Life-Threatening *Mycoplasma hominis* Mediastinitis

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*Mycoplasma hominis* infections are easily missed because conventional methods for bacterial detection may fail. Here, 8 cases of septic mediastinitis due to *M. hominis* are reported and reviewed in the context of previously reported cases of mediastinitis, sternum wound infection, pleuritis, or pericarditis caused by *M. hominis*. All 8 patients had a predisposing initial condition related to poor cardiorespiratory function, aspiration, or complications related to coronary artery surgery or other thoracic surgeries. Mediastinitis was associated with purulent pleural effusion and acute septic symptoms requiring inotropic medication and ventilatory support. Later, the patients had a tendency for indolent chronic courses with pleuritis, pericarditis, or open sternal wounds that lasted for several months. *M. hominis* infections may also present as mild sternum wound infection or as chronic local pericarditis or pleuritis without septic mediastinitis. Treatment includes surgical drainage and debridement. Antibiotics effective against *M. hominis* should be considered when treating mediastinitis of unknown etiology.

*Mycoplasma hominis* is a small bacterium that lacks a typical bacterial peptidoglycan cell wall. Because of this property, it is not visualized on bacterial gram stains and is resistant to antibiotics affecting peptidoglycan synthesis (such as β-lactam agents and vancomycin). It is rarely associated with infection, but it is frequently isolated from the urogenital and respiratory tracts of asymptomatic healthy individuals. Rates of colonization in the urogenital tract range from 21% to 54% among women and from 4% to 13% among men [1]. Rates of colonization in the upper respiratory tract have been reported to range from 1% to 3% among healthy adults, and colonization has been found in up to 8% of adults with chronic respiratory illnesses [2] and in up to 30% of children with chronic tonsillitis [3]. *M. hominis* infections are predominantly associated with the genitourinary tract; these infections occur particularly during the peripartum period and after abortions and are responsible for cases of postpartum fever, cesarean section wound infection, pelvic inflammatory disease, and pyelonephritis. Acquisition of the organism during delivery may cause meningitis, brain abscesses, and eye infections in the newborn.

*M. hominis* may cause nongenitourinary infections in adults; and cases of septicemia, wound infections, meningitis, brain abscesses, arthritis, and respiratory tract infections have been reported [4–6]. The route of infection has been identified as either the urinary tract via urethral catheterization or the respiratory tract. Many patients with nongenitourinary infections have been described to have predisposing factors for infection, including immunosuppression, trauma, or poor cardiorespiratory function.

Here, we report eight cases of mediastinitis caused by *M. hominis* and review them in the context of previously reported cases of sternum wound infection, pleuritis, mediastinitis, or pericarditis due to *M. hominis*. Analysis of the cases revealed the life-threatening nature of the infection, the tendency for pleural and pericardial effusions, and the predilection for a late chronic course.

**Methods**

*M. hominis* was isolated by use of conventional anaerobic bacteriologic techniques. Samples were streaked on plates with Fastidious Anaerobe Agar (Lab M, Bury, United Kingdom) that were supplemented with 5% defibrinated horse blood. The plates were incubated in anaerobic jars at 35°C. *M. hominis* appeared as pinpoint transparent colonies after several days of incubation.

The preliminary identification of *M. hominis* was made if the colonies had a negative gram-stain and if disk diffusion testing showed a typical antibiotic susceptibility pattern: resistance to penicillin and erythromycin and susceptibility to clindamycin and tetracycline. Definite identification was based on PCR analysis [7].

The Etest (AB BIODISK, Solna, Sweden) was used for antimicrobial susceptibility testing. This method has been shown to give results comparable with those obtained by broth and agar dilution techniques [8]. MICs for each antibiotic were interpreted.
Table 1. Summary of newly reported cases of Mycoplasma hominis mediastinitis.

