A 54-year-old woman was admitted to the hospital because of respiratory failure, hypotension, and a cavitary lesion in the lung.

She had rheumatoid arthritis but had otherwise been well until approximately 1 week before admission, when upper respiratory symptoms, cough, and shortness of breath developed. On the day of admission, shortness of breath worsened. She called her physician, who advised her to go to a hospital for evaluation. While she was preparing to leave her home, her symptoms increased in severity; she collapsed, and emergency medical services (EMS) were called.

When they arrived, the patient was unconscious and showing minimal respiratory effort; the pulse was not palpable. Cardiopulmonary resuscitation was initiated with chest compressions and ventilation by means of a mask attached to a handheld bag-valve system, and she was taken to the emergency department of another hospital.

On arrival at the other hospital, the patient was being manually ventilated; the blood pressure was 110/70 mm Hg, the pulse barely palpable at 110 beats per minute, and the temperature 38.9°C. The pupils were 3 mm in diameter and minimally reactive to light, the oral mucosa was dry, the breath sounds were diminished over the right lung fields, and the extremities were cold and cyanotic. An electrocardiogram showed a sinus rate of 120 beats per minute, with evidence of left ventricular hypertrophy and repolarization abnormalities. The results of analysis of arterial blood gases are shown in Table 1. Naloxone was administered, and the trachea was intubated with the use of etomidate and succinylcholine. After the intubation procedure, a large amount of bright-red blood was suctioned from the endotracheal tube. Mechanical ventilation was begun. Laboratory-test results are shown in Table 1.

A chest radiograph showed an endotracheal tube in place, with its tip 4.5 cm above the carina; diffuse air-space opacity was seen throughout the right lung, with dense consolidation surrounding a central cavity, 6 cm in diameter, in the right upper lobe and patchy air-space opacity in the left lower lobe. A right pleural effusion was layered posteriorly; there was no pneumothorax. The osseous thorax appeared intact. A central intravenous catheter was placed in the right internal jugular vein.
The blood pressure suddenly decreased to 70/44 mm Hg with pulseless electrical activity. Phenylephrine, normal saline, sodium bicarbonate, potassium chloride, ceftriaxone, vancomycin, and azithromycin were administered intravenously. Chest radiography repeated 24 minutes after the first study revealed a large right-sided tension pneumothorax, displacement of the mediastinal structures to the left, and complete collapse of the right lung. Air-space opacity in the left lower lobe was unchanged. All tubes and catheters appeared to be in appropriate positions. An angiographic catheter was introduced into the inferior right lateral hemithorax, and there was immediate release of air under pressure. A thoracic surgeon inserted a chest tube in the second right intercostal space; the tube was connected to a chest drainage system that included a water-seal chamber, and a marked air leak was noted. A follow-up chest radiograph showed partial reexpansion of the right upper lobe. The mediastinum was shifted to the left; there was a poorly defined opacity in the left lung and no pleural effusion. The endotracheal tube terminated in the upper thoracic trachea, and the central venous catheter in the superior vena cava. Laboratory-test results are shown in Table 1. The patient was transferred to this hospital.

The patient had had arthritis for 10 years, characterized predominantly by asymmetric swelling of the joints of the hands and feet; she had a negative test for rheumatoid factor and variably positive antinuclear-antibody titers (1:40 to 1:80 in ribosomal or nucleolar patterns). She was treated sequentially with nonsteroidal antiinflammatory drugs (NSAIDs), sulfasalazine, and methotrexate, with partial relief. Two and a half years before admission, while taking methotrexate, a flare occurred, with swelling of the joints of the hands and feet, carpal tunnel syndrome, and morning stiffness; the dose of methotrexate was increased, but she then had hair loss, and abnormal results of liver-function tests were reported. Two years before admission, methotrexate was discontinued, and adalimumab was begun, with prompt and complete relief of symptoms. Three months before admission, at routine follow-up with her rheumatologist, she felt well, with no joint pain or stiffness, and the physical examination was normal. The erythrocyte sedimentation rate was 13 mm per hour, and the serum level of antibody to cyclic citrullinated peptide was 145 U per milliliter (normal, <20). A diagnosis of Graves’ disease had been made 11 years earlier; the disease was treated with radioactive iodine. She had hypercholesterolemia and allergic rhinitis and had undergone hysterectomy and bilateral salpingo-oophorectomy 2 years earlier because of leiomyomas. Both her parents had had hypertension; her mother had rheumatoid arthritis and had had a myocardial infarction when she was in her 40s. The patient was divorced, worked in an office, and had grown children. She did not smoke or drink alcohol and had no known drug allergies. Medications included ezetimibe, simvastatin, levothyroxine, and adalimumab (40 mg weekly, subcutaneously).

