

## Pleural Empyema Caused by *Gemella* Species: A Rare Condition

Cristina Senent, José Norberto Sancho, Eusebi Chiner, Jaime Signes-Costa, Ana Camarasa, and Ada Luz Andreu

Secció de Pneumologia, Hospital Universitari Sant Joan d'Alacant, Sant Joan d'Alacant, Alacant, Spain

Three cases of pleural empyema caused by *Gemella* species—2 caused by *Gemella morbillorum* and 1 caused by *G haemolysans*—are reported. Microbiological characteristics, predisposing factors, and treatment are reviewed and all cases published in the literature are analyzed.

**Key words:** *Gemella morbillorum*. *Gemella haemolysans*. Pleural empyema.

Empiema pleural por microorganismos del género *Gemella*: una complicación infrecuente

Se describen 3 casos de empiema pleural por microorganismos del género *Gemella*, 2 por la especie *G. morbillorum* y uno por *G. haemolysans*. Se revisan las características microbiológicas, los factores predisponentes y las pautas de tratamiento, y se exponen los casos publicados en la literatura médica.

**Palabras clave:** *Gemella morbillorum*. *Gemella haemolysans*. Empiema pleural.

### Introduction

Microorganisms of the *Gemella*<sup>1</sup> species are gram-positive cocci and facultative anaerobes which—like other human commensal bacteria—are opportunistic pathogens and may cause serious local and systemic infections, mainly in immunodepressed patients. The species *G morbillorum* and *G haemolysans* are the most important pathogens. *G haemolysans* can cause endocarditis<sup>2</sup> and meningitis,<sup>3</sup> while *G morbillorum* causes endocarditis, especially of native valves,<sup>4,5</sup> septic arthritis,<sup>6</sup> and meningitis,<sup>7</sup> among others. Respiratory tract infections caused by *Gemella* species have rarely been reported but they can cause lung abscesses,<sup>8,9</sup> necrotizing pneumonia,<sup>10,11</sup> and pleural empyemas,<sup>8,10,12-19</sup> while there are few publications referring to pleural involvement and these describe isolated cases.

We report 3 cases of pleural empyema caused by *Gemella* species, 2 caused by *G morbillorum*, and 1 caused by *G haemolysans*. We also review articles published in medical literature to date.

The protocol for identification was as follows. Gram staining revealed gram-positive cocci grouped together in chains. Samples were cultured on Columbia blood agar

base and chocolate agar with incubation in an anaerobic chamber. After 48 hours of incubation,  $\alpha$ -hemolytic, catalase-negative colonies were obtained that showed better growth in the anaerobic medium. Microorganisms were identified as *G morbillorum* and *G haemolysans* by means of the API 20 Strep system (CAPI System, BioMérieux, La Balme Les Crottes, Montalieuvercien, France).

Antimicrobial susceptibility was ascertained with the Kirby-Bauer disk diffusion method.

### Case Descriptions

#### Patient 1

The first patient was a 45-year-old male ex-smoker (30 pack-years) with an intake of 30 g of alcohol a day, a history of hypertension, and recently diagnosed atrial fibrillation. He was admitted for fever, right-sided pleuritic pain, shivering, and general malaise, with onset 25 days earlier. Of note in his clinical examination was obesity and symptoms of right pleural effusion. A chest x-ray and a computerized tomography (CT) scan showed right-sided, loculated pleural effusion with thickened visceral pleura and underlying condensation in the right lower lobe (Figure 1a). Diagnostic thoracocentesis was performed and a purulent, greenish, putrid fluid was obtained. Culture of this fluid revealed the growth of *G morbillorum* susceptible to penicillin, cephalosporins, and aminoglycosides. Treatment commenced with a chest drain (total volume 1200 mL), fibrinolytics, and cefotaxime at a dose of 1 gram every 6 hours intravenously, as well as levofloxacin (500 mg every 12 hours, intravenously), for 16 days. Oral cefuroxime (500 mg every 12 hours) was then added, and treatment lasted for 26 days. A subsequent follow-up examination revealed minimal residual basal pleural thickening

Correspondence: Dr E. Chiner  
Secció de Pneumologia, Hospital Universitari Sant Joan d'Alacant  
Ctra. Alicante-Valencia, s/n  
03550 Sant Joan d'Alacant,  
Alacant, Spain  
E-mail: chiner\_eus@gva.es