<table>
<thead>
<tr>
<th>Patient no.:</th>
<th>Previous disease(s) and predisposing factor(s)</th>
<th>Initial operation(s) and/or perioperative complication(s)</th>
<th>Start of symptoms</th>
<th>Lung infiltration(s) and/or effusion(s)</th>
<th>Associated infection(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: 78, M</td>
<td>Two episodes of heart infarction within 1 mo before surgery resulting in cardiac failure with EF of 30%, cardiac arrhythmias, and unstable signs</td>
<td>Emergency coronary artery bypass surgery</td>
<td>Day 4, postoperatively febrile; day 5, sternal pain; day 6, purulent discharge from sternal wound, CRP level up to 250 mg/L, septic symptoms</td>
<td>Day 7, CT scan, pneumonia in left lower lobe, left pleural fluid; CT scan on day 15 revealed findings the same as on day 7 with formation of left-sided atelectasis</td>
<td>None</td>
</tr>
<tr>
<td>2: 68, M</td>
<td>Smoked for 40 y, ventilatory dysfunction, hypertension; gallbladder operation 19 y ago; heart infarction 7 mo before operation resulting in cardiac failure, EF of 30%</td>
<td>Coronary artery bypass surgery perioperative counterpulsation; day 2, hemiplegia</td>
<td>Day 12, febrile, septic, CRP level up to 400 mg/L; subsequently purulent discharge from sternum wound</td>
<td>Day 9, left pleural fluid; day 60 CT scan, bilateral pleural fluid; day 90 CT scan, pneumonia in left lower lobe, pleural fluid</td>
<td>None</td>
</tr>
<tr>
<td>3: 44, M</td>
<td>Hypertension and psoriasis, atrial fibrillation, septicemia with warfarin treatment; symptoms of coronary heart disease for 1 y before operation, EF of 57%</td>
<td>Coronary artery bypass surgery, low cardiac output after surgery, inotropic medication</td>
<td>Day 6, febrile; day 7, septic, CRP level up to 350 mg/L, drainage from sternal wound</td>
<td>Day 7 CT scan, pleural effusion, especially on left side; day 13 CT scan, pneumonia in left upper lobe, atelectasis in left lower lobe</td>
<td>None</td>
</tr>
<tr>
<td>4: 51, M</td>
<td>Smoked for 35 y, family history of coronary heart disease; symptoms of coronary heart for 2 y attacks of cardiac infarction within 4 mo before operation, EF of 57%</td>
<td>Emergency coronary artery bypass surgery because of cardiac infarction after coronary angiography</td>
<td>Day 2, febrile, septic, disoriented; day 12, discharge from sternal wound</td>
<td>Day 4, left-sided atelectasis; day 12 CT scan, pericardial and bilateral pleural effusion; day 60, right-sided pleural effusion</td>
<td>Staphylococcus epidermidis in trachea on day 12</td>
</tr>
<tr>
<td>5: 58, M</td>
<td>Cardiac infarction 1 y before surgery resulting in cardiac insufficiency, EF of 53%</td>
<td>Coronary artery bypass surgery; day 1, ventricular fibrillation resternotomy, evacuation of hematoma, counterpulsation</td>
<td>Febrile; subsequently, discharge from sternum leading to sternotomy, on day 9, CRP level up to 250 mg/L</td>
<td>CT scan before day 9, pleural effusion</td>
<td>S. epidermidis in sternal wound on day 19</td>
</tr>
<tr>
<td>6: 51, M</td>
<td>Chronic reflux esophagitis, dysphagia, big esophageal diverticulum</td>
<td>Thoracotomy and excision of diverticulum, fundoplication and Heller’s myotomy; intraoperative rupture of right main bronchus, postoperative esophageal perforation</td>
<td>Day 1, febrile, improvement after closure of esophageal perforation; day 10, poor respiratory function, CRP level up to 100 mg/L</td>
<td>Day 1, right-sided atelectasis; day 13 CT scan, left-sided mediastinal abscess, pericardial and pleural effusion; day 27 CT scan, left-sided empyema and pericardial fluid</td>
<td>Coagulase-negative staphylococcus in sternal wound specimen obtained on day 17</td>
</tr>
<tr>
<td>7: 42, M</td>
<td>Long history of alcohol abuse, acute pancreatitis 4 y before admission; previous hiatal hernia with esophageal ulcer</td>
<td>None</td>
<td>Was found hypotonic at home; septic of admission cardiac arrest, aspiration, and resuscitation on the day of admission, CRP level up to 300 mg/L</td>
<td>CT scan revealed pleural effusion</td>
<td>Streptococcus pyogenes facial abscesses and sepsis on day 1</td>
</tr>
<tr>
<td>8: 48, F</td>
<td>Alcohol abuse, tobacco smoker, chronic laryngitis, poor oral hygiene</td>
<td>None</td>
<td>Pain and swelling on the right side of the mandible for 5 d before admission; septic of admission, hypotonic, and resuscitation</td>
<td>Day 1 neck CT scan, submandibular abscess; day 2, bilateral pleural effusion, mediastinal edema; day 6, pleural fluid and pneumonic infiltrates on left side; day 9 CT scan, fluid collections in mediastinum, peritoneal fluid</td>
<td>Actinomyces neck abscess</td>
</tr>
</tbody>
</table>

