MAYO CLINIC

77-Year-Old Man With a Painful Left Knee, Anemia, and Renal Insufficiency

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A 77-year-old man presented to a community emergency department with acute left knee pain and swelling 1 day after a minor fall from his truck. Radiography of the knee did not detect fracture. Because of increasing pain, swelling, and erythema, he presented 3 days later to a community orthopedist for further evaluation. He had no systemic symptoms of fever and chills and no history of gout, pseudogout, or knee operation.

The patient's medical history was notable for an elevated creatinine concentration, hypertension, dyslipidemia, and an episode of pneumonia requiring hospitalization in the early spring, 7 months before presentation with left knee pain. His medications included aspirin (81 mg/d), coenzyme Q10 (200 mg/d), levothyroxine (137 μg/d), metoprolol succinate (50 mg twice daily), simvastatin (20 mg/d), and one multivitamin daily.

On physical examination, his vital signs were notable only for a new oxygen requirement of 2 L by nasal cannula to maintain an oxygen saturation of 94%. He was in obvious pain. His lungs were clear on auscultation, and cardiac examination revealed a regular heartbeat with no murmurs. His left knee was markedly erythematous, edematous, and painful on palpation and passive range of motion. He was unable to actively move his left leg at the knee because of the pain. The joint was aspirated, and laboratory examination of the specimen revealed a white blood cell (WBC) count of more than 46.0×10^9/L ($<1.5 \times 10^8$/L) as well as positively birefringent calcium pyrophosphate dihydrate crystals. His initial laboratory results at presentation were remarkable for the following (reference ranges provided parenthetically): hemoglobin, 9.8 g/dL (13.5-17.5 g/dL) with a mean corpuscular volume of 92.7 fL (81.2-95.1 fL); WBC count, 22.4×10^9/L ($3.5\text{-}10.5 \times 10^9$/L). An electrolyte panel was remarkable only for a sodium level of 131 mmol/L (135-145 mmol/L). In addition, cultures of the synovial fluid were positive for bacterial growth consistent with a diagnosis of septic arthritis.

1. Which *one* of the following is the *most likely* bacterial cause of septic arthritis in this patient?

a. *Mycoplasma hominis*
b. *Neisseria gonorrhoeae*
c. *Staphylococcus aureus*
d. *Streptococcal pneumoniae*
e. *Borrelia burgdorferi*

Concomitant crystal-induced and septic arthritis can occur, as in this patient, but is not common. *Mycoplasma hominis* is a very rare cause of septic arthritis and is usually seen in patients who are immunocompromised and have recently undergone pelvic surgical manipulation.[1] *Neisseria gonorrhoeae* is a common cause of septic arthritis in sexually active young adults but is less likely in an elderly patient. The most common cause of septic arthritis in immunocompetent adults is *Staphylococcus aureus*, which is the most likely cause in our patient; *Streptococcus pyogenes* is the second most common cause, and *S pneumoniae* is the third most common cause.[2] In about half the cases of *S pneumoniae* joint infections, there is no other clinically apparent focus of pneumococcal infection.[2] Our patient's synovial fluid cultures were positive for *S pneumoniae*. *Borrelia burgdorferi* is the agent responsible in Lyme disease–associated arthritis. This arthritis usually presents in a patient with a history of untreated Lyme disease and is usually reactive in nature with no organisms actually present within the synovial fluid.

The patient was promptly transferred to our hospital for emergent irrigation and debridement. Six of 6 blood specimens obtained at admission also grew *S pneumoniae*. Treatment with intravenous ceftriaxone was

See end of article for correct answers to questions.

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initiated. Chest radiography, lumbar puncture, and echocardiography revealed no signs of pneumonia, meningitis, or valvular vegetations. In one study, 36% of patients with pneumococcal arthritis had concomitant pneumonia, 15% had meningitis, and 6% had endocarditis.[2] Although *S pneumoniae* is a less common cause of septic arthritis, it is the most common cause of bacterial pneumonia and can also cause otitis media and meningitis. Along with young children and immunocompromised individuals, adults over the age of 65 years are at higher risk for invasive disease and should be vaccinated.

2. On the basis of current recommendations, this patient *should* have received the pneumococcal conjugate vaccine (PCV13) and the pneumococcal polysaccharide vaccine (PPSV23) on which *one* of the following regimens?

a. Age 60, PCV13 followed by the PPSV23 6 months later
b. Age 60, PPSV23 followed by the PCV13 8 weeks later
c. Age 65, PCV13 followed by the PPSV23 12 months later
d. Age 65, PCV13 followed by the PPSV23 8 weeks later
e. Age 65, PPSV23 alone

In June 2015, the Advisory Committee on Immunization Practices updated recommendations for vaccine-naive immunocompetent adults, stating that at age 65, they should receive first PCV13 followed by the PPSV23 1 year or more later.[3] This new recommendation extends the interval between doses from a previous recommendation of 6 months. Adults aged 65 years or older who previously were vaccinated with only PPSV23 should receive a dose of PCV13 1 year or more later.[3] Younger patients (aged 19-64 years) who have chronic heart disease, chronic lung disease, diabetes mellitus, alcoholism, or chronic liver disease or are cigarette smokers should be vaccinated with a dose of PPSV23.[4] Immunocompromised or asplenic (functional or anatomic) patients aged 19 years or older should receive both pneumococcal vaccinations with the interval between PCV13 and PPSV23 doses being shorter (≥8 weeks) and should be revaccinated at 5 years with PPSV23.[4]

On admission to our hospital, it was noted that the patient had received the pneumococcal polysaccharide vaccine (Pneumovax 23) 1 year before this hospitalization and received the pneumococcal conjugate vaccine (Prevnar 13) 9 months after receiving the Pneumovax 23. Despite having received both vaccinations, our patient had been hospitalized in the early spring with pneumonia and is now hospitalized with pneumococcal bloodstream infection and septic arthritis, suggesting that he may have a susceptibility to infection by this organism. Further blood testing on admission for treatment of his septic left knee revealed the following: creatinine, 2.1 mg/dL (0.8-1.3 mg/dL); calcium, 8.7 mg/dL (8.9-10.1 mg/dL); normocytic anemia (hemoglobin, 11.1 g/dL [13.5-17.5 g/dL]); total protein, 10.6 g/dL (6.3-7.9 g/dL); and albumin, 1.9 g/dL (3.5-5.0 g/dL).

3. Which *one* of the following is the *most likely* underlying factor in this patient's susceptibility to pneumococcal infection?

a. Multiple myeloma
b. Amyloidosis
c. Sickle cell disease
d. Celiac disease
e. Human immunodeficiency virus (HIV)

Interestingly, all of these options can lead to a functional asplenia and susceptibility to encapsulated organisms. Given the patient's presentation, including acute infection, normocytic anemia, and elevated creatinine and total protein levels, a diagnosis of multiple myeloma must be excluded. The best combination of tests to screen for multiple myeloma consists of serum protein electrophoresis, serum immunofixation, and the serum free light chain assay. In this patient, serum protein electrophoresis revealed a gamma globulin level of 3.5 g/dL (0.6-1.6 g/dL) and a monoclonal M protein spike of 3.3 g/dL with an IgGκ M protein, suggesting a likelihood of multiple myeloma. Multiple myeloma can result in immune dysfunction and increased risk for infection, particularly with encapsulated organisms like *S pneumoniae*. Mechanisms include reduced humoral immunity with a decrease in normal polyclonal antibody and defects in lymphocyte