A patient with deteriorating pulmonary melioidosis rapidly recovered after treatment with ceftazidime. To prevent possible relapses, an oral maintenance regimen of amoxicillin and clavulanic acid was prescribed for a period of three months. Melioidosis is caused by *Pseudomonas pseudomallei*. It is an insidious disease because of its variable clinical presentation, possible long-term asymptomatic carriage, broad-spectrum resistance to first-line antibiotics, and high mortality rate. As in our patient, the diagnosis should be particularly considered when there is reduced immunologic resistance and previous exposure in endemic areas, such as Southeast Asia. 

(Chest 1992; 101:555-57)

The spread of tropical diseases increases with growing worldwide travel activity and the influx of refugees into the Western world. Unfamiliarity with infectious diseases that are not endemic in a certain area causes delay in establishing the appropriate diagnosis, which may have severe consequences for morbidity and mortality. Melioidosis, which is endemic in Southeast Asia and is caused by *Pseudomonas pseudomallei*, is a potentially life-threatening disease with poor clinical responsiveness to a large number of antibiotics. Ceftazidime monotherapy has recently been shown in a prospective study to halve the mortality rate. 1

We present the clinical course of a family practitioner who returned to The Netherlands from a vacation in Thailand.

**CASE REPORT**

A 47-year-old man was admitted to the hospital because of fever, coughing, and roentgenographic evidence of a lesion in the left lung. Mild aortic insufficiency had been diagnosed 15 years previously, and multiple sclerosis had been diagnosed two years previously. His health had been fairly good during the previous three months, however, and he was not using any medication. He had never had any pulmonary disease. He smoked 20 cigarettes a day.

During October 1990 he was on holiday in the northwestern part of Thailand, where he was able to travel around without major problems. To avoid the risk of food poisoning, he ate as little as possible, leading to a weight loss of approximately 3 kg. At the end of his journey he became ill, complaining of general fatigue and coughing. Three days after his return to The Netherlands, his temperature increased to 39.5°C; he was producing small quantities of sputum; and he experienced left-sided chest pain during breathing. There were no gastrointestinal symptoms. Being a medical doctor, he started taking amoxicillin, 750 mg twice a day. Three days later, however, he became progressively ill and visited a chest physician.

Chest roentgenography revealed a solitary mass in the left upper lobe; central cavitation of this lesion could not be excluded (Fig 1, top). Review of a chest x-ray film obtained at the beginning of October 1990 showed clear lung fields. Laboratory studies disclosed an erythrocyte sedimentation rate of 44 mm/h, a white blood cell count of 8,300/mu mm (normal differential), and normal glucose and creatinine concentrations. Two days later the patient’s clinical situation deteriorated. Bronchoscopy was performed after prophylactic administration of amoxicillin and gentamicin because of aortic insufficiency. Thereafter, he was transferred to our hospital for further evaluation and treatment.

On physical examination the patient was found to be moderately ill. His temperature was 40°C, the blood pressure was 130/50 mm Hg, and the pulse rate was 96 beats per minute. There were no skin abnormalities, and no lymphadenopathy was detected. Some crackles were heard over the left lung on deep inspiration. There was a soft cardiac murmur due to the aortic insufficiency. The abdomen was normal.

A second chest roentgenogram showed that the mass in the left upper lobe was not as sharply defined as it had been two days earlier, and there was progressive infiltration in the left lung (Fig 1, center). Echocardiography showed only the known aortic insufficiency. Gram staining of sputum and bronchoalveolar lavage fluid revealed Gram-negative rods.

Treatment was started with intravenous administration of gentamicin, 120 mg twice a day; cefazolin, 1 g three times a day; and erythromycin, 1 g three times a day. The next day the patient became progressively more ill, with a blood pressure of 95/60 mm Hg and a pulse rate of 88 beats per minute. The lung sounds were unchanged. Arterial blood gas analysis (*FIO₂ = 0.21*) showed a *PO₂* of 97 mm Hg, a *PCO₂* of 19.5 mm Hg, a pH of 7.49, and a base excess of -5.1 mmol/L. The hemoglobin level was 6.7 mmol/L, and the white blood cell count was 17,600/mu mm. Because of threatening septicemia, the patient was temporarily transferred to the intensive care unit.

 Cultures of sputum and bronchoalveolar lavage fluid yielded orange colonies with a smooth or wrinkled appearance on routinely used sheep-blood nutrient agar under aerobic conditions. The growth was accompanied by a distinctive earthy odor. Microscopically, bipolar Gram-negative rods were seen with a tuft of three flagella per pole. *Pseudomonas pseudomallei* was identified with

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use of an API NF system (Analytab Products, France) and was
confirmed by the Dutch Reference Laboratory, Bilthoven. All blood
cultures remained sterile. The antibiogram is shown in Table 1. On
the basis of these findings, melioidosis was diagnosed.

Antimicrobial therapy was changed to ceftazidime monotherapy,
2 g three times a day, which caused rapid improvement of the
patient's clinical condition. His temperature and blood pressure
normalized within two days. He was treated with ceftazidime
intravenously for four weeks. At the time of discharge from the
hospital the roentgenographic abnormalities had disappeared (Fig
1, bottom), although there was still an increased lung volume with
flattened diaphragms. This was confirmed by a pulmonary function
test revealing a lowered Dco and an increased total lung capacity of
124 percent of predicted.

Antimicrobial therapy was continued with orally administered
amoxicillin-clavulanic acid for three months after discharge.