NOTE: BAL, bronchoalveolar lavage; Cm, clindamycin; Cprf, ciprofloxacin; CRP, C-reactive protein level; Ctx, cefotaxime; Czid, cefazidime; DIC, disseminated intravascular coagulation; Dox, doxycycline; EF, ejection fraction; Em, erythromycin; Flu, fluconazole; Imi, imipenem; Mtx, metronidazole; Ofx, ofloxacin; Rif, rifampin; Vm, vancomycin.
<table>
<thead>
<tr>
<th>Specimen positive for <em>M. hominis</em></th>
<th>Antimicrobial therapy</th>
<th>Revision operation(s)</th>
<th>Serious sequela(e)</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural fluid obtained on day 22, identification on day 28</td>
<td>Day 6, Imi, Vm, Em, Flu; day 28, Cm, Cpf x, Rif, Flu</td>
<td>Day 15, resternotomy, irrigation through drains</td>
<td>Deterioration despite resternotomy; day 28, CT scan, bilateral lower lobe, atelectasis, fluid and gas collections in mediastinum, disorientation</td>
<td>General condition improved after specific medication against mycoplasma was started on day 28</td>
</tr>
<tr>
<td>Sternal wound specimen obtained on day 16, identification on day 21</td>
<td>Day 9, Czd; day 12, Imi, Vm, Flu; day 21, Cm added</td>
<td>Day 16, resternotomy, sternum disintegrated, mediastinal drainage</td>
<td>Recovery slow despite antimycoplasmal therapy; transaminase and alkaline phosphatase levels increased, albumin level normal</td>
<td>Day 150, laparotomy, purulent fluid beneath liver, bowel necrosis, death</td>
</tr>
<tr>
<td>Sternal wound specimen obtained on day 8, identification on day 14</td>
<td>Day 6, Vm; day 14, Ofx</td>
<td>Day 8, resternotomy, serious fluid mixed with blood in sternal wound, bilateral pleural fluid drained, lavage started; day 26, omentoplasty of sternum</td>
<td>Day 11, respiratory insufficiency</td>
<td>General condition improved after specific medication was started on day 14; extubated on day 17; Ofx therapy continued for several months; sternum remained unstable and painful</td>
</tr>
<tr>
<td>Sternal wound specimen obtained on day 12, identification on day 33</td>
<td>Day 2, Ctx; day 12, Vm, Imi, Flu; day 90, Dox; day 120, Cm</td>
<td>Debridement, drainage, and irrigation</td>
<td>Day 4, liver dysfunction with encephalopathy</td>
<td>Day 20, extubated, liver function and encephalopathy resolved, sternal wound remained open for 22 mo; Cm therapy continued up to 24 mo; sternum remained unstable and painful</td>
</tr>
<tr>
<td>Mediastinum specimen obtained on day 19 during 3rd resternotomy, identification on day 29</td>
<td>Vm, Imi, Mtz, Flu; day 29, Cpf x and Cm added</td>
<td>Day 1, resternotomy; day 9, 2d resternotomy, drainage, and irrigation of mediastinum; day 19, 3d resternotomy, complete excision of sternum because of necrosis plas tia with pectoral muscles</td>
<td>Slow recovery, sternal wound would open for 40 d</td>
<td>General condition improved gradually after 3rd resternotomy and administration of antimycoplasmal therapy; instability related to removal of sternum</td>
</tr>
<tr>
<td>Left pleural drainage obtained on day 21, identification on day 30</td>
<td>Day 1, Imi; day 17, Vm, Imi, Flu; day 30, Dox added</td>
<td>Day 2, closure of esophageal perforation, paraesophageal abscesses evacuated pleural cavities and retro mediastinal spaces drained; day 17, drainage of pericardial and pleural effusion</td>
<td>Persistent mediastinal abscesses and pericardial fluid</td>
<td>Day 33, 250 mL of pericardial fluid drained, gradual improvement of general condition</td>
</tr>
<tr>
<td>BAL fluid obtained on day 2, identification on day 9</td>
<td>Day 1, Imi; day 40, Cm, Czd, Vm, Mtz</td>
<td>Laparotomy on day 34 for treatment of gastroduodenal hemorrhage</td>
<td>Bilateral pneumonia, rhabdomyolysis, labile hemodynamics DIC</td>
<td>Initial response to therapy, septic symptoms reappeared on day 40; death on day 60 after several episodes of gastrointestinal bleeding related to DIC</td>
</tr>
<tr>
<td>Left pleural fluid obtained on day 6, identification day 13</td>
<td>Day 1, Ctx, Mtz; day 4, Imi, Flu; day 13, Cm, Vm</td>
<td>Day 2, cervical incision and drainage, right-sided pleural drain; day 13, right-sided thoracotomy, drainage; day 24, rethoracotomy</td>
<td>Gradual slow improvement after last thoracotomy on day 24</td>
<td></td>
</tr>
</tbody>
</table>
as susceptible, intermediate resistant, or resistant was done according to a standard reported elsewhere [9].

Results

Altogether 8 patients were found to have M. hominis mediastinitis in the Helsinki University Central Hospital during 1991–1998. Of the 8 patients, 5 had undergone coronary artery bypass grafting, 1 underwent surgery for diverticulum of the esophagus, and 2 were admitted to the hospital in septic shock. The clinical features of the patients are summarized in table 1.

All 8 patients were immunocompromised because they had either underlying conditions or complications related to surgery. Patients 1 and 2 (table 1) had a preoperative ejection fraction of 30%. Patient 3 (ejection fraction, 57%) was receiving warfarin treatment that predisposed to sternal hematoma. Patient 4, who had the highest preoperative ejection fraction (72%), underwent emergency coronary artery bypass surgery because of heart infarction related to coronary angiography. Patient 5 (ejection fraction, 53%) developed postoperative ventricular fibrillation.

