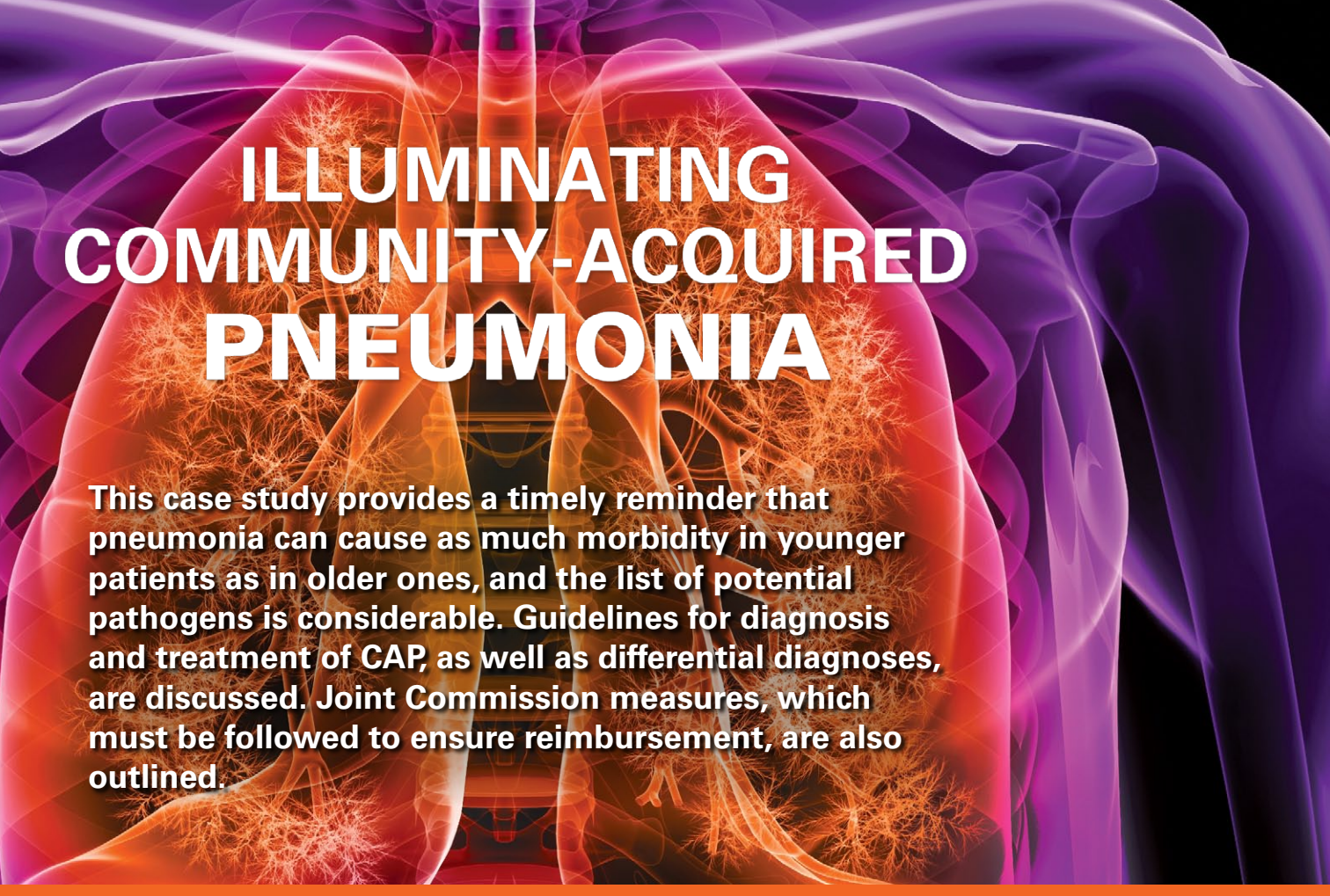

ILLUMINATING COMMUNITY-ACQUIRED PNEUMONIA

This case study provides a timely reminder that pneumonia can cause as much morbidity in younger patients as in older ones, and the list of potential pathogens is considerable. Guidelines for diagnosis and treatment of CAP, as well as differential diagnoses, are discussed. Joint Commission measures, which must be followed to ensure reimbursement, are also outlined.