On examination, she was intubated and unconscious, with central and peripheral cyanosis and no spontaneous movements. There were bounding femoral and carotid pulses; radial pulses were absent. The blood pressure was 105/70 mm Hg, the pulse 115 beats per minute, and the temperature 38.1°C; respirations were by mechanical ventilation, and the oxygen saturation could not be measured. The pupils were 4 mm and constricted to 3 mm on exposure to light; the neck was supple, and the breath sounds were coarse. The extremities were cold, and the skin was mottled. The remainder of the examination was normal.

Air was escaping through the chest tube, with a volume loss of 300 to 400 ml for every 500- to 600-ml breath. Analysis of the urine revealed 3+ albumin and blood, 5 to 10 red cells and 3 to 5 white cells per high-power field, and moderate numbers of bacteria; a toxicology screen was positive for benzodiazepines. Other laboratory-test results are shown in Table 1. Specimens of blood and urine were cultured. Vecuronium (10 mg) was administered intravenously immediately on arrival, the administration of normal saline and phenylephrine was continued, and norepinephrine was administered at a dose that would result in a systolic blood pressure greater than 90 to 100 mm Hg; calcium carbonate, bicarbonate, vasopressin, vancomycin, ceftriaxone, and clindamycin were also administered. A chest radiograph revealed a pneumothorax with collapse of the right middle and lower lobes and multifocal patchy opacities in the remaining lungs, a chest tube in the right middle lung field, the endotracheal tube at the level of the thoracic inlet, and the internal jugular catheter in the superior vena cava.