Patient 6, who underwent surgery for diverticulum of the esophagus, had intraoperative perforation of the right bronchus and postoperative perforation of the esophagus. Patients 7 and 8, who were admitted to the hospital because of septic hypotension, were alcoholics; both of these patients were resuscitated on the day of admission.

In all 8 patients, the first signs of infection were fever and/or sepsis. Of the 6 patients who had undergone previous surgery, 5 developed fever within 1 week after surgery, and 1 developed fever 12 days after surgery. After the onset of fever, the general condition of the patients became rapidly worse; they developed septic symptoms, disorientation, and cardiorespiratory dysfunction requiring inotropic medication and ventilatory support. Subsequently, there was purulent discharge from chest wounds in patients who had undergone previous surgery.

Infections were characterized by effusions in pleural and pericardial cavities. CT revealed pleural effusions in all patients and pericardial effusion in 2 patients. The technique for coronary artery surgery involved opening the left pleural cavity and preparation of the left internal mammary artery, which led to collections of fluid in the left pleural cavity and formation of small areas of atelectasis in the left lung. Operative trauma may predispose to M. hominis infection, which was characterized by purulent effusion especially in the left pleural cavity in patients who had undergone coronary artery bypass surgery.

There was considerable delay in the diagnosis of M. hominis infection. After a sample was obtained, microbiological identification of mycoplasm took an average of 9.1 days (range, 5–21 days). After the onset of fever, diagnosis of mycoplasmal infection took an average of 17.9 days (range, 8–31 days). The delay in microbiological identification was because M. hominis grew only slowly on the culture plates used, which were not optimized for mycoplasmal growth but were rather used to detect various different pathogens. M. hominis was isolated from pleural or mediastinal fluid specimens from patients 1, 5, 6, and 8. M. hominis was the only organism isolated from these samples. Staphylococcal growth was found in cultures of superficial sternum wound specimens from patients 5 and 6; however, staphylococci were not recovered from pleural or mediastinal fluid samples from these patients.

M. hominis was isolated from sternum wound specimens from patients 2, 3, and 4. M. hominis was the only organism isolated from these specimens. M. hominis was recovered from a bronchoalveolar lavage (BAL) fluid specimen from patient 7. No other organisms were found in this BAL fluid sample, and the quantity of colonies on the culture plate was high (BAL samples were evaluated with a semiquantitative scale). It is possible that M. hominis strains isolated from the sternal wounds or BAL fluid may have represented superficial colonization with M. hominis. However, the large quantity of M. hominis colonies and the lack of other organisms suggest that M. hominis played a pathogenetic role in clinical disease. The quantities of M. hominis colonies on the culture plates may even be underestimated, since the plates were not specifically designed for M. hominis isolation.

All 8 strains were susceptible to clindamycin (MIC range, 0.03–0.06 μg/mL) and tetracycline (MIC range, 0.125–0.25 μg/mL; table 2). Susceptibility to ciprofloxacin was variable, and all strains were resistant to tobramycin (table 2). All strains were resistant to erythromycin (assessed by disk diffusion testing). All patients except patient 7 underwent revision operations because of pleural empyema and for removal of necrotic tissue. Patients 5 and 8 underwent 3 major operations to control infection. Revision operations included omentoplasty and musculus pectoralis major flap surgery. The importance of local drainage and debridement is highlighted in the case of patient 4, who responded initially to surgical treatment without specific antimicrobial therapy against M. hominis, which was not started until day 90.

After the initial septic phase of infection, infections tended

<table>
<thead>
<tr>
<th>Isolate no.</th>
<th>Clindamycin (μg/mL)</th>
<th>Tetracycline (μg/mL)</th>
<th>Ciprofloxacin (μg/mL)</th>
<th>Tobramycin (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.06 (S)</td>
<td>0.125 (S)</td>
<td>4.0 (R)</td>
<td>8 (R)</td>
</tr>
<tr>
<td>2</td>
<td>0.06 (S)</td>
<td>0.25 (S)</td>
<td>0.5 (S)</td>
<td>8 (R)</td>
</tr>
<tr>
<td>3</td>
<td>0.06 (S)</td>
<td>0.25 (S)</td>
<td>2.0 (I)</td>
<td>8 (R)</td>
</tr>
<tr>
<td>4</td>
<td>0.03 (S)</td>
<td>0.125 (S)</td>
<td>2.0 (I)</td>
<td>8 (R)</td>
</tr>
<tr>
<td>5</td>
<td>0.06 (S)</td>
<td>0.25 (S)</td>
<td>0.5 (S)</td>
<td>16 (R)</td>
</tr>
<tr>
<td>6</td>
<td>0.06 (S)</td>
<td>0.25 (S)</td>
<td>1.0 (S)</td>
<td>16 (R)</td>
</tr>
<tr>
<td>7</td>
<td>0.06 (S)</td>
<td>0.125 (S)</td>
<td>0.5 (S)</td>
<td>8 (R)</td>
</tr>
<tr>
<td>8</td>
<td>0.06 (S)</td>
<td>0.25 (S)</td>
<td>2.0 (I)</td>
<td>16 (R)</td>
</tr>
</tbody>
</table>

NOTE. MICs were interpreted as susceptible (S), intermediate resistant (I), and resistant (R) according to the standard of the National Committee for Clinical Laboratory Standards [9].
to follow a chronic course. Sternal wounds tended to close slowly with continuous purulent discharge. Patient 4 had a sternal wound open for 22 months and required long courses of antimicrobial therapy. Patient 2 developed a collection of necrotic fluid beneath the liver 5 months after the initial operation that may have been caused by Mycoplasma hominis. Subsequently, he developed intestinal necrosis and died.