**DISCUSSION**

Melioidosis is primarily endemic in Southeast Asia,
but occasional cases have arisen in Africa, Europe,
and North and South America.2,3 Thailand has the
highest incidence, especially in the northeastern part
of the country. Although the disease can be acquired
all year round, melioidosis is mainly acquired in the
rainy season from May until October.

*Pseudomonas pseudomallei*, the causative agent of
melioidosis, can contaminate the soil, especially
of rice fields, and infection can occur by direct contact
or inhalation of dust or water droplets. The incubation
period may be a few days, but the microorganism can
also remain dormant, and asymptomatic infection may
persist in humans for many years before the
appearance of clinical disease.4,5 Under certain physical
conditions, particularly those that compromise the
immune status, asymptomatic carriage may result in
overt disease with a nonspecific and variable presenta-
tion.

Our patient visited northeastern Thailand at the
end of the rainy season. Shortly after his return to
The Netherlands he became progressively ill with
signs of pneumonia, not indicative of any particular
causative microorganism. The appropriate diagnosis
was considered only after microscopic examination of
the direct Gram stain of the bronchoalveolar lavage
fluid showed the abundant presence of Gram-negative
rods. By that time, however, his clinical condition had
already deteriorated severely, with transfer to the
intensive care unit. Identification of the bacteria as
*P pseudomallei* was accomplished after another 48 h.
Blood cultures remained sterile during this hospital
stay.

Pulmonary melioidosis usually presents as a non-
specific pneumonia with fever, dyspnea, and expec-
toration of small quantities of purulent sputum, som-
times accompanied by hemoptysis and chest pain.3

Roentgenographic findings are usually localized, ie,
uni- or bilobar or segmental infiltrates, mostly in the
upper lobes (70 to 90 percent). Multiple small cavities
with a diameter of 0.5 to 1 cm may be present.

**Figure 1.** Serial chest roentgenograms. *Top:* Solitary mass in the
left upper lobe. *Center:* Progressive infiltration in the left lung at
the time of hospital admission. *Bottom:* Resolution at discharge
from hospital.

Although melioidosis is associated with conditions
of reduced resistance to infection, such as diabetes
Table 1—Minimum Inhibitory and Bactericidal Concentrations of Various Antimicrobial Agents against Patient’s Isolate of Pseudomonas pseudomallei

<table>
<thead>
<tr>
<th>Antimicrobial Agent</th>
<th>MIC, mg/L</th>
<th>MBC, mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>&gt;32</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Amoxicillin plus clavulanic acid</td>
<td>8/4</td>
<td>6/4</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Imipenem</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>&gt;16</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>&gt;16</td>
<td>&gt;16</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Sulfonamide</td>
<td>2</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Trimethoprim plus sulfamethoxazole</td>
<td>0.06/0.13</td>
<td>8/128</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&gt;2</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>0.05</td>
<td>1</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>&gt;1</td>
<td>&gt;1</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>&gt;4</td>
<td>&gt;4</td>
</tr>
</tbody>
</table>

*MIC = minimum inhibitory concentration; MBC = minimum bactericidal concentration.

mellitus and chronic renal diseases, 30 percent to 50 percent of the patients are previously healthy. Our patient suffered from multiple sclerosis, which is also known to affect immune function. Septic melioidosis is an acute, life-threatening infection with a mortality rate between 40 percent and 80 percent even with appropriate therapy. As in our patient, the localized form of melioidosis, which is thought to precede septicemia, accounts for approximately 40 percent of the cases. The lungs and the liver are the organs that are most frequently involved (30 percent to 60 percent).3

The treatment of choice in severe melioidosis has recently been suggested to be the third-generation β-lactam ceftazidime, which reduced mortality in a prospective study by 50 percent compared with the conventional regimen consisting of the combination of chloramphenicol, doxycycline, trimethoprim, and sulfamethoxazole.1 These better results were mainly accomplished in the first 48 h of treatment. Excellent in vitro susceptibility of P pseudomallei to imipenem has been reported, but clinical effectiveness still remains to be established.7 Clinical responses are very poor to first- and second-generation β-lactams and to aminoglycosides, which, as was the case initially in our patient, are widely used as empiric antibiotics in the treatment of pneumonia and septicemia. Considering atypical pneumonia as a differential diagnosis and using erythromycin or doxycycline with or without rifampicin will also have no clinical effect in melioidosis.

In view of the relatively high mortality of 20 percent in localized pulmonary melioidosis, it is of paramount importance to start adequate therapy as soon as possible. At the initiation of ceftazidime treatment, our patient’s condition was becoming critical, with severely impaired lung function and impending septicemia. Nevertheless, he rapidly improved within 48 h, and ceftazidime treatment was continued for four weeks.

The optimal duration of antimicrobial therapy has not yet been established, and current usage varies between six weeks and six months.2,3 Long-term intravenous therapy possibly followed by an oral maintenance regimen is necessary because of the high relapse rate.3 This might be due to the capacity of the microorganism to survive and multiply in phagocytes, making it a facultative intracellular organism.7 Because of the well-known high relapse rate of melioidosis, we preferred a maintenance regimen for a longer period. Despite moderate sensitivity evidenced in the antibiogram, oral treatment with amoxicillin-clavulanic acid was chosen because of its relative safety and preliminary positive results in clinical practice.9,10

ACKNOWLEDGMENTS: The minimum inhibitory and minimum bactericidal concentrations were determined by the staff of the Laboratory of Medical Microbiology, Canisius Wilhelmina Ziekenhuis, Nijmegen, The Netherlands. The technical assistance of Mrs P. Vinke was highly appreciated, as was the secretarial support by Mrs B. Peeters.

REFERENCES


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