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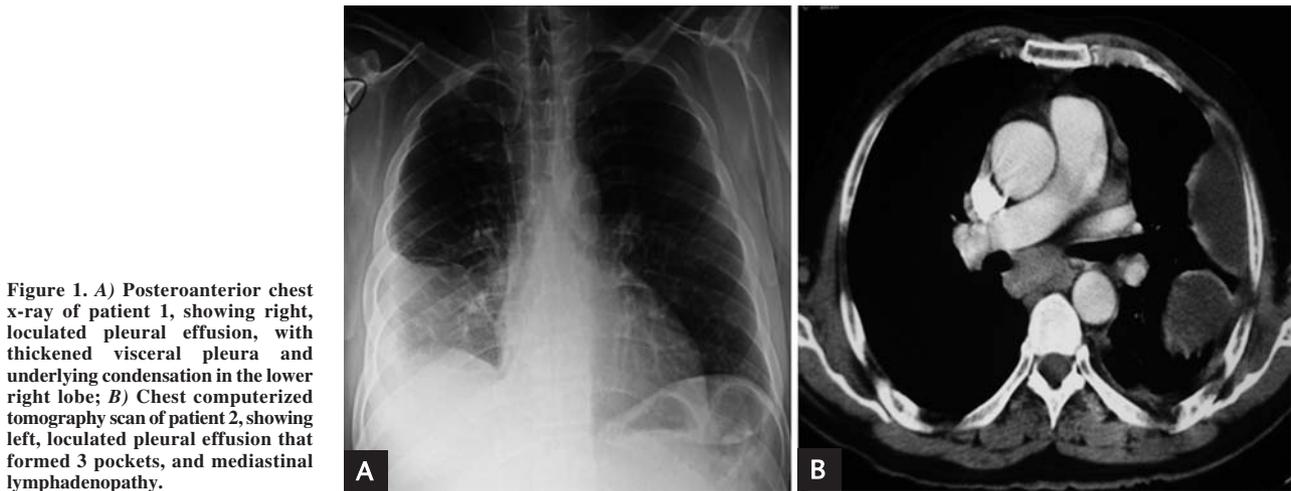


Figure 1. A) Posteroanterior chest x-ray of patient 1, showing right, loculated pleural effusion, with thickened visceral pleura and underlying condensation in the lower right lobe; B) Chest computerized tomography scan of patient 2, showing left, loculated pleural effusion that formed 3 pockets, and mediastinal lymphadenopathy.

in the right lung. While in hospital, the patient developed a perianal abscess that required surgical drainage but no microbiological samples were available.

#### Patient 2

The second patient was a 59-year-old male former active smoker (40 pack-years), with an alcohol intake of 40 g a day and a history of personality disorder with dysthymia and somatization, benzodiazepine abuse which required 2 hospital admissions for drug-induced coma, and an episode of bronchial aspiration. The patient suffered from untreated sleep apnea-hypopnea syndrome, features of chronic bronchitis, and alcohol-induced chronic liver disease. The patient was admitted for a fever of 40°C that started 15 days earlier, pleuritic chest pain in the left hemithorax, shivering, and malaise. In the physical examination, symptoms of pleural effusion in the lower half of the left hemithorax were notable. Chest x-ray and CT scan showed loculated pleural effusion in the left lung that formed 3 pockets of fluid (basal posterior, lateral and apicoposterior), and mediastinal lymphadenopathy (Figure 1b). Diagnostic thoracocentesis yielded a greenish, thick and putrid fluid with growth of *G morbillorum* susceptible to penicillins and cephalosporins, and intermediate susceptibility to aminoglycosides. The patient was initially treated with a chest drain (total volume 1270 mL), fibrinolytics, and imipenem (500 mg intravenously every 6 hours) for 4 days. Once the microbiological results were available, amoxicillin-clavulanic acid was administered intravenously (2 g every 8 hours) for 4 days and then orally (875/125 mg every 8 hours) until day 24 of treatment. The clinical and radiologic outcome was satisfactory.