Discussion

In addition to mediastinitis, Mycoplasma hominis may cause wound infections, abscesses, arthritis, osteitis, peritonitis, pneumonia, meningitis, and sepsis. Extragenital infections due to Mycoplasma hominis have been reviewed elsewhere [4, 6]. In general, infections involving the mediastinum tended to follow a course that was more severe than those of other Mycoplasma hominis infections. Previously reported cases of mediastinitis, sternum wound infection, pleuritis, or pericarditis due to Mycoplasma hominis are summarized in table 3 [4, 5, 10–26]. The high mortality rate among these patients highlights the severity of these infections. Most deaths occurred in patients who underwent transplantation surgery (8 of 15), 1 death occurred in 13 patients who underwent reconstructive cardiac surgery, and 2 deaths occurred in 7 patients with other underlying diseases.

These infections can roughly be categorized into 3 different clinical entities: acute septic mediastinitis; indolent chronic sternum wound infection, pericarditis, or pleuritis lasting for months; and acute mild sternum wound infection or pleuritis lasting <1 month.

Patients with acute septic mediastinitis usually presented within 2 weeks after a surgical procedure. These patients had the following symptoms, as mentioned in the temporal order of presentation: tenderness of the sternal wound, high-grade fever, purulent discharge from the wound, pleural and sometimes pericardial effusion, and disorientation. All of our 8 patients had septic mediastinitis. They all had cardiorespiratory insufficiency which required respiratory assistance and inotropic medication. Several previously described patients had a clinical picture of septic mediastinitis, including patient 9 [10] (table 3), patient 10 [12], patient 12 [14], patient 29 [23], and patient 22 [18]. After the acute phase, infections tended to follow a chronic course with persistent pleural effusion, open sternal wound, and malunion of the sternum. In 1 instance, empyema with pleural effusion recurred 7 months after surgery and the initial clinical infection due to Mycoplasma hominis (patient 10) [12]. These patients usually required multiple operations, including drainage of effusion, debridement, musculus pectoralis major flap surgery, and omentoplasty for closure of open sternal wounds.

In some cases, infection followed a localized chronic course with low-grade fever but without septic symptoms. Patient 23 (table 3) had an open sternal wound and fluid in the anterior mediastinum 1 week after surgery that took 3 months to heal [13]. Patient 11 developed an open sternal wound 4 weeks after surgery that took 5 months to heal [13]. Infection sometimes manifested as late as 18 months after surgery as pleural effusion and purulent pericarditis with pericardial thickening and lymphocytic inflammation (patient 26) [22]. Patient 25 had prosthetic valve endocarditis lasting for 5 months, which was ultimately treated with heart transplantation [20]. Patient 30 was a newborn with massive pericardial effusion whose mother had had a florid illness 2 weeks before delivery [24]. The newborn was treated with clindamycin and by creation of a pleuropericardial window at the age of 42 days.

Some patients had acute sternum wound infection or pleuritis without septic symptoms that lasted <1 month. Patient 16 (table 3) had sternum wound infection 4 days after surgery which healed rapidly [16], and patient 27 developed sternum wound infection 5 days after surgery, which healed within 1 month [16]. Patient 24 was a neonate with sternum wound infection after Rashkind balloon atrial septostomy and subsequent arterial switch operation to treat transposition of the great arteries [19]. The baby recovered rapidly after surgical drainage and debridement and administration of clindamycin.

Diagnosis of mycoplasmal infections is difficult because gram staining of effusion or purulent discharge does not reveal bacteria; only the presence of neutrophils is shown. Routine bacterial cultures may be negative since mycoplasmas are highly fastidious and require enriched culture media for growth [27]; selective agents may be used to prevent the growth of other organisms. Mycoplasma hominis is the least fastidious of the mycoplasmas and may be identified on routine bacteriologic culture plates only after several days of incubation; it forms pinpoint-sized colonies that are easily overlooked and best detected under magnification. Identification of mycoplasmal colonies on culture plates can be facilitated by the use of direct immunofluorescence techniques [27]. Routine automated blood culture systems may miss the presence of mycoplasmas, because their growth on liquid media is small, and cultures yield at most a faint haze that is best detected by comparison with medium that has not been inoculated [28, 29]. They can be detected in blood by subculture from seemingly negative blood culture bottles. Detection of Mycoplasma hominis by PCR assay [30] or antigen detection methods [31] directly in clinical specimens may prove useful in the diagnosis of Mycoplasma hominis infections.