David A. Farcy MD, Joseph C. Chan, MD, and David Rabinowitz

CASE

A 44-year-old woman presents to the ED with fever, blood-tinged productive cough, and shortness of breath of several days' duration. Her symptoms began 5 days earlier with a productive cough, nasal congestion, and sore throat after she returned from a trip to York, England. She visited her primary care physician 2 days prior to the ED presentation and was started on prednisone 20 mg daily. Over-the-counter medications have not provided symptom relief. In fact, the patient reports worsening of shortness of breath as well as pleuritic chest pain, rusty sputum, cough-associated emesis, and chills without fever. Her medical history is unremarkable, and her surgical history includes hysterectomy and breast augmentation. She denies any tobacco, alcohol, or illicit drug use.

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Physical examination reveals a temperature of 37°C; heart rate, 106 beats/min with a regular rhythm; respiratory rate, 20 breaths/min; blood pressure, 91/57 mm Hg; and oxygen saturation, 90% on room air. Exam findings are notable for dyspnea and diaphoresis. The patient's lips and oral mucosa are dry. Right basilar rhonchi and diffuse crackles are noted on lung auscultation. Laboratory values include a white blood cell count of 4,080 cells/µL with a differential of 66% segmented neutrophils, 14% nonsegmented neutrophils, and 8% lymphocytes; hematocrit, 42.7%; and platelet count, 174,000 cells/µL. The results of coagulation studies are normal. Basic metabolic panel is normal without anion gap. Arterial blood gas analysis (performed during administration of supplemental oxygen at 3 L/min by nasal cannula) reveals a pH of 7.47; Pco_2, 31 mm Hg; Po_2, 70 mm Hg; arterial oxygen saturation, 94.9%; and calculated HCO_3 concentration, 22.6 mmol/L. An ECG demonstrates sinus tachycardia without evidence of ischemia. A chest radiograph (Figure 1) shows an area of consolidation involving the right lower lung, consistent with right lower lobe pneumonia.