A central arterial catheter was inserted. A sur-
Table 1. Results of Laboratory Tests.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference Range, Adults†</th>
<th>Other Hospital</th>
<th>This Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>On Arrival</td>
<td>1 Hr 17 Min after Arrival</td>
</tr>
<tr>
<td>Arterial base excess (mmol/liter)</td>
<td></td>
<td>−29.0</td>
<td>−20.0</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.35–7.45</td>
<td>6.88</td>
<td>6.97</td>
</tr>
<tr>
<td>Fraction of inspired oxygen (per liter)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Partial pressure of arterial carbon dioxide (mm Hg)</td>
<td>35–42</td>
<td>87.70</td>
<td>30.30</td>
</tr>
<tr>
<td>Partial pressure of arterial oxygen (mm Hg)</td>
<td>80–100</td>
<td>78.00</td>
<td>113.00</td>
</tr>
<tr>
<td>Bicarbonate (mmol/liter)</td>
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<td>10.3</td>
<td>8.7</td>
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<tr>
<td>Oxygen saturation (%)</td>
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<td>96.0</td>
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<tr>
<td>Allen test</td>
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<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>36.0–46.0 (women)</td>
<td>38.3</td>
<td>40.4</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.0–16.0 (women)</td>
<td>13.5</td>
<td>13.8</td>
</tr>
<tr>
<td>White-cell count (per mm³)</td>
<td>4500–11,000</td>
<td>3700</td>
<td>2500</td>
</tr>
<tr>
<td>Differential count (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>40–70</td>
<td>42</td>
<td>31</td>
</tr>
<tr>
<td>Band forms</td>
<td>0–10</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>22–44</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Monocytes</td>
<td>4–11</td>
<td>15</td>
<td>0</td>
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<tr>
<td>Eosinophils</td>
<td>0–8</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Atypical lymphocytes</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Myelocytes</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Metamyelocytes</td>
<td>0</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Platelets (per mm³)</td>
<td>150,000–350,000</td>
<td>162,000</td>
<td>136,000</td>
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<tr>
<td>Partial-thromboplastin time (sec)</td>
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<td>42.4</td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>10.3–13.2</td>
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<td>16.4</td>
</tr>
<tr>
<td>International normalized ratio</td>
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<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Sodium (mmol/liter)</td>
<td>135–145</td>
<td>141</td>
<td>139</td>
</tr>
<tr>
<td>Potassium (mmol/liter)</td>
<td>3.5–5.0</td>
<td>2.9</td>
<td>4.4</td>
</tr>
<tr>
<td>Chloride (mmol/liter)</td>
<td>100–108</td>
<td>110</td>
<td>113</td>
</tr>
<tr>
<td>Carbon dioxide (mmol/liter)</td>
<td>23.0–31.9</td>
<td>11</td>
<td>15.0</td>
</tr>
<tr>
<td>Urea nitrogen (mg/dl)</td>
<td>8–25</td>
<td>50</td>
<td>63</td>
</tr>
</tbody>
</table>
A surgical consultant placed a second chest tube in the right lateral chest, and the first tube was clamped; however, the air leak persisted. The anesthesia service was consulted, and the endotracheal tube was advanced down the left mainstem bronchus, with resolution of the leak from the chest tube on the right; however, repeated assessments of the levels of arterial blood gases (Table 1) showed insufficient oxygenation, so the endotracheal tube was withdrawn to above the level of the carina. Bronchoscopic examination with alveolar lavage of the right lung, performed at the bedside by thoracic surgeons, revealed edema and inflammation and no endobronchial lesions. During the procedure, hypotension with pulseless electrical activity developed; cardiopulmonary resuscitation was instituted, with restoration of a pulse. The patient was transferred to the surgical intensive care unit 5.5 hours after her arrival in the emergency department.

Contact precautions were instituted. Metabolic and respiratory acidosis persisted, despite the administration of pressors and bicarbonate. Levels of amylase and lipase were normal; other test results are shown in Table 1. Additional episodes of pulseless electrical activity occurred, and resuscitation efforts failed. The patient was pronounced dead 8 hours after arrival in the emergency department.

An autopsy was performed.

**Differential Diagnosis**

_Dr. Michael E. Weinblatt:_ May we review the radiographic studies?

_Dr. Gerald F. Abbott:_ The initial chest radiograph from the other hospital (Fig. 1A), obtained with the patient in the supine position, shows extensive air-space opacity throughout the right lung, with dense consolidation in the right upper lobe surrounding a well-demarcated cavity that is approximately 6 cm in diameter. There is patchy air-space opacity in the left lower lobe. There is a veil of increased density across the entire right hemithorax, which suggests the presence of a pleural effusion that is layered posteriorly. A second chest radiograph from the other hospital (Fig. 1B) shows a new, right internal jugular catheter extending to the superior vena cava and a right tension pneumothorax, with air extending down into the costodiaphragmatic sulcus. There is virtual collapse of the entire right lung, with some
aeration remaining in the apex; a shift of the mediastinal structures toward the left; and increased density in the left lung, a feature consistent with atelectasis. A third chest radiograph obtained shortly thereafter (Fig. 1C) shows a chest tube in place in the right hemithorax, partial reexpansion of the right lung, but persistent consolidation, atelectasis, and pneumothorax. There is mild interstitial pulmonary edema in the left lung.

A representative chest radiograph obtained after transfer to this hospital (Fig. 1D) shows a second chest tube in place in the right hemithorax and almost complete resolution of the pneumothorax. There is increasing diffuse air-space opacity in both lungs, a feature consistent with pulmonary edema and bilateral pleural effusions.