All 8 strains in our series were susceptible to clindamycin and tetracycline (table 2). Susceptibility to ciprofloxacin was variable, and all strains were resistant to tobramycin. All strains were resistant to erythromycin; disk diffusion testing revealed this resistance, which is in agreement with previous reports indicating resistance of Mycoplasma hominis to erythromycin and also the newer macrolides. MICs of clindamycin were similar to those reported elsewhere for Mycoplasma hominis [32, 33]. It should be noted, however, that clindamycin may not be effective against Ureaplasma urealyticum, which may coexist in Mycoplasma hominis infections. Although all the strains were susceptible to tetracy-
Table 3. Summary of data on previously reported cases of mediastinitis, sternum wound infection, pleuritis, or pericarditis caused by *Mycoplasma hominis*.

<table>
<thead>
<tr>
<th>Patient group, patient no., age (y), sex</th>
<th>Specimen(s) positive for <em>M. hominis</em></th>
<th>Concurrent organism(s) and/or infection(s)</th>
<th>Associated underlying condition(s) and/or previous surgery</th>
<th>Therapy</th>
<th>Outcome</th>
<th>Ref(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who underwent transplantation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1: 43, M</td>
<td>Sternum wound specimen</td>
<td>Coagulase-negative staphylococci, diphteroids</td>
<td>Cardiac transplantation, cyclosporine, corticosteroid, antithymocyte globulin</td>
<td>Cm, Dox</td>
<td>Died</td>
<td>[5]</td>
</tr>
<tr>
<td>2: 43, F</td>
<td>Blood, pleural space specimen</td>
<td>Herpes simplex virus esophagitis and tracheobronchitis</td>
<td>Cardiac transplantation, cyclosporine, corticosteroid, antithymocyte globulin</td>
<td>Cm, Dox</td>
<td>Died</td>
<td>[5]</td>
</tr>
<tr>
<td>3: 55, M</td>
<td>Sternum wound specimen</td>
<td>Enterobacter cloacae bacteremia</td>
<td>Cardiac transplantation, cyclosporine, corticosteroid, antithymocyte globulin</td>
<td>Cm, Dox</td>
<td>Died</td>
<td>[5]</td>
</tr>
<tr>
<td>4: 63, M</td>
<td>Mediastinum specimen</td>
<td></td>
<td>Cardiac transplantation, cyclosporine, corticosteroid, azathioprine</td>
<td>Cm, then Dox, Cm; drainage, debridement, and irrigation</td>
<td>Resolved</td>
<td>[10]</td>
</tr>
<tr>
<td>5: 30, F</td>
<td>Mediastinum and sternum wound specimens, respiratory secretions</td>
<td>Multiple organisms in respiratory secretions</td>
<td>Heart-lung transplantation, cyclosporine, corticosteroid, antithymocyte globulin</td>
<td>Dox, Cm, Gm; drainage</td>
<td>Died</td>
<td>[11]</td>
</tr>
<tr>
<td>6: 31, F</td>
<td>Sternum wound specimen, BAL fluid</td>
<td></td>
<td>Heart-lung transplantation, cyclosporine, corticosteroid, antithymocyte globulin</td>
<td>Cm, Dox; debridement ×3</td>
<td>Died</td>
<td>[5]</td>
</tr>
<tr>
<td>7: 43, F</td>
<td>Mediastinum and sternum wound specimens, respiratory secretions</td>
<td>Multiple organisms in respiratory secretions</td>
<td>Heart-lung transplantation, cyclosporine, corticosteroid, azathioprine</td>
<td>Dox, Cm, Gm; drainage</td>
<td>Died</td>
<td>[11]</td>
</tr>
<tr>
<td>8: 43, F</td>
<td>Sternum wound, specimen, BAL fluid</td>
<td></td>
<td>Heart-lung transplantation, cyclosporine, corticosteroid, azathioprine</td>
<td>Cm, Dox</td>
<td>Died</td>
<td>[5]</td>
</tr>
<tr>
<td>9: 48, M</td>
<td>Mediastinum specimen, pleural fluid</td>
<td><em>Ureaplasma urealyticum</em> in mediastinum and pleural fluid specimens</td>
<td>Heart-lung transplantation, cyclosporine, corticosteroid, azathioprine</td>
<td>Cm, Dox</td>
<td>Died</td>
<td>[5]</td>
</tr>
</tbody>
</table>
| 10: 48, M                              | Mediastinum and sternum wound specimens | *Ureaplasma urealyticum* in mediastinum and sternum wound specimen, *Pseudomonas* bacte-
|                                           |                                       | remia, *Candida albicans* mucosal infections | Heart-lung transplantation, cyclosporine, corticosteroid | Vm, Czd, Pp, Vm, then Dox; Cm, debridement | Resolved | [10]   |
| 11: 41, M                              | Sternum wound specimen                | Coagulase-negative staphylococcus in sternum wound specimen | Heart-lung transplantation | Vm, Em; debridement ×2 | Resolved | [13]   |
| 12: 34, M                              | Pleural fluid, BAL fluid, lung tissue | *U. urealyticum* in lung tissue | Heart-lung transplantation, cyclosporine, corticosteroid, azathioprine | Vm, Czd, Imi, then Dox; debridement | Resolved | [14]   |
| 13: 50, M                              | Pleural fluid, BAL fluid              |                                           | Lung transplantation, cyclosporine, corticosteroid, azathioprine, transmission of mycoplasma from donor | Vm, Czd, TMP-SMZ, then Cpf; drainage | Resolved | [15]   |
| 14: 65, M                              | Pleural fluid, BAL fluid              |                                           | Lung transplantation, cyclosporine, corticosteroid, azathioprine, transmission of mycoplasma from donor | Vm, Czd, TMP-SMZ, then Cpf; drainage | Resolved | [15]   |
| 15: 31, M                              | Pleural fluid                         | *Bacteroides fragilis*                   | Pancreatic transplantation, diabetes mellitus, cyclosporine, corticosteroid, azathioprine | Cm, debridement ×3 | Died    | [5]    |
Patients who underwent coronary artery bypass surgery or other reconstructive cardiac surgery