#### Patient 3

The third case was a 50-year-old female ex-smoker with stage 4 colon cancer. She had undergone surgery 7 years ago and had received several cycles of chemotherapy. She was admitted to hospital after 3 days of fever of 39°C, cough, purulent sputum, and pleuritic pain in the right hemithorax. Her symptoms indicated pleural effusion in the lower two thirds of the right hemithorax. Chest x-ray and CT scan showed a bilateral pleural effusion with right-sided predominance and loculations in its upper part, pulmonary infiltrate in the lower right lobe with abscessed areas and multiple pulmonary nodules related to previously diagnosed metastases (Figure 2). Thoracocentesis showed a serosanguineous, thick fluid with growth of



Figure 2. Chest computerized tomography scan of patient 3, showing bilateral pleural effusion of right predominance with loculations in its upper part, pulmonary infiltrate in the lower right lobe with abscessed areas and multiple pulmonary nodules related to previously diagnosed metastases.

*G haemolysans* susceptible to penicillin, cephalosporins, and aminoglycosides. The patient was treated with a chest drain (1670 mL) and fibrinolytics together with intravenous amoxicillin-clavulanic acid (1 g every 8 hours) and levofloxacin (500 mg every 12 hours) for 10 days, before switching to oral administration (amoxicillin-clavulanic acid, 875/125 mg every 8 hours; levofloxacin, 500 mg every 24 hours) until she had completed 21 days of treatment. Her clinical and radiologic outcome was favorable.

#### Discussion

*Gemella* species are gram positive, facultative anaerobic, catalase negative cocci described for the first time in 1917 by Tunnicliff.<sup>20</sup> The name of the genus was officially proposed by Berger in 1961<sup>1</sup> and included just 1 species at that time, *G haemolysans*, previously known as *Neisseria haemolysans*.<sup>21</sup> A second *Gemella* species, *G morbillorum*, was added in 1988. This was previously classed as a

Review of Published Cases of Pleural Empyema Caused by *Gemella morbillorum*

Authors	Year	No.	Age, y	Predisposing Factor	Antibiotic Treatment	Duration, d
García del Busto et al <sup>2</sup>	1995	1	38	Poor mouth hygiene	CFX + TOB	–
Da Costa et al <sup>8</sup>	1996	1	–	Dental surgery, CF	–	–
Hayashi e Ito <sup>3</sup>	1996	1	44	Dental caries, diabetic ketoacidosis, CLN + PAP	28	–
Marcos Sánchez et al <sup>15</sup>	2000	1	68	Bronchiectasis, monthly roxithromycin	IMP ERT	30 20
Signes-Costa et al <sup>10</sup>	2000	1	47	Smoker, laryngectomy, microaspiration	CTX CFR	30
Canet et al <sup>16</sup>	2001	1	75	AF, embolic CVA, aphasia + dysphagia	IMP AMX-C	70
Poulose <sup>17</sup>	2002	1	–	–	None	–
García-Lechuz et al <sup>19</sup>	2002	4	54 (36-75)	1. HIV+ IVDA, PTB 2. Alcohol abuse 3. COPD, alcohol abuse 4. Diabetes, hypertension	AMX-C CTX + AZT IMP + CFX CFX + SXT AMX-C + CFZ + CLN	10 4 14 – – –
Valipour et al <sup>18</sup>	2005	1	26	Epilepsy, IVDA	–	–
Vezeris et al <sup>14,a</sup>	1999	1	71	Smoker, COPD, carcinoma of the larynx, microaspiration	AMX-C	–

Abbreviations: AF, atrial fibrillation; AMX-C, amoxicillin-clavulanic acid; AZT, aztreonam; CF, cardiac failure; CFR, cefuroxime; CFX, ciprofloxacin; CFZ, cefazolin; CLN, clindamycin; COPD, chronic obstructive pulmonary disease; CTX, cefotaxime; CVA, cerebrovascular accident; ERT, erythromycin; HIV+, human immunodeficiency virus infection; IMP, imipenem; IVDA, intravenous drug abuse; PAP, panipipenem; PTB, pulmonary tuberculosis; SXT, co-trimoxazole; TOB, tobramycin.

<sup>a</sup>Empyema caused by *Gemella haemolysans*.