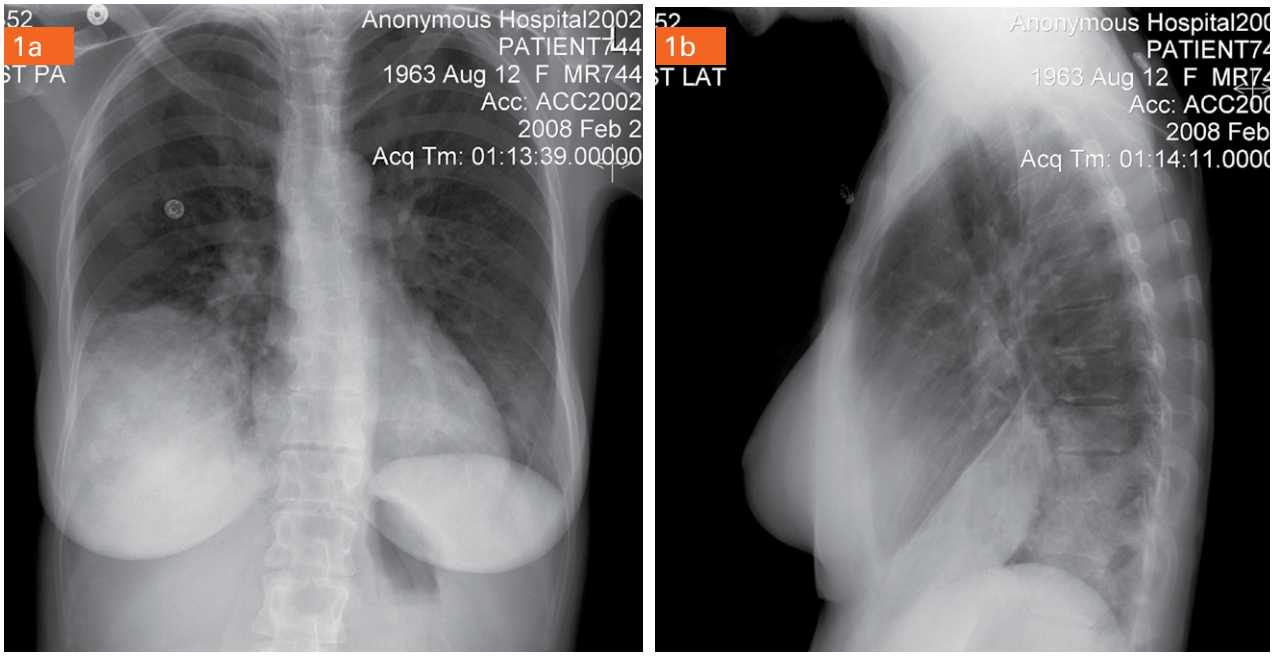

FIGURE 1. Right lower lobe pneumonia. 1a. Initial PA view obtained on arrival, showing consolidation of right lower lung zone. **1b.** Lateral view.

The patient is started on IV fluids (0.9% normal saline) and levofloxacin 750 mg IV almost immediately after pan culture is performed and blood work is sent to the lab. Within 2 hours of the patient's arrival, it is evident that her condition is worsening and she is in septic shock: Her hypotension has not reversed after administration of 3 L of normal saline. Despite use of a nonrebreather mask, the patient develops worsening hypoxemia, marked by an oxygen saturation of 89%. She subsequently becomes more tachycardic, and a repeat chest radiograph (Figure 2, page 16) reveals bilateral lower lobe consolidation. In addition, a repeat arterial blood gas analysis is performed with the patient receiving 100% F_{IO_2} via nonrebreather mask; the following values are obtained: pH, 7.21; P_{CO_2}, 59 mm Hg; P_{AO_2}, 60 mm Hg; and oxygen saturation, 89%. The patient now has acute respiratory distress syndrome (ARDS), defined as sudden onset of bilateral infiltrates and a P_{AO_2}/F_{IO_2} ratio less than 200 mm Hg without evidence of left heart failure. She undergoes successful rapid sequence intubation without difficulty. Etomidates are not used because of the association with adrenal insufficiency and septic shock.[1] Early, goal-directed therapy for sepsis is initiated and the patient undergoes central venous catheterization of the internal jugular vessel to ascertain central venous pressure (CVP). This is recorded at 6 mm Hg; her central venous oxygen saturation (S_{CVO_2}) is 59.5%. Normal saline is administered to maintain a CVP of 8 to 12 mm Hg, and the antibiotic spectrum is broadened to include vancomycin, which is added empirically to cover methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia. Despite aggressive fluid resuscitation, the patient remains hypotensive, requiring norepinephrine to achieve normotension. Dobutamine is started and titrated to achieve a S_{CVO_2} greater than 70%. After 8.75 hours in the ED, the patient is transferred to the medical ICU.

During hospitalization, the patient's blood cultures remain negative. Bronchoscopy is performed, and cultures of bronchial alveolar lavage (BAL) fluid from the right lower lobe yield *Streptococcus pyogenes* at 10,000 to 100,000 CFU/mL. Cultures of bronchial brushings of the right lower lobe yield *Streptococcus pyogenes* at 100 to 900 CFU/mL. Sputum cultures demonstrate growth of the same organism.

DIAGNOSING CAP

Community-acquired pneumonia (CAP) is defined as pneumonia that is not acquired in hospitals or long-term care facilities. In the United States, an estimated 5.6 million cases of CAP occur annually, at an estimated cost of $8.4 billion.[2] CAP is commonly encountered by emergency physicians, and it is important to be familiar with the disease and the bacterial pathogens that serve as etiologies of CAP. It is crucial to recognize that the causes of CAP can include usual as well as unusual pathogens.

In 2001, influenza and pneumonia were the seventh leading cause of mortality in the United States, with an age-adjusted death rate of 21.8 per 100,000 persons.[3] Following the advent of the influenza and pneumococcal vaccines, there has been a decrease in the mortality rate associated with these illnesses. In 2005, influenza and CAP dropped to the eighth leading cause of death.[4] However, CAP remains a leading cause of mortality.

