Case 13

This 40-year-old male with multisystem failure secondary to bilateral pneumonia was transferred to our hospital via helicopter. He had presented to his local physician 3 days previously complaining of fevers, malaise, and vague respiratory symptoms. He was given amantadine for suspected influenza. His condition became progressively worse, with shortness of breath and a fever to 40.5°C, and he was admitted to an outside hospital 24 h prior to transfer. A laboratory examination revealed abnormal liver and renal function. Therapy with Timentin (ticarcillin-clavulanic acid) and trimethoprim-sulfamethoxazole was begun. On admission, he underwent a bronchoscopic examination which revealed mildly inflamed airways containing thin, watery secretions. A Gram stain of bronchial washings obtained at bronchoscopy is shown in Fig. 1. Based on these findings, he was begun on appropriate antimicrobial therapy. Culture results are shown in Fig. 2.

Despite appropriate antimicrobial agents and supportive therapy, the patient never recovered adequate pulmonary function and died 9 months later in a long-term care facility.

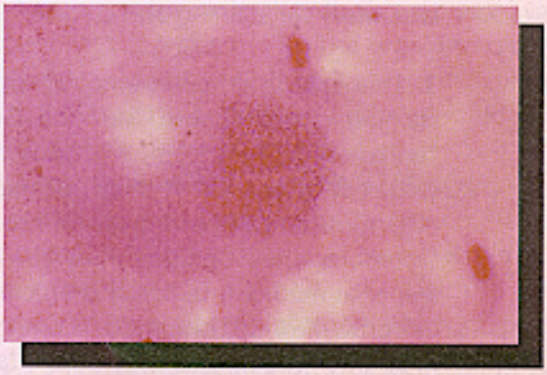

Figure 1

1. Which organisms are common causes of community-acquired bacterial pneumonia?

2. What are bronchial washings and how are they obtained?

3. On the basis of the Gram stain of the bronchial washings and the patient's presentation, what is the most likely cause of this patient's catastrophic infection? Why must the laboratory be notified if this organism is considered in the differential diagnosis?

4. What techniques other than culture can be used to detect this organism within 24 h of obtaining the culture?

5. What is the epidemiology of this organism?

6. What is the appropriate antimicrobial agent for treatment of this infection? Which other gram-negative respiratory pathogen is treated with this agent?

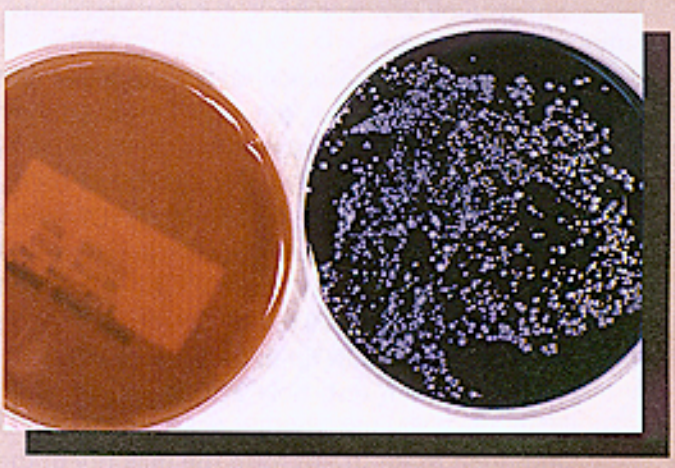

Figure 2

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Case Discussion

1. The common causes of community-acquired pneumonia are *Streptococcus pneumoniae; Haemophilus influenzae; Mycoplasma pneumoniae; Staphylococcus aureus,* frequently following an initial infection with influenza virus; *Klebsiella pneumoniae,* especially in the elderly and alcoholics; and *Legionella pneumophila. Chlamydia pneumoniae* (TWAR) is a recently described organism that also causes community-acquired pneumonia.

2. Bronchial washings are obtained during bronchoscopic examination. The bronchoscope is introduced, and a small volume of saline is injected into the bronchi through a channel in the bronchoscope. The mixture of saline and bronchial secretions is then suctioned from the bronchi through the bronchoscope and sent to the laboratory for staining and culture.

3. This patient has *L. pneumophila* pneumonia. *L. pneumophila* is an aerobic, poorly staining gram-negative rod. The Gram stain in Fig. 1 is what is known as an "enhanced" Gram stain, and thus the organisms appear more readily than they would with the Gram stain technique typically used. Legionellae are fastidious organisms and will not grow on media routinely used for cultivation of respiratory secretions. The laboratory must be informed that this organism is suspected so that a special medium, buffered charcoal yeast extract (BCYE) agar, which will support the growth of this organism, is used. This is the medium showing growth in Fig. 2. In addition, BCYE with antibiotics is used as a selective medium. Since *Legionella micdadei,* another species that may cause a clinically identical syndrome, may be inhibited by BCYE with antibiotics, BCYE without antibiotics must be used as well.

