

Not just a usual community-acquired infection

Friday, 01 July 2005

A 64-year-old male presented to the Emergency Room of the local hospital in a rural area of Greece complaining of fever, shortness of breath, productive cough, and mild low back pain. He had no previous hospitalizations.

The patient's symptoms suggest a lower respiratory tract (LRT) infection as the most likely diagnosis. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are common etiologic agents in patients with community acquired LRT infections. In addition, atypical bacteria including *Mycoplasma*, *Chlamydia*, *Legionella*, and *Rickettsiae* species are the cause of a considerable proportion of lower respiratory tract infections that varies in different age groups. Also, several viruses including influenza, parainfluenza, and adenoviruses may cause LRT infection, especially during the winter session.

The patient was a farmer. His past medical history was significant for a work-related injury in the lower back 10 years ago. He consumed alcohol, about half a liter of wine per day, for 20 years. He did not smoke. He never traveled outside Greece.

The details of the medical history and the habits of the patient suggest additional possible pathogens for his LRT infection, mainly *Klebsiella pneumoniae*, given the history of alcoholism. Because of his occupation, leptospirosis should be considered in the differential diagnosis. In addition, brucellosis should be also considered given that the patient lives in a rural area in Greece where the infection is endemic. It should be noted that brucellosis may cause manifestations from the respiratory system.

The patient's condition deteriorated despite the administration of antimicrobial treatment (ceftriaxone 1 g every 12 hours i.v. and clarithromycin 500 mg every 12 hours p.o.) at the local hospital. He was transferred to a tertiary hospital in Athens, two days after his admission at the local hospital. He presented with temperature 38.5 °C, heart rate 108/min, and tachypnea (45 breaths/min). Physical examination on admission revealed crackles in the base of the left lung and the upper right lung. Routine laboratory testing showed white blood cell count 8,800/mm³, neutrophils 88%, erythrocyte sedimentation rate 104 mm/1st hour, serum urea 57 mg/dl and creatinine 1.4mg/dl. Gram stain of a sputum specimen showed about 20 neutrophils per optic field. Chest x-rays on admission showed infiltrates in the left lower and the right upper lobe (figure 1). Arterial gas testing showed PaO₂/FiO₂=240, arterial pH = 7.48, and PCO₂=28 mmHg.

The patient's worsening condition despite the use of appropriate antimicrobial treatment for community-acquired pneumonia suggests several possibilities. First, that the pathogen responsible for his pneumonia was indeed one of the most commonly implicated micro-organisms in LRT infections, namely *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, or an atypical pathogen that was however resistant to the administered agents. There is an increasing proportion of pneumococcal isolates with full resistance to penicillin in several countries during the last years. Although still a controversial issue, it seems that the majority of evidence supports that the outcome of patients who receive treatment with ceftriaxone for pneumonia due to *Streptococcus pneumoniae* with full resistance to penicillin is worse than with vancomycin or other agents with activity against this pathogen. Second, the pathogen may be one not included in the above list of microorganisms. Someone should also consider other etiologic agents such as staphylococci, streptococci other than *Streptococcus pneumoniae*, anaerobes, and Gram-negative bacteria other than *Klebsiella pneumoniae*. In addition, mycobacteria, mainly *Mycobacterium tuberculosis*, should be always considered in the differential diagnosis in patients with LRT infection. It should be also noted that antibacterial agents would not influence the natural history of a viral LRT infection, except if a secondary bacterial infection had already developed. Non-infectious causes of lung infiltrates should also be included in the differential diagnosis at this stage.

Because of deterioration of his condition, antimicrobial treatment with vancomycin 1 gr every 12 hours i.v. and ciprofloxacin 400 mg every 12 hours i.v. was started. Treatment with ceftriaxone continued, while clarithromycin was stopped. Despite the change of the regimen of antibiotics, the patient's condition continued to deteriorate and he was transferred to the intensive care unit (ICU), after a three-day hospitalization in the medical ward. On admission to the ICU, he was intubated due to severe respiratory failure (PaO₂/FiO₂ ratio 175, arterial pH 7.21, PaCO₂=59 mm Hg). Laboratory testing showed white blood cell count =11,100/mm³ (polymorphonuclear cells = 89%), hemoglobin = 9.9 g/dl, hematocrit = 32%, platelets = 103,000/ mm³, serum urea 131 mg/dl, serum creatinine 1.7 mg/dl, C-reactive protein = 16.4 mg/dl, fibrinogen 935 mg/dl, and D-dimmer 544 ig/l. A CT-scan of the chest showed extensive infiltrates in both lungs with pneumoceles (figure 2).

What's your diagnosis? (Please click below for the response)

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The patient's symptoms suggest a lower respiratory tract (LRT) infection as the most likely diagnosis. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are common etiologic agents in patients with community acquired LRT infections. In addition, atypical bacteria including *Mycoplasma*, *Chlamydia*, *Legionella*, and *Rickettsiae*

species are the cause of a considerable proportion of lower respiratory tract infections that varies in different age groups. Also, several viruses including influenza, parainfluenza, and adenoviruses may cause LRT infection, especially during the winter session.