Pneumonia is an infection of the lungs that has a multitude of clinical manifestations and symptoms. These include, but are not limited to, cough (with or without sputum), fever, chills, fatigue, dyspnea, rigor, headache, myalgia, and pleuritic chest pain. Certain pneumonia-causing pathogens, such as *Legionella*, may cause abdominal pain. The physical exam may reveal accessory respiratory muscle use, bronchial breath sounds, tachypnea, and diaphoresis, and rhonchi or rales may be heard on lung auscultation. According to the American Thoracic Society guidelines for the diagnosis and treatment of CAP, a chest radiograph should be obtained in all patients in whom pneumonia is suspected—not only to establish the diagnosis but also to identify potential complications (such as pleural effusion or multilobar involvement).[5] Two-view chest radiographs remain the gold standard to diagnose CAP, although they may be less sensitive in the early stages of pneumonia and cannot be used to identify the specific pathogen.[5,6] Laboratory tests for pneumonia have low sensitivity: Traditionally, blood cultures reveal a probable pathogen in 5% to 14% of cases, while sputum culture sensitivity is 40% to 50%.[5] Urinary antigen assay seems to have a higher diagnostic value for pneumococcal pneumonia, with sensitivity of 50% to 80% and specificity greater than 90%.[5]

The utility of BAL has gained widespread acceptance in the diagnosis of pneumonia. The diagnostic threshold is 10^4 or 10^5 CFU/mL. In a recent review of bronchoscopic BAL in the diagnosis of ventilator-associated pneumonia, a sensitivity of 42% to 93% and a specificity of 45% to 100% were reported.[7] However, bronchoscopy is not easily performed, nor is it often available in the ED. Another study found that blindly obtained samples taken in the ICU and sent for BAL or mini-BAL had sensitivities of 74% to 97% and 63% to 100%, respectively. Specificities were 74% to 100% and 66% to 96%, respectively.[8] We recommend sending blindly obtained tracheal aspirate for culture prior to antibiotic therapy, as long as antibiotic care is not delayed.

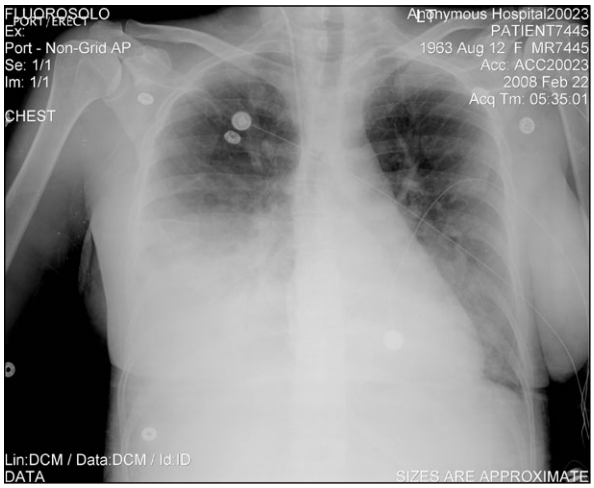

FIGURE 2. Right pleural effusion (air bronchogram clearly visible).

Historically, CAP has been categorized as typical or atypical. Typical pneumonia is usually caused by *Streptococcus pneumoniae* (both penicillin-sensitive and penicillin-resistant strains), *Haemophilus influenzae* (both ampicillin-sensitive and ampicillin-resistant strains), and *Moraxella catarrhalis* (all strains are penicillin resistant). *Staphylococcus aureus* (both penicillin-sensitive and penicillin-resistant strains), *Streptococcus pyogenes*, or group A streptococcus (GAS; all strains are penicillin sensitive) are less common causes. Rare causes include *Neisseria meningitidis*, *Pasteurella multocida*, anaerobes, or aerobic gram-negative bacteria. Atypical pneumonia is caused by influenza, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydophila psittaci*, *Legionella* species, adenovirus, and others (Table 1).[5,9,10] Treatment of CAP is based on the presumptive diagnosis suggested by the physical examination, laboratory results, and patient demographics (Table 2).[5]

TABLE 1. Causes of Community-Acquired Pneumonia and Treatment Recommendations[a]

