A case of rapidly progressive empyema caused by *Streptococcus anginosus* group bacteria in a young male patient

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**ABSTRACT**

Introduction: The *Streptococcus anginosus* group bacteria (SAG; formerly *Streptococcus milleri*) are facultative anaerobes that rarely cause pneumonia but have been increasingly found in empyema. Several reports have suggested that patients with SAG empyema commonly have underlying comorbidities that include diabetes mellitus and malignancy. Case Report: A 30-year-old male with no past medical history presented with progressive shortness of breath and pleuritic chest pain despite recent treatment with azithromycin. Lung examination was significant for decreased tactile fremitus, decreased breath sounds, and egophony over the left lower lobe. Laboratories demonstrated leukocytosis with marked bandemia. Chest X-ray revealed marked opacification of the left hemithorax and CT chest showed left lung collapse and multiple loculations over the left lower lobe. Intravenous ceftriaxone and clindamycin were initiated, and two left chest tubes drained 2500 ml of pus; however, the patient had intermittent fevers. Thoracotomy was performed on day nine of admission, from which a repeat pleural fluid culture revealed *Streptococcus anginosus* that was sensitive to penicillin G, and the patient improved clinically with a resolved leukocytosis. Conclusion: This was a case of severe empyema in a young male with no underlying medical comorbidity. It is important to conduct appropriate tests to effectively treat the disease as bacteriology changes over time and antibiotic resistance is becoming more prevalent.

Keywords: Antibiotic choice, Empyema, *Streptococcus anginosus*, Thoracotomy

INTRODUCTION

Pleural empyema is defined as bacterial infection of the pleural space that results in either pus or the presence of bacterial organisms on Gram stain. Pleural empyema can be an outcome of complicated parapneumonic effusions, frequently requiring invasive procedures such as thoracostomies and thoracotomies in addition to antibiotic therapy. The incidence of empyema is increasing worldwide and rises by 3% per year in the United States [1]. The reason is not known, though it is suspected that it may be due to the increasing number of patients living with chronic disease and risk factors (e.g. heart disease, diabetes, obesity, tobacco and alcohol...
use), and increased identification and coding of pleural empyema [1]. Up to half of the four million patients who suffer from pneumonia each year will develop a parapneumonic effusion [2]. More than 65,000 patients suffer from pleural empyema each year in the United Kingdom and United States, with an estimated $500 million US dollars in hospital costs [3].

The *Streptococcus anginosus* group bacteria (SAG; formerly known as *Streptococcus milleri*), consists of *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*. These three microorganisms were ultimately distinguished via advanced technology by DNA homology, polypeptide patterns of whole cells, and phenotypic characteristics [4]. SAG are facultative anaerobes, Gram-positive, catalase-negative cocci, and exhibit variable hemolysis patterns. They are part of the normal flora in the oral cavity and gastrointestinal tract but have been documented to cause a variety of infections including dental abscesses, central nervous system abscesses (epidural and subdural spaces), thoracic infections (pneumonia, empyema, mediastinitis), and abdominal infections (liver abscess, cholangitis, subphrenic abscess, peritonitis) [5–7]. Several reports have suggested that patients with SAG empyema commonly have underlying comorbidities that include diabetes mellitus and malignancy [8–9]. This report presents a case of severe empyema in a young male with no underlying medical comorbidity.

**CASE REPORT**

A 30-year-old male without prior medical history was admitted to the hospital for increasing shortness of breath and pleuritic chest pain. The patient was treated with oral azithromycin for community-acquired pneumonia diagnosed by chest X-ray showing a left lower lobe infiltrate a week prior (Figure 1). Social history was significant for smoking tobacco and polysubstance use. Review of systems was positive for chills, cough, and diaphoresis.

On initial assessment, the patient had a heart rate of 112 beats per minute, blood pressure of 123 mmHg/79 mmHg, respiratory rate of 16 breaths per minute, temperature of 98.0°F, and borderline hypoxia of 92% oxygen on room air. On physical examination, the patient was in no acute distress and spoke in full sentences, but appeared diaphoretic. Oral cavity examination revealed poor dentition with tooth decay. There was no cervical, supraclavicular, or infraclavicular lymphadenopathy on palpation. Cardiovascular examination was significant for tachycardia but demonstrated no murmurs, rubs, or gallops. Lung examination was significant for absent breath sounds, decreased tactile fremitus, and egophony over the left lower lobe in addition to mild crackles over the right lower lobe. Laboratories revealed a white blood count (WBC) of 27,500 cells/μL with 16% bandemia. Laboratory values are shown in Tables 1–3. His urine toxicology results were positive for cocaine, opiates, tetrahydrocannabinol, and phencyclidine. Chest X-ray showed opacification of the left hemithorax (Figure 2), and computed tomography revealed left lung collapse with a large, multiloculated left pleural effusion (Figure 3). On day one, two left chest tubes were placed which evacuated a total of 2500 ml of frank pus. Gram stain of the fluid showed Gram-positive coci in chains. Pleural fluid culture grew *Gemella morbillorum* and revealed glucose of 92 mg/dL, pH 7.3, protein less than 3.0 g/dL, WBC 18,000 cells/μL with 72% neutrophils, and lactate dehydrogenase of 719 U/L. Blood cultures remained negative.