This case demonstrates the catastrophic nature of this illness in some previously healthy patients. Key findings in this case include hepatic and renal dysfunction, as well as the finding of thin, watery secretions, which are characteristic of pneumonia with this infection. Patients with bacterial pneumonia due to most other bacterial agents typically have thick, purulent secretions.

4. Culture for *L. pneumophila* typically takes up to 5 days before colonies are visible. Given this organism's potential for causing catastrophic illness, as we saw in this patient, more rapid diagnostic techniques are important in optimizing the management of this disease. *L. pneumophila* can be rapidly detected in two ways: by performing a direct fluorescent antibody (DFA) test and by detecting a urinary antigen. Both tests have been used in clinical settings. The DFA test has a sensitivity of 60 to 70% as compared with culture; i.e., 3 or 4 of 10 patients who are culture positive for *L. pneumophila* will not be detected by this test. However, the DFA test takes only 2 h, compared with up to 5 days for culture to become positive, so it is useful. The urinary antigen test, now available as an enzyme immunoassay, is more sensitive than the DFA test, but is only positive for strains of *L. pneumophila* group 1. Although these strains form the majority of the cases of *Legionella* infection, other

groups of *L. pneumophila* and other *Legionella* spp. cause a significant proportion (20 to 40%) of clinical cases. For these reasons, culture continues to be essential. In the near future, nucleic acid amplification procedures (such as PCR [polymerase chain reaction]) may become the procedure of choice since the sensitivity may approach that of culture and the turnaround time may be only a few hours.

5. *L. pneumophila* was first recognized as a cause of pneumonia when an outbreak of pneumonia of unknown etiology called Legionnaires' disease occurred in 1976 during an American Legion convention in Philadelphia. The source of the organism was traced to the air conditioning system at one of the convention hotels. Exposure to water containing *L. pneumophila* is believed to be the major mode of transmission. A number of studies have shown *L. pneumophila* to be the etiologic agent in nosocomial outbreaks of pneumonia. A common theme in all of these outbreaks was the aerosolization of water contaminated with *L. pneumophila*. The organism grows in air conditioning systems, shower heads, tap water, and sinks. It is very difficult to eradicate from hospital water supplies, although superheating and hyperchlorination of water have both been used with various degrees of success.

Despite concern about nosocomial outbreaks of *L. pneumophila* infection, sporadic community-acquired cases are probably more common in the United States. Chronic lung disease, immunosuppression, and advancing age all have been implicated as risk factors. Our patient had none of these. A possible risk factor in this patient may have been viral infection prior to his *Legionella* infection. Although prior viral infection is not recognized as a risk factor for *L. pneumophila* pneumonia, it is well recognized that bacterial superinfection can follow viral pneumonia, and this patient's original presentation may have been due to a virus such as influenza virus. Alternatively, *L. pneumophila* can cause a "flu-like" prodrome, and all his symptoms could be explained by this infection.

6. Erythromycin is the therapy of choice. This agent is usually considered to be active only against two gram-negative rods which cause infection in the respiratory tract, *Legionella* spp. and *Bordetella pertussis*. A key characteristic of this antimicrobial agent is its ability to penetrate into white cells. This characteristic is probably important therapeutically since *Legionella* spp. survive and multiply within macrophages. Beta-lactam drugs have been proven ineffective against *L. pneumophila* due in part to its ability to produce a β-lactamase. Although clinical experience is limited, the drugs clarithromycin and azithromycin are chemically closely related to erythromycin and both appear to have good in vitro activity against *L. pneumophila*. The quinolone agent ciprofloxacin has been used with some success in cases in which ototoxicity, a side effect of high doses of intravenous erythromycin, has necessitated a change from erythromycin to another drug. Finally, rifampin, which achieves excellent levels within eukaryotic cells, has been used in combination with erythromycin with some success in some severe *Legionella* infections.

References

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2. **Yu, V.** 1995. *Legionella pneumophila* (Legionnaire's disease), p. 2087–2097. *In* G. L. Mandell, J. E. Bennett, and R. Dolin (ed.), *Principles and Practice of Infectious Diseases,* 4th ed. Churchill Livingstone, Inc., New York.