Pathogen	Recommended therapy	Alternative therapy
Streptococcus pneumoniae	Penicillin G, amoxicillin, fluoroquinolone	For drug-resistant *S pneumoniae*: vancomycin, linezolid If allergic to penicillin: macrolide, clindamycin, doxycycline, fluoroquinolone
Mycoplasma pneumoniae	Macrolide, a tetracycline	Fluoroquinolone
Haemophilus influenzae		
Non–β-lactamase-producing	Amoxicillin	Fluoroquinolone, doxycycline, azithromycin, clarithromycin
β-lactamase-producing	Second- or third-generation cephalosporin, amoxicillin-clavulanate	Fluoroquinolone, doxycycline, azithromycin, clarithromycin
Chlamydophila pneumoniae	A tetracycline	Macrolide[9]
Legionella species	Fluoroquinolone, azithromycin	Doxycycline
Staphylococcus aureus		
Methicillin-susceptible	Antistaphylococcal penicillin	Cefazolin, clindamycin
Methicillin-resistant	Vancomycin or linezolid	Trimethoprim-sulfamethoxazole
Streptococcus pyogenes, group A streptococcus[10]	Penicillin	Clindamycin
Respiratory viruses (influenza A and B, adenovirus, respiratory syncytial virus, and parainfluenza)	Supportive care; prevent secondary bacterial infections	

[a] Adapted from Mandell et al.[5] Data from Oba[9]; Bartlett.[10]

Joint Commission Measures

The Joint Commission, together with the Centers for Medicare and Medicaid Services, the Infectious Diseases Society of America, the American Thoracic Society, the American Society of Emergency Room Physicians, and the CDC, has established a set of performance measures for the treatment of patients with pneumonia. The following measures must be followed to guarantee a full reimbursement[11]:

- Blood cultures performed in ICU patients within 24 hours before or after arrival to the hospital
- Blood cultures performed in ED patients before antibiotic administration
- Administration of antibiotics in the ED within 6 hours of patient arrival
- Pneumococcal screening and vaccination
- Influenza screening and vaccination
- Appropriate antibiotic selection for immunocompetent patients
- Smoking-cessation counseling, if patient has used tobacco within the past 12 months.

Failure to perform one of the aforementioned measures will result in a significantly lower rate of reimbursement and, thus, will directly affect the income received by the provider.

CASE DIAGNOSIS

The patient presentation described above details a rapidly worsening case of pneumonia in a healthy woman. The microorganism that seemed to fit the clinical picture and the radiographic findings was MRSA because of the patient's rapid clinical dete-

TABLE 2. Community-Acquired Pneumonia Treatment Recommendations

INPATIENT

Non-ICU

- Respiratory fluoroquinolone (level I evidence)
- β-lactam + macrolide (level I evidence)

ICU

- β-lactam + either azithromycin (level II evidence) or respiratory fluoroquinolone (level I evidence)[a]

OUTPATIENT

Patients without comorbidities or use of antimicrobials within previous 3 months

- Macrolide (level I evidence)
- Doxycycline (level III evidence)

Patients with comorbidities

- Respiratory fluoroquinolone (level I evidence)
- β-lactam + macrolide (level I evidence)

OUTPATIENT cont.

In regions with high levels of macrolide-resistant infection[b]

- Respiratory fluoroquinolone (level III evidence)
- β-lactam + macrolide (level III evidence)

SPECIAL CONCERNS

If *Pseudomonas* is a consideration

- Antipneumococcal, antipseudomonal β-lactam[c,d] + either ciprofloxacin or levofloxacin (level III evidence)
  or
- Above β-lactam[c,d] + aminoglycoside + azithromycin (level III evidence)
  or
- Above β-lactam[c,d] + aminoglycoside + antipneumococcal fluoroquinolone (level III evidence)

If community-acquired MRSA is a consideration

Add vancomycin or linezolid (level III evidence)

Adapted from Mandell et al.[5]
[a] For penicillin-allergic patients, respiratory fluoroquinolone and aztreonam are recommended.
[b] For patients without comorbidities.
[c] Ticarcillin, piperacillin, ceftazidime, cefepime, imipenem, or meropenem.
[d] For penicillin-allergic patients, substitute aztreonam for β-lactam.

rioration.[12] Recently, the CDC reported 10 cases of MRSA CAP in previously healthy patients whose median age was 17.5 years. Six of the 10 patients died; all who died had multilobar infiltrates much like those in our patient.[13] MRSA CAP is typically associated with influenza virus infection or influenza-like illness. Our patient's previous complaints could easily have been due to influenza. She was started on vancomycin and an emergent infectious disease consult was obtained.