16: 46, M  Blood, sternum wound specimen  
Coronary artery bypass surgery  
Tet  
Resolved [16]

17: 48, M  Mediastinum and sternum wound specimens  
Coronary artery bypass surgery  
Dox, Cm, Tm; drainage  
Resolved [11]

18: 48, M  Pleural fluid, sternum wound specimen  
Coronary artery bypass surgery  
Cm, Dox; debridement × 3  
Resolved [5]

19: 62, M  Mediastinal tissue, pericardium specimen  
*Staphylococcus epidermidis* in mediastinum and pericardium specimens  
Coronary artery bypass surgery  
Vm, Em, then Cm, then Dox  
Resolved [4]

20: 62, M  Mediastinum specimen  
Coronary artery bypass surgery  
Cman, then Dox; drainage, debridement, and irrigation  
Resolved [10]

21: 63, M  Sternal wound specimen  
U. urealyticum in sternum wound specimen  
Coronary artery bypass surgery, diabetes  
Vm, Ctri, then Cm, Dox, Gm; debridement and drainage  
Resolved [17]

22: 64, M  Pleural fluid, sternum wound specimen  
Coronary artery bypass surgery  
Clfox, Gm, Vin; debridement  
Died [18]

23: 71, M  Sternal wound specimen  
Coronary artery bypass surgery  
Vm, Pip, Tm, then Cm, Dox; debridement and drainage  
Resolved [19]

24: 0, F  Pleural fluid, sternum wound specimen  
Coagulase-negative staphylococci  
Transposition of great arteries, Rashkind balloon atrial septostomy and arterial switch surgery  
Vm, Dox, Rif; heart transplantation  
Resolved [20, 21]

25: 25, M  Blood, sternum wound specimen  
Haemophilus influenzae in trachea specimen  
Aortic valve xenograft surgery  
Dox, debridement and drainage  
Resolved [22]

26: 31, M  Pericardium specimen  
Aortic valve replacement surgery  
Dox; debridement and drainage  
Resolved [23]

27: 56, M  Blood, sternum wound specimen  
*Haemophilus influenzae* in trachea specimen  
Aortic valve xenograft surgery  
Amp, then Tet, Em; debridement and drainage  
Resolved [16]

28: 24, M  Pleural fluid, blood, ankle wound specimen  
C. albicans  
Chronic active hepatitis, corticosteroids  
Died [25]

29: 37, F  Pleural fluid, peritoneum specimen  
Multiple trauma, multiple fractures, ankle wound  
Chronic active hepatitis, corticosteroids  
Em; debridement  
Resolved [5]

30: 21, M  Endocardium specimen  
Systemic lupus erythematosus, aortic valve replacement surgery  
Cm, Dox, Rif; heart transplantation  
Resolved [20, 21]

31: 21, M  Pericardial fluid  
Klebsiella in sputum  
Aspiration pneumonia, empyema  
Clfox, Cm, Pen, Em; empyema tube  
Resolved [4]

32: 0, F  Pericardial fluid  
Klebsiella in sputum  
Aspiration pneumonia, empyema  
Clfox, Cm, Pen, Em; empyema tube  
Resolved [4]

33: 58, M  Blood, blood, urine  
Staphylococci and *Escherichia coli* bacteremia  
Systemic lupus erythematosus  
Dox; drainage  
Resolved [22]

34: 24, M  Blood, lung specimen  
Multiple trauma, multiple fractures, ankle wound  
Chronic active hepatitis, corticosteroids  
Em; debridement  
Resolved [25]

35: 74, M  Pleural fluid, bone, urine  
Systemic lupus erythematosus  
Chronic lymphocytic leukemia, carcinoma of prostate, corticosteroids  
Em; treatment of urinary retention  
Resolved [26]