**Figure 1. Chest Radiographs Obtained with Portable Equipment.**

An initial chest radiograph (Panel A) shows an endotracheal tube in an appropriate position and extensive air-space opacity throughout the right lung, with dense consolidation in the right upper lobe surrounding a cavity, 6.0 cm in diameter, right pleural effusion, and patchy air-space opacity in the left lower lobe. A repeat chest radiograph (Panel B) shows a right internal jugular catheter extending to the superior vena cava and a right tension pneumothorax with collapse of the right lung and shift of the mediastinal structures to the left. A subsequent chest radiograph (Panel C) shows a right chest tube in place, with partial reexpansion of the right lung but persistent consolidation, atelectasis, and pneumothorax, as well as mild interstitial pulmonary edema in the left lung. A chest radiograph obtained after transfer to this hospital (Panel D) shows a second right chest tube in place and almost complete resolution of the pneumothorax. There is increasing diffuse air-space opacity in both lungs, a feature consistent with pulmonary edema and bilateral pleural effusions.
both lungs, a feature consistent with pulmonary edema, and there are bilateral pleural effusions.

Dr. Weinblatt: This 54-year-old woman with rheumatoid arthritis and a negative test for rheumatoid factor was admitted to the hospital with respiratory failure, hypotension, fever, and a cavitary lesion in the lung, and she died several hours later. What caused the cavitary process? The differential diagnosis includes the rheumatic disease itself, a malignant tumor, and infection.

**PULMONARY MANIFESTATIONS OF RHEUMATOID ARTHRITIS**

Rheumatoid arthritis can have pulmonary complications. Rheumatoid nodules in the lung are most common in patients who have a positive test for rheumatoid factor and also have subcutaneous rheumatoid nodules. Pulmonary rheumatoid nodules can cavitate and can occasionally but rarely lead to bronchopulmonary fistulas. Pulmonary nodules with cavitation may occur in patients with rheumatoid arthritis who have occupational exposure to coal dust, silica, or asbestos, which is called Caplan’s syndrome. Other pulmonary processes seen in patients with rheumatoid arthritis include interstitial fibrosis, pleuritis, pleural effusions, bronchiectasis, bronchiolitis, pulmonary hypertension, and rarely, pulmonary vasculitis. Other rheumatologic diseases that could produce a cavitary process include types of pulmonary vasculitis, most notably Wegener’s granulomatosis.

The fact that this patient tested negative for rheumatoid factor and did not have subcutaneous nodules makes it unlikely that she had rheumatoid nodules in the lung that cavitated. She had no occupational exposures, and the other manifestations of rheumatoid lung disease are not consistent with her presentation. Although Wegener’s granulomatosis can progress to catastrophic lung disease, including pulmonary hemorrhage, there is nothing in this patient’s history to suggest this diagnosis.

**MALIGNANT TUMORS**

Patients with rheumatoid arthritis may be at increased risk for some types of malignant tumors, including both nodal and extranodal lymphomas; this risk may be increased by the immunosuppressive therapy used for the treatment of the arthritis. However, the rapid evolution of this patient’s illness makes a malignant tumor highly unlikely.

**INFECTIONS**

The history of fever and the rapid progression of the illness over a period of 1 week strongly suggest that the pulmonary process was an infection. Patients with rheumatoid arthritis are at an increased risk for bacterial infections. In a population-based study from Rochester, Minnesota, patients with rheumatoid arthritis had nearly twice the risk of infection, including lung infections, as control patients. This increased risk could be attributable to the disease itself, treatment of the disease, or a combination of the two.

**TREATMENT OF RHEUMATOID ARTHRITIS**

This patient received a variety of treatments for rheumatoid arthritis over a 10-year period. Initially, she received NSAIDs. These reduce the morning stiffness, pain, and swelling associated with the disease but do not modify the course of the illness, which is associated with joint deformity, fatigue, weight loss, anemia, and premature death. The treatment of rheumatoid arthritis has evolved substantially in recent decades with the introduction of disease-modifying antirheumatic drugs (DMARDs), which actually slow or stop the progression of the disease instead of simply alleviating symptoms.