The diagnosis of GAS pneumonia was made by BAL. The patient's hospital course was complicated by septic shock.

GAS PNEUMONIA

Patients diagnosed with GAS are often younger and otherwise healthy. GAS, along with MRSA, has been named an emerging pathogen by the CDC.[14,15] Multiple cases of GAS pneumonia have been reported in York, England, where the patient had recently traveled.[16] The incidence of GAS pneumonia, as reported in a population-based surveillance study of Ontario residents, ranged from 0.16 per 100,000 people in 1992 to 0.35 per 100,000 in 1999.[17] The mortality rate from GAS pneumonia has been reported to be as high as 38%; by comparison, the reported mortality rate from pneumococcal pneumonia ranges from 12% to 20%.[17-19] Factors reported to be independently associated with increased mortality are streptococcal toxic shock syndrome (STSS), increased age, female sex, and coexisting medical conditions such as diabetes, HIV infection, cancer, chronic lung disease, heart disease, and alcohol abuse.[18-21] Death from GAS is usually rapid, with a median survival of 2 days.[17] GAS with STSS is associated with bacteremia in 80% of cases.[22] In the patient discussed above, blood cultures were negative; the diagnosis of GAS was confirmed by BAL culture.

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Some strains of GAS produce exotoxins and superantigens that can cause severe inflammatory responses leading to septic shock and multiple organ failure. In one study, lack of antibodies against the virulent M protein appeared to increase morbidity and mortality.[23] In another study, Husmann et al found that strains of GAS B514 with hyaluronic acid capsules had a selective advantage to survive in the upper respiratory tract and showed increased incidence of pneumonia once the host was colonized with these strains.[24]

Complications of GAS pneumonia can lead to STSS, toxic shock syndrome, septic shock, and ARDS.[25] Aggressive, goal-directed therapy must be initiated promptly. This should include empiric antibiotics, aggressive fluid resuscitation to achieve a CVP of 8 to 12 mm Hg, vasopressors to maintain systolic blood pressure above 90 mm Hg, and inotropes if $Scvo_2$ is less than 70%. Other therapies to consider include drotrecogin alfa (activated) and stress-dose corticosteroids.[22,26] A 2008 study found that although steroids did not decrease mortality, they did expedite weaning from vasopressors.[27] Intubation with mechanical ventilation should be performed as needed. In ARDS, the recommendation is to use low tidal volume (6 mL/kg) to maintain plateau pressure below 30 cm H_2O during mechanical ventilation.[28]

CASE RESOLUTION

The patient was intubated and respiration was supported by mechanical ventilation. Her hypotension was treated with IV fluids (normal saline, lactated Ringer solution, 5% dextrose in 1/2 normal saline, albumin) and vasopressors. She initially received antibiotics empirically, with linezolid and levofloxacin chosen for probable community-acquired MRSA and other common CAP pathogens. After GAS was confirmed, treatment was switched to ceftriaxone. The patient developed multisystem failure that included severe cardiomyopathy with an ejection fraction of 20%, as well as severe oliguric renal failure secondary to prerenal azotemia from her septic shock. Her initial urinary output was less than 10 mL/h. In the ICU, the patient developed anion gap metabolic acidosis, which was likely secondary to hypotension. Her APACHE II score was 21, and a decision was made not to administer drotrecogin-alfa (activated) because of concerns regarding hemoptysis. Her lowest pH was 7.14. With extensive hydration and treatment of her infection, she regained kidney function, her cardiac function improved rapidly, and she was extubated the following week.

CONCLUSION

Emergency physicians need to be aggressive in recognizing the presentation of CAP, initiating treatment, and anticipating complications. Following current CAP guideline measures for management of both typical and atypical pneumonia, including MRSA pneumonia and streptococcal pneumonia, is essential for both treatment and reimbursement.

The future of CAP diagnoses will be based, mainly, on producing a rapid bedside test that has acceptable sensitivity and specificity. With the emergence of resistant CAP-causing strains comes the necessity for physicians to review the status of local antibiotic resistances and tailor treatment based on such resistances. □

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