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What's your diagnosis?

The characteristic CT scan finding of the pneumoceles suggests that *Staphylococcus aureus* is the most likely cause of the pneumonia. There is an increasing frequency of community-acquired pneumonia (CAP) due to *Staphylococcus aureus*, even in immunocompetent persons. In addition, a considerable proportion of the isolated pathogens from these cases are staphylococci resistant to several classes of antibiotics, including antistaphylococcal penicillins.

The culture of a sputum specimen was negative. However, two specimens of blood cultures taken from different peripheral veins grew *Staphylococcus aureus*. The isolated strain was resistant to amoxicillin, amoxicillin/clavulanic acid, ampicillin/sulbactam, first, second and third generation cephalosporins including ceftriaxone, antistaphylococcal penicillins including oxacillin, carbapenems, tetracycline, and aminoglycosides. The strain was sensitive to clindamycin, erythromycin, clarithromycin, vancomycin, teicoplanin, linezolid, cotrimoxazole, and fluoroquinolones. Treatment with linezolid (600 mg every 12 hours i.v.) and clindamycin (600 mg every 8 hours i.v.) was started. Vancomycin and ceftriaxone were stopped, while ciprofloxacin was continued.

The lack of the response to the treatment with vancomycin led to the appropriate decision for a change of the antimicrobial regimens. Linezolid, clindamycin, and cotrimoxazole attain good concentrations in the lung parenchyma and

subsequently were good options for inclusion in the treatment. The presence of renal dysfunction was another good reason to consider the discontinuation of vancomycin.

A bronchoscopy was performed the day after the admission to the ICU that revealed dirty secretions of high viscosity in the affected lung lobes. A bronchoalveolar lavage (BAL) was performed to help clearing the bronchi and obtain specimens for microbiological studies. Specimens from the BAL fluid grew *Staphylococcus aureus* with the same in vitro antimicrobial susceptibility pattern with the blood isolate.

A gradual improvement of the patient was noted after the last modification of the antibiotics and the bronchoscopy. He was extubated 10 days after his admission to the ICU and was discharged from the ICU in good condition two days later.

Fortunately, the last antibiotic regimen seems to control the LRT infection. The appropriate duration of the antimicrobial treatment in patients with severe CAP due to *Staphylococcus aureus* is probably 3 weeks. Part of this treatment may be given by per os treatment (for example in our case, linezolid 600 mg every 12 or 24 hours depending on the severity of the infection, and clindamycin 300 mg every 8 hours) when the patient's condition permits it.

While the respiratory status of the patient was improving, he complained of low back pain especially on ambulation. There was no tenderness on pressure of the lumbar spine. In addition, neurological examination was normal. A CT scan of the lumbar spine did not show any appreciable abnormal findings.

Of note, the patient complained of mild low back pain at his presentation at the initial local hospital. His symptom was obviously underestimated since it was probably considered a manifestation related to his previous injury in the area, exacerbated by the febrile episode. However, the continuation of low back pain despite the improvement of pneumonia suggests another possibility related to the current health problem of the patient, namely the presence of an extrapulmonary focus of the staphylococcal infection in the spinal area. Despite the lack of findings of the CT scan of the lumbar spine, additional investigation is necessary to clarify the cause of the low back pain. A MRI of the lumbar spine is the test with the highest yield.

The MRI of the lumbar spine showed destructive changes of the L4-L5 and L5-S1 intervertebral disks, an epidural abscess extending from the twelfth thoracic to the first sacral vertebra with maximum width of 7 mm, and heterogeneity of the bodies of the fourth and fifth lumbar as well as the first sacral vertebra (figure 3).

The MRI findings are suggestive for a severe inflammatory process of the spine, apparently due to *Staphylococcus aureus*. Since the patient has no neurological symptoms or signs and despite the severity of the spinal infection, medical management with prolonged appropriate antimicrobial treatment can be employed to avoid an operation in the area.

The patient received treatment with clindamycin 300 mg every 8 hours p.o. and ciprofloxacin 500 mg every 12 hours po for 6 months. He noted a gradual improvement of his low back pain. In addition, both erythrocyte sedimentation rate and C-reactive protein levels gradually normalized during the 6-month per os antimicrobial treatment. A MRI of the spine performed at the end of the treatment showed absence of active infection in the area. The patient continued to be well without any residual back pain or respiratory symptoms during the 18-month follow-up.

A good outcome was achieved, as evidenced by the follow up tests including the spinal MRI and the lack of symptoms during the one and a half years of follow up after the discontinuation of treatment. Both clindamycin and ciprofloxacin attain good concentrations in the bones and the muscles even when they are administered per os, thus they are good options for the necessarily prolonged treatment of a spinal and paraspinal MRSA infection.