Treatment with DMARDs is now begun as soon as the diagnosis of rheumatoid arthritis is made, since early institution of therapy reduces the morbidity and perhaps the mortality associated with rheumatoid arthritis. This patient received sulfasalazine followed by methotrexate; methotrexate is now the most popular DMARD worldwide. Because of abnormal results of liver-function tests, methotrexate was stopped, and anti–tumor necrosis factor (TNF) therapy was begun for control of her rheumatoid arthritis. There are three anti-TNF therapies approved for use in the United States: infliximab and adalimumab (monoclonal antibodies) and etanercept (a soluble TNF receptor). All three drugs decrease the signs and symptoms of rheumatoid arthritis, have a beneficial effect on quality of life and function, and reduce the structural progression of joint disease. This patient was receiving adalimumab, a fully humanized monoclonal antibody, which is self-administered (40 mg subcutaneously, generally every other week) with or without methotrexate. As with all anti-TNF therapies, the clinical response is better when added to methotrexate.

Although most patients have clinical responses
to anti-TNF therapies within 2 to 4 weeks, infections are potentially serious complications. TNF is a cytokine that is an important mediator of inflammation and immune regulation and has a role in the function of monocytes, neutrophils, B cells, and T cells. Thus, it is not surprising that blocking its effects could produce susceptibility to infections. What infections is this patient at risk for because of this treatment?

**Bacterial Infections**

A higher rate of bacterial infections, including pulmonary infections, has been reported among patients with rheumatoid arthritis who are receiving anti-TNF therapy than among those who are not receiving these therapies, but this is not a universal finding. Many of these patients are also taking corticosteroids, and the role of these agents in the increased risk must be considered.

Pneumococcal infection is a particular concern for patients receiving anti-TNF therapy, since TNF-α appears to be important in the clearance of infection with *Streptococcus pneumoniae*. There have been case reports of fatal infection with *S. pneumoniae* in patients receiving anti-TNF therapy. We recommend that all patients receive a pneumococcal vaccine before starting anti-TNF therapy. We were not told whether this patient had been vaccinated.

We also need to consider methicillin-resistant *Staphylococcus aureus* (MRSA) infection and cavitary secondary to aspiration pneumonia with a mixed bacterial infection. There was no history of skin lesions to suggest MRSA and no history of altered mental status or difficulty swallowing to increase the risk of aspiration, so these causes are unlikely.

**Mycobacterial Infection**

Tuberculosis has been seen with anti-TNF therapy. TNF is critical for the control and containment of intracellular pathogens by means of the formation of granulomas. During the initial development of infliximab and adalimumab, there were only rare reports of tuberculosis. Since the approval of the drugs by the Food and Drug Administration, an increasing number of cases of tuberculosis have been reported. Infection typically becomes manifested relatively soon after the start of therapy (mean, 12 weeks), suggesting reactivation of latent infection rather than primary infection. More than half the patients are on other immunosuppressive therapies, and half have extra-pulmonary tuberculosis, including disseminated tuberculosis. The relative risk of the development of tuberculosis among patients with rheumatoid arthritis who receive TNF blockers is estimated to be 4 times as high as that among patients with rheumatoid arthritis who do not receive these agents, and close to 20 times as high as that in the normal population.

This patient had a negative purified protein derivative (PPD) test for mycobacterium tuberculosis exposure before starting therapy, but because of anergy, patients with rheumatoid arthritis may be PPD-negative despite having latent infection. Risk factors for exposure to tuberculosis, such as family history, occupational and travel history, or immigration from an area where the disease is endemic, must be ascertained to help determine the risk of latent disease before anti-TNF therapy is begun. Since this patient had been receiving adalimumab for 2 years, if this were tuberculosis, it would most likely be a new primary infection.