NOTE:  
AmB, amphotericin B; Amp, ampicillin; BAL, bronchoalveolar lavage; Claz, cefazolin; Cfox, cefoxitin; Cm, clindamycin; Cman, cefamandole; Cpfx, ciprofloxacin; Ctax, cefotaxime; Cthn, cephalothin; Ctri, ceftriaxone; Czid, ceftazidime; Dox, doxycycline; Em, erythromycin; Gm, gentamicin; Imi, imipenem; Pen, penicillin; Pp, piperacillin; Ref, reference; Rif, rifampin; Tet, tetracycline; Tm, tobramycin; TMP-SMZ, trimethoprim-sulfamethoxazole; Vm, vancomycin.
cline, up to 15% of clinical isolates of M. hominis have been reported to be tetracycline-resistant [32, 33]. The new quinolone trovafloxacin has been shown to be effective against Mycoplasma species in vitro [34].

Treatment of infections involved drainage, debridement, and specific antimicrobial therapy. The importance of surgical treatment is evident from a case report of a patient who responded to surgical therapy alone (patient 11 [13]; table 3). M. hominis sternum wound infections were sometimes refractory to therapy, and despite specific antimicrobial therapy, debridement, and reconstructive operations, there was a tendency for mal-union of the sternum.

Other mycoplasmas have also been found in infections involving the mediastinum. U. urealyticum may, although infrequently, coexist in M. hominis infections (table 3) and has been found alone in one case of pericarditis after heart transplantation [22]. Mycoplasma pneumoniae has been implicated as a pathogen in cases of pericarditis [22, 35-38].

All 8 of the patients in our series had identifiable factors that predisposed them to infections. The specific mechanisms predisposing to mycoplasmal infection may have involved formation of atelectasis, collection of secretions in bronchial or thoracic cavities, or hemorrhage. Specific antibodies may be important in defense against mycoplasmal infections, since mycoplasma-specific antibodies alone have been reported to inhibit the growth of mycoplasmas in vitro [39]. Keeping in mind the possible protective role of antibodies, we retrospectively looked for serum γ-globulin levels. It is surprising that patient 2 had an increased γ-globulin level (22.0 g/L) 4 months after the onset of M. hominis mediastinitis. This finding may indicate that he had a normal antibody-mediated immune response. Alternatively, mycoplasmal infection may have resulted in unspecific synthesis of γ-globulin without the development of protective antibodies specific to M. hominis. Unspecific synthesis of immunoglobulins has been observed in M. pneumoniae infections; they have been reported to be associated with the formation of circulating immune complexes [40] and autoantibodies [41].

Analysis of successive M. hominis strains cultured from synovial fluid from a patient with chronic arthritis over a 6-year period revealed that M. hominis isolates possess surface antigen variation [42]. One of these variable surface antigens was found to be an immunogenic lipoprotein important in the adhesion of mycoplasmas to eukaryotic cells called the variable adherence-associated antigen (Vaa). Variants of the progenitor M. hominis strain were found to have size variation caused by gain or loss of central repetitive sequences in the vaa lipoprotein gene and sequence divergence in the distal C-terminal portion of the vaa gene [43]. Because antibodies to the Vaa lipoprotein inhibit adherence of M. hominis to host cells [44], antigenic variation in the Vaa lipoprotein may help M. hominis to escape immune surveillance. Other surface antigens of M. hominis may also exhibit variation; for example the P120 surface protein, whose sequences have been shown to be highly variable between different strains [45]. The P135 surface protein Lpm1 has been shown to contain multiple repetitive sequences that may be prone to mutations leading to antigenic variation [46].

M. hominis is a potent inducer of epithelial cells secreting neutrophil chemoattractant cytokines such as IL-8 and epithelial cell-derived neutrophil-activating peptide (ENA-78) [47]. This property may contribute to the tendency of infected patients to develop pleural and pericardial effusions. The ability of M. hominis to attract neutrophils is intriguing in light of the findings that mycoplasmas bind spontaneously to neutrophils and remain viable inside neutrophils when phagocytosed in the absence of antibody [39]. The intracellular location may enable M. hominis to multiply freely when protected from antibody-mediated host defenses.

Although M. hominis infections are uncommon, the bacterium may be a more prevalent pathogen than previously reported studies have indicated. Because isolation of the organism is difficult, M. hominis infection may be frequently missed or misdiagnosed. One should suspect M. hominis infection when gram staining reveals abundant neutrophils but no bacteria. When a case is suspected, the clinical bacteriologic laboratory should be consulted for isolation of M. hominis, and empirical antibiotic treatment against mycoplasmas should be considered. It should be noted that because of the tendency for chronic infection, long-term antimicrobial treatment against M. hominis should be administered. However, surgical drainage and debridement are key to recovery, since patients respond to therapy with surgical treatment alone. Because hematomas, collections of fluid, and atelectasis appear to predispose to M. hominis infections, the use of atraumatic surgical technique and good hemostasis cannot be overemphasized in preventing these infections.

References
9. National Committee for Clinical Laboratory Standards. Performance stan-