*Streptococcus* species. Today, *G haemolysans*, *G morbillorum*, *G bergeriae* and *G sanguinis* have all been classed as *Gemella* species based on DNA hybridization and 16S ribosomal RNA gene sequencing.<sup>21</sup>

*G haemolysans* has been found in 30% of pharyngeal swabs taken from the oral cavities and upper respiratory tracts of healthy individuals,<sup>23</sup> whereas *G morbillorum* has also been found as a component of the human flora in the intestine and urogenital system.<sup>21,24</sup>

Due to their opportunistic nature, these species are capable of causing certain infections, the most common of which are septicemia,<sup>25</sup> infections of the nervous system,<sup>3,26</sup> arthritis,<sup>6</sup> liver abscesses,<sup>27</sup> and endocarditis.<sup>4,5</sup> Cases of respiratory tract infections have been described such as necrotizing pneumonia,<sup>10,11</sup> lung abscesses,<sup>8,9</sup> and even colonization of the tuberculous cavity. However, the appearance of pleural empyema is considered exceptional. In a review of medical literature using MEDLINE we only identified 12 cases of pleural empyema caused by *G morbillorum*<sup>8,10,12,13,15-19</sup> and 1 case caused by *G haemolysans*.<sup>14</sup>

The Table shows the characteristics of the 13 cases. Our study of 3 patients is one of the largest to have been published, with the exception of the review by García-Lechuz et al,<sup>19</sup> who described 4 cases of pleural empyema caused by *Gemella* species over a period of 4 years. The case described by Signes-Costa et al<sup>10</sup> was, however, treated in our department but we did not include it in this study since it has already been published; together with this case we would have treated a total of 4 cases over a period of 7 years.

Among the underlying conditions presented by patients with this type of infection, intravenous drug addiction,<sup>5,18,19</sup> diabetes,<sup>13,19</sup> cardiovascular disease,<sup>8</sup> and alcohol abuse<sup>19</sup>

are notable, as was the case in the 2 patients from this study infected by *G morbillorum*, and cancer,<sup>29</sup> as was the case in the third patient described here. All cases were characterized by immunodepression. Predisposing factors include poor mouth hygiene and prior dental procedures, which due to the disruption in the mucosa, could facilitate hematogenous dissemination,<sup>8,12,13</sup> as well as microaspiration of oropharyngeal secretions that would facilitate bronchogenic dissemination, which we believe could have occurred in patient 2 given the past medical history and ingestion of drugs.

It is notable that patient 2 presented an anal abscess that was surgically drained during its clinical course and that we believe could be related to hematogenous dissemination caused by *G morbillorum*, although samples were not cultured. The appearance of perianal abscess caused by this microorganism has not been described previously.

Response to treatment is usually favourable,<sup>18</sup> as was the case in our 3 patients, although there may be complications when sepsis or shock are present,<sup>11,24</sup> especially in immunodepressed patients.

Information on the antimicrobial susceptibility of these species is limited. Low resistance to aminoglycosides and high resistance to trimethopim-sulfametoxazole<sup>11</sup> has been described. Antibiotic susceptibility resembles that of *Streptococcus viridans*,<sup>30</sup> therefore penicillin or ampicillin are the drugs of choice. Indeed, there are authors that recommend empirical treatment with penicillin G sodium,<sup>16</sup> although occasional resistance to penicillin is argued as a rationale to commence treatment with beta-lactamases and aminoglycosides or, failing this, vancomycin.<sup>18</sup> In cases of pleural empyema, there is insufficient information on the duration of treatment and so it is recommended to prolong treatment for at least 4 weeks<sup>10,13</sup> or until the

empyema is evacuated,<sup>16</sup> as management of these patients is based on drainage of the empyema with therapeutic thoracentesis<sup>12</sup> or chest drain.<sup>10,13,15,16,18</sup> Cure following application of this measure without the need for antibiotic treatment has even been described.<sup>17</sup> In our patients no penicillin resistance was found and patients followed antibiotic treatment with beta-lactamases for 3 to 4 weeks with a satisfactory clinical and radiologic outcome. In the 3 patients from our study we performed chest drainage—which exceeded 1000 mL in volume in all cases—and administered fibrinolytics.

To conclude, in the case of a patient with empyema, we must consider the possibility of infection caused by *Gemella* species, especially in immunodepressed patients or those having recently undergone digestive tract or dental procedures, or those patients with suspected nasopharyngeal microaspiration.

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