Atypical mycobacterial infections have also been reported in patients receiving anti-TNF therapy. However, such infections would be unlikely to produce the rapidly progressive, fulminating disease seen in this patient.

**Fungal Infection**

Fungal infections, including histoplasmosis, coccidioidomycosis, and aspergillosis, have also been seen in patients receiving anti-TNF therapy. The lack of a history of travel to an area where these infections are endemic and the rapid progression of the process make most fungal infections unlikely in this case.

**Summary**

This patient’s course is most consistent with a rapidly progressive lung infection leading to a cavitary lung disease. In view of its pace, the disease was probably caused by an encapsulated bacterium, rather than by a mycobacterium or fungus, and the most common pathogen to cause overwhelming disease in this context would be *S. pneumoniae*. Because of the risk of the development of severe infections in patients with rheumatoid arthritis who take methotrexate, TNF blockers, or both, patients, primary care physicians, and other health care workers need to be aware of the importance of rapid recognition and early treatment of infections in these patients. We recommend that patients taking these medications receive pneumococcal and influenza vaccines an-
nually. Patients must be aware that they need to be evaluated promptly if they have a fever or other signs of infection. Delay in diagnosis and initiation of therapy for an infection can have catastrophic consequences, as it did in this case.

**Clinical Diagnosis**

Bacterial pneumonia with abscess formation and cavitation.

**Dr. Michael E. Weinblatt’s Diagnosis**

Bacterial pneumonia with abscess formation and cavitation, most likely due to *S. pneumoniae*.

**Pathological Discussion**

Dr. Aashiyana F. Koreishi: At autopsy, the combined weight of the lungs was 1818 g (reference range, 685 to 1050), and there was a right pleural effusion (150 ml). The right upper lobe was densely consolidated and contained a cavity, 8.5 cm in diameter (Fig. 2A). We did not find gross evidence of a communication between the cavity and either the pleural space or a bronchus. This suggests that the abscess did not rupture spontaneously, in which case we would have expected to see a large defect in the pleura. A defect due to a needle injury could have been too small to detect on gross examination. On histologic examination, congested lung tissue with thrombosed vessels surrounded the cavity (Fig. 2B). The alveolar spaces were filled with fibrin and histiocytes, with necrosis. Colonies of bacteria were seen along interlobular septa and bronchovascular bundles (Fig. 2C), a feature consistent with growth along pulmonary lymphatic vessels. Gram’s staining of a tissue specimen revealed abundant gram-positive cocci, predominantly in chains, both free in the air spaces and within macrophages (Fig. 2C, inset). A culture of premortem bronchial washings was positive for group A beta-hemolytic streptococcus (*S. pyogenes*). Blood cultures were negative. Multiple thrombi were present in the microvasculature of the lungs, heart, and kidneys (Fig. 2D), a finding consistent with disseminated intravascular coagulation. The kidneys showed acute tubular injury. Additional findings included mild left ventricular hypertrophy and coronary artery disease.

Group A beta-hemolytic streptococcus is an uncommon cause of pneumonia, accounting for less than 1% of community-acquired cases. Pneumonia accounts for approximately 11% of invasive infections by group A beta-hemolytic streptococcus. Risk factors for pneumonia are similar to those for invasive group A beta-hemolytic streptococcus overall, and they include diabetes mellitus, congestive heart failure, chronic lung disease, malignant tumors, and immunosuppression. Pneumonia in this context produces a severe interstitial or confluent bronchopneumonia, which is often necrotizing and, as in the present case, may lead to abscess formation and cavitation. Infection can show an erysipelas-like spread through lymphatic vessels, as it did in this case, and may cause pleural effusions and empyema.