Commentary

Staphylococcus aureus has been reported to be the etiologic agent in considerably different proportions of patients with CAP in various studies (1). In a study of 392 patients with CAP diagnosed in the emergency department of a Spanish hospital, 228 had the etiologic agent identified with noninvasive microbiological investigations; among them *Staphylococcus aureus* was responsible for 2 (0.9%) cases (2). In a study of 318 patients with CAP necessitating hospitalization in Switzerland, it was found that *Staphylococcus aureus* was responsible for 1.6% of cases (3). On the other hand, *Staphylococcus aureus* was reported to be a common etiologic agent (18%) in patients who presented with septic shock due to CAP (4). In addition, it seems that the pathogen is a more common cause of CAP among the elderly (up to 26%) than in younger patients (5-7).

Unfortunately, there is an alarming increase of the incidence of community-acquired infections due to *Staphylococcus aureus* resistant to methicillin (MRSA) during the recent years in many countries. Community-acquired MRSA infections of various human systems and organs, including CAP, affect various populations (8-9). This is considered by many investigators to be among the most important public health issues related to antimicrobial resistance. The increasing incidence of nosocomial and community-acquired MRSA infections contributes to the increasing use of glycopeptides. However, isolates with intermediate and full resistance to glycopeptides have been recently reported.

Newer agents, such as linezolid, daptomycin, and quinopristin/dalfopristin are valuable options for the treatment of serious Gram-positive bacterial infections. Linezolid is indicated for the treatment of nosocomial pneumonia as well as CAP. The minimum inhibitory concentration (MIC) of various antimicrobial agents for 150 MRSA isolates recovered from hospitalized patients was studied; the MIC₉₀ was 2.0 mg/ml for vancomycin and teicoplanin (range 0.5-2.0 mg/ml and 0.125-2.0 mg/ml, respectively), and 0.5 mg/ml for pristinamycin and linezolid (range 0.125-0.75 mg/ml and 0.125-0.5 mg/ml, respectively) (10). In addition, a randomized clinical trial and a large body of anecdotal data indicate the trimethoprim/sulfamethoxazole may be considered for the treatment of MRSA infections (11).

An interesting observation in the discussed case was that the patient improved after the bronchoalveolar lavage (BAL) with the bronchoscopy. Although there are no data to suggest a therapeutic role of the BAL in patients with pneumonia, the clearance of the airways by the inflammatory fluid may help in the ventilation of the lungs and the decrease of the local microbial counts. In general, the role of bronchoscopy in the management of CAP remains unclear. In severe cases necessitating tracheal intubation and in ventilator-associated pneumonia (VAP) bronchoscopy could help clinicians to identify respiratory pathogens, to remove tenacious bronchial secretions and to resolve atelectasis. Evaluation of patients by fiberoptic bronchoscopy together with BAL is a safe modality with an adequate diagnostic yield that made it possible to determine the etiology of the pulmonary infiltrates seen in chest x-rays. The use of quantitative cultures of the BAL effluent to distinguish between contamination and lower respiratory tract infection, thus avoiding unnecessary antibiotic use with its sequelae such as increased resistant organisms, antibiotic-related complications, and increased hospitalization costs seems to be gaining supporters. In a recent meta-analysis of RCTs it was found that bronchoscopy, although did not alter mortality, affected antibiotic use and prescribing (12).

Another interesting point regarding the management of infections that is frequently overlooked by clinicians is that localized symptoms or signs in an area other than the site of infection may represent a remote focus of infection due to the same pathogen. This obviously happened in the case discussed here, where the mild back pain that was one of the presenting symptoms was caused by an extra-pulmonary focus of MRSA infection in the spinal area.

Measurements of C-reactive protein and erythrocyte sedimentation rate are not helpful in evaluating the significance of back pain in patients with LRT infections because they can increase by the LRT infection alone. In addition, CT scan of the spine especially if it does not include a phase with the use of an intravenously administered radio-contrast agent, may underestimate the significance of early findings of infection in the area. In practice the only imaging modality for the diagnosis of infection in the spinal area which combines high sensitivity with satisfactory specificity is MRI. The MRI is the method of choice for direct demonstration of extension of an infection, such as the development of a paraspinal phlegmon or an epidural abscess and neural compression. Although spinal MRI helps making the diagnosis of a spinal infection easier and quicker compared with other imaging tests, repeated neurological and spinal examination are essential in any patient with a known focus of infection and spinal pain or tenderness.

Staphylococcus aureus is the commonest etiologic agent of spinal epidural abscess since it is the responsible pathogen for at least half of cases (13-14). Although the surgical treatment was considered a necessary part of the management of patients with spinal epidural abscess for a long time, accumulating evidence during the last two decades suggested that this infection can be safely and effectively treated with antibiotics alone, especially if the causative microorganism is known, and the neurological status is not impaired (15).

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Acknowledgements

This case was prepared for our website by Argyris Michalopoulos, M.D.