonischemic cardiomyopathy, and/or arrhythmia, including 4 who had long-term AF, but none of the 13 had been experiencing long-term CHF prior to the onset of the pneumonia.

The same precipitating factors that were identified in these patients were also identified in patients who had MI or arrhythmia. Nine (69%) were hypoxic at admission, and 6 (46%) had hemoglobin levels of $\leq 10$ gm/dL. Four (30%) of 13 patients experiencing CHF died during the hospitalization.

**DISCUSSION**

Occam’s Razor, the law of parsimony, urges physicians to seek a unifying diagnosis. However, when one condition predisposes to—or is associated with—another, consideration of concomitant diagnoses is prudent. Of 170 consecutive patients who were hospitalized for pneumococcal pneumonia, 33 (19.4%) experienced $\geq 1$ major myocardial event, including 12 who had MI, 8 who had major arrhythmias, and 13 who experienced worsening CHF. Because some patients with MI also had arrhythmias and CHF, and some who had arrhythmias experienced worsening CHF, there were actually a total of 46 major cardiac events observed in these 33 patients. The concurrence of pneumonia and a new cardiac event was often unrecognized, especially in the first 12–24 h of hospitalization, resulting in some patients not receiving antibiotics for pneumonia and others not receiving cardiac monitoring or anticoagulant therapy.

An association between cardiac events and pneumonia was noted in the first half of the 20th century [12], when prospective studies [22–24] documented electrocardiographic changes that were consistent with ischemia in 2%–22% of cases and AF or atrial flutter in $\sim 6\%$ of cases. The recent medical literature has generally not addressed the concurrence of pneumonia and new cardiac events. For example, a description of coronary artery disease and pulmonary disease in patients who presented to an emergency center did not mention the coexistence of the 2 in any patient [25]. One very recent study [26] that specifically sought noncardiac conditions in patients who had acute MI, however, found that 7.2% of these patients had pneumonia; the authors emphasized, as do we, the tendency of admitting physicians to confine their assessment to a single diagnosis.

We used strict criteria for diagnosing MI—namely, electrocardiographic changes that corresponded to an area of the myocardium supplied by a single coronary artery, together with elevated troponin I levels and ancillary evidence, including noninvasive stress testing and echocardiography [14]. We did not include patients who had elevated troponin I levels without electrocardiographic evidence of MI, a laboratory finding that has been documented in patients in intensive care units [13, 27]. Although, in such cases, elevations of troponin I levels probably indicate myocardial injury, the pathogenesis remains uncertain. The correlation between high circulating levels of IL-6 and TNF-$\alpha$ and an increased troponin I level might indicate a global effect of inflammatory cytokines on the myocardium [10, 28]. Interestingly, 1 study of all patients in an intensive care unit who had elevated troponin levels found evidence of pneumococcal infection in a substantial proportion [13].

We found AF to be the most common serious arrhythmia. Pneumonia was at the top of Friedberg’s long list of noncardiac conditions that cause AF [12], and present-day support for this concept derives from a study of all patients admitted to a hospital with AF as a secondary condition; the leading primary diagnosis was CHF (13%), followed by pneumonia (7%) [29]. We also noted the frequent coexistence of CHF in 71% of our patients with AF. Ventricular tachycardia in 1 patient occurred prior to antibiotic administration—an important point because fluoroquinolones and macrolides may increase the risk for ventricular arrhythmias [30].

The strong association between pneumococcal pneumonia and CHF and the difficulty in clinically differentiating between these 2 conditions was so well recognized in the early 20th century that some physicians routinely prescribed digitalis for pneumonia [31, 32] and penicillin for CHF [33]. In modern times, measuring serum B–natriuretic peptide levels facilitates this distinction [34]. In the setting of acute dyspnea, a serum B–natriuretic peptide level of $>500$ pg/mL predicts a high probability of decompensated CHF if severe sepsis and septic shock are excluded [35, 36]. Only 1 of 13 CHF patients had septic shock; the others met criteria only for sepsis.
Several mechanisms may explain the association between pneumonia and acute cardiac events (figure 1). Epidemiological studies have shown that physical stress is associated with a 2- to 10-fold increased risk for acute MI [3–6], perhaps reflecting disruption of an atherosclerotic plaque followed by thrombosis and acute MI [1, 2]. Infection, which increases myocardial oxygen demand due to fever and tachycardia and decreases oxygenation of the blood via ventilation-perfusion mismatch, is analogous to extreme physical stress. Most of our patients were hypoxic at some time early in their hospitalization, and 58% also had severe anemia (hemoglobin level, ≤10 g/dL). Infection also increases levels of C-reactive protein, fibrinogen, and inflammatory cytokines, which may increase the risk for thrombogenesis and which independently predict an increased likelihood for acute coronary syndromes [7, 8, 37–39]. Two epidemiological studies have shown 5–6-fold increases in the incidence of MI following respiratory tract infection [40] or urinary tract infection [41]. Interestingly, in 8 of 12 patients with MI, the hospital admission for pneumonia was the first at which CAD was diagnosed. Perhaps the replacement of aspirin with acetaminophen/ibuprofen for treatment of fever contributes to an increased occurrence of MI in acute pneumonia.

The pathogenesis of arrhythmia and CHF in pneumonia is also multifactorial (figure 1), including increased myocardial demand for oxygen, lowered blood oxygen levels, and suppression of ventricular function by elevated levels of cytokines [9]. Biventricular impairment of intrinsic myocardial contractility, which may be present in 50% of patients with severe sepsis or septic shock [16], was documented in several of our patients using echocardiography. Tachycardia and especially AF contribute to CHF and worsen myocardial contractility [42], which is consistent with our finding that 10 patients who were experiencing CHF had AF. Taken together, these factors help explain the finding that, overall, 24 (14%) of 170 patients with pneumococcal pneumonia had new or worsening CHF.

Because this is an uncontrolled case series, it is possible that other illnesses, such as chronic obstructive pulmonary disease or gastrointestinal bleeding, that adversely affect oxygen demand due to fever and tachycardia and decreases oxygenation of the blood via ventilation-perfusion mismatch, contributes to an increased occurrence of MI in acute pneumonia. Nonetheless, we found that the concurrence of a cardiac event with pneumococcal pneumonia strongly correlated with in-hospital mortality. Our overall in-hospital mortality rate in patients with pneumococcal pneumonia was 12.4%. Within this group, 9 (27.3%) of 33 patients who had concomitant cardiac events died, compared with 12 (8.8%) of 137 patients who did not experience cardiac events (P<.008, by χ² test; OR, 3.9).

In summary, 19.4% of patients who were admitted to a hospital for pneumococcal pneumonia had ≥1 concurrent major cardiac event. Confidence in a unifying diagnosis may lead initially to consideration of one, rather than both conditions. This frequency of the association is surprisingly high, considering the paucity of recent literature on the subject.

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