The mortality rate for group A beta-hemolytic streptococcal pneumonia is as high as 38%, higher than that for necrotizing fasciitis (26%) and invasive infections overall (12%). Toxic shock syndrome is reported to occur in about one third of cases of group A beta-hemolytic streptococcus pneumonia. The consensus definition of toxic shock syndrome includes hypotension (systolic blood pressure of ≤90 mm Hg) in combination with two or more of the following: acute renal failure, coagulation abnormalities, liver-function abnormalities, acute respiratory distress syndrome, generalized rash, and necrotizing fasciitis. This patient had hypotension, abnormal results of liver-function tests, coagulation abnormalities, and histologic evidence of disseminated intravascular coagulation and acute tubular injury, and therefore she met the criteria for the toxic shock syndrome.

Dr. Morton N. Swartz (Infectious Disease): Is there any histologic evidence in other parts of the lung of hyaline-membrane formation to suggest an influenza viral infection followed by invasive streptococcal infection?

Dr. Koreishi: There was no evidence of diffuse alveolar damage.

Dr. Nancy Lee Harris (Pathology): Dr. Weinblatt, do you have any information on the occurrence of group A beta-hemolytic streptococcal infections in patients who are taking TNF blockers?

Dr. Weinblatt: There has been one report of the toxic shock syndrome due to the occurrence of this organism in a patient receiving etanercept, and I had a patient receiving etanercept in whom the toxic shock syndrome occurred in association
with group A beta-hemolytic streptococcal infection. This organism is not commonly associated with anti-TNF therapy.

_Dr. Margaret Seton_ (Rheumatology): We see patients who come from overseas and have been treated for tuberculosis in the past. Should these patients receive TNF blockers?

_Dr. Weinblatt_: For patients who have a risk of latent infection with resistant tuberculosis, I consult with our infectious-disease colleagues about the best antimicrobial regimen before starting anti-TNF therapy.

**ANATOMICAL DIAGNOSIS**

Invasive group A beta-hemolytic streptococcal infection, with acute necrotizing bronchopneumonia with cavitation and with evidence of the toxic shock syndrome, in a patient treated with anti-TNF antibody.

Dr. Weinblatt reports receiving consulting fees from Can-Fite, EntreMed, Horizon Therapeutics, Idera Pharmaceuticals, Reata Pharmaceuticals, Rigel, VBL, Abbott, Amgen, Astellas Pharma, Avidimer, AstraZeneca, Biogen Idec, Bristol-Myers Squibb, Celsion, CombinatoRx, Crescendo Bioscience, Cytokine PharmaSciences, Ensemble Discovery, Genentech, GlaxoSmithKline, Sandou Hexal, Hollis-Eaton, Medarex, Medimmune, Merck, Millennium Pharmaceuticals, Novartis, Pfizer, Roche, Sanofi-Aventis, Serona, Teva

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**Figure 2. Findings at Postmortem Examination.**

A gross photograph of the right lung (Panel A) shows dense consolidation in the upper lobe, with a central cavity, 8.5 cm in diameter (inset). Histologic evaluation of the right upper lobe (Panel B, hematoxylin and eosin) shows diffusely inflamed and necrotic lung tissue with multiple thrombosed vessels (arrow) surrounding the cavity. Clusters of bacteria (Panel C, hematoxylin and eosin) are seen surrounding the thrombosed vessel that is identified in Panel B. Gram-positive cocci in chains are seen (Panel C, inset, Brown–Hopps stain). In the kidney (Panel D), thrombi are seen within glomerular capillary loops (arrowheads). Several renal tubules are dilated (arrows), with flattened epithelial cells, loss of nuclei, sloughing of cells into the tubular lumens, and irregular luminal outlines.
Pharmaceuticals, Velcura, Xphos Technologies, Centocor, Wyeth, and UCB; holding stock options in Can-Fite, Celsion, Entremed, Merrimack, and VBL; receiving lecture fees from Abbott; and receiving grant support from Amgen, Abbott, Bristol-Myers Squibb, Genentech, Millennium Pharmaceuticals, Biogen Idec, and Crescendo. Dr. Abbott reports receiving royalties from Amisys and Thieme Medical Publishers. No other potential conflict of interest relevant to this article was reported.

REFERENCES


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