![Figure 1: Chest X-ray one week prior to admission: Left lower lobe infiltrate and possible small left effusion suggesting pneumonia.](image1)

![Figure 2: Chest X-ray on admission: Marked opacification of left hemithorax. There is collapse of much of the left lung with possible multiloculated pleural effusions and a left apical hydropneumothorax.](image2)
Table 1: Basic metabolic profile, lactic acid, and LDH on admission

| Reference Range and Units                  | Value |
|--------------------------------------------|-------|
| Sodium                                     | 132 mEq/L |
| Potassium                                  | 4.2 mEq/L |
| Chloride                                   | 97 mEq/L |
| Carbon dioxide                             | 25 mmol/L |
| Anion Gap                                  | 10 mEq/L |
| Glucose                                    | 129 mg/dL |
| BUN                                        | 30 mg/dL |
| Creatinine                                 | 1.2 mg/dL |
| Calcium                                    | 7.8 mg/dL |
| Estimated GFR                              | >60 ml/min/1.73 m2 |
| BUN/Cr Ratio                               | 25 |
| Lactic acid                                | 1.7 mmol/L |
| Serum LDH                                  | 94 U/L |

Abbreviations: BUN=blood urea nitrogen; Cr=creatinine; GFR=glomerular filtration rate; LDH=lactate dehydrogenase.

Table 2: Complete blood count with differential during hospital course

| Reference Range | D1  | D3  | D4  | D5  | D7  | D8  | D9  | D10 | D11 | D13 | D15 | D18 | D19 | D20 |
|-----------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| WBC             | 27.5| 24.8| 23.1| 31.4| 24.7| 32.3| 31.3| 33.9| 23.9| 13.2| 8.6 | 6.9 | 7.4 | 9.2 |
| Hb              | 11.1| 10.3| 10.5| 11.3| 10.6| 10.9| 10  | 8.4 | 8   | 7.9 | 7.2 | 7.1 | 7.5 | 7.8 |
| Hct             | 33.5| 32.1| 32  | 35.6| 33  | 34  | 30.3| 24.9| 23.8| 24.4| 22  | 21.4| 22.8| 23.4|
| Plt             | 239 | 250 | 245 | 327 | 352 | 371 | 328 | 288 | 315 | 361 | 339 | 299 | 297 | 316 |
| SegNeut         | 68  | 70  | 76  | 71  | 64  | 68  | 77  | 84  | 85  | 75  | 67  | 60  | n/a | 76  |
| Bas             | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 1   | 1   | 1   | n/a | 1   |
| Eos             | 0   | 0   | 1   | 1   | 1   | 3   | 0   | 0   | 0   | 1   | 1   | 1   | n/a | 0   |
| Lymph           | 2   | 3   | 10  | 17  | 11  | 15  | 13  | 6   | 8   | 17  | 23  | 30  | n/a | 18  |
| Mono            | 13  | 9   | 2   | 11  | 14  | 3   | 6   | 4   | 7   | 7   | 9   | 9   | n/a | 6   |
| Abs Neut        | 18.7| 17.4| 17.6| 22.3| 15.8| 22  | 24.1| 28.5| 20.2| 9.9 | 5.7 | 4.1 | n/a | 7   |

Abbreviations: D=day; WBC=white blood count; Hb=hemoglobin; Hct=hematocrit; Plt=platelet count; Seg Neut=segmented neutrophils; Bas=basophils; Eos=eosinophils; Lymph=lymphocytes; Mono=monocytes; Abs Neut=absolute neutrophils.

Table 3: Liver profile

| Reference Range and Units | D2  | D4  | D5  | D8  | D11 |
|---------------------------|-----|-----|-----|-----|-----|
| Albumin                   | 2.5 | 2   | 2   | 2.1 | 1.7 |
| Total bilirubin           | 2.4 | 2.3 | 1.6 | 1.1 | 0.6 |
| Direct bilirubin          | 1.8 | n/a | n/a | n/a | 0.3 |
| ALP                       | 65  | 101 | 126 | 106 | 96  |
| AST                       | 8   | 34  | 49  | 23  | 24  |
| ALT                       | 11  | 24  | 40  | 35  | 22  |
| Total protein             | 5.7 | 5   | 5.3 | 6   | 5   |
| Globulin                  | 3.2 | 3   | 3.3 | 3.9 | 3.3 |
| Alb/Glob ratio            | 0.8 | 0.7 | 0.6 | 0.5 | 0.5 |

Abbreviations: ALP=alkaline phosphatase; AST=aspartate transaminase; ALT=alanine transaminase; Alb=albumin; Glob=globulin
Hospital Course and Treatment

The patient was initially treated with ceftriaxone and clindamycin in addition to serial thoracostomies with local tissue plasminogen activator administration. However, adequate drainage of multiple loculations was still not achieved (Figures 4–5). The patient had persistent leukocytosis and intermittent fevers, thus requiring thoracotomy nine days after admission. Pleural culture obtained during the procedure revealed *Streptococcus anginosus* sensitive to penicillin and resistant to clindamycin, erythromycin, and tetracycline. The patient’s antibiotic course was changed to intravenous penicillin G (Table 4). After surgery, the patient felt better and the leukocytosis resolved to a WBC of 6,900 cells/μL, eight days post-thoracotomy (Figure 6). On day 20, he was discharged home on oral penicillin with instructions to take 500 mg every eight hours for eight weeks. The patient did not follow up with us as an outpatient.
DISCUSSION

This relatively young patient was ultimately found to have rapidly progressive empyema caused by Streptococcus anginosus, a pathogen not commonly known to cause empyema in the United States. In such a patient who did not improve on empiric antibiotic therapy, it is important to order appropriate diagnostic tests such as pleural fluid cultures, Gram stain, and antimicrobial susceptibility testing to identify the pathogen which will guide treatment. The empiric antibiotic therapy for this patient included clindamycin since aspiration pneumonia was considered as a possible cause in light of his risk factors (i.e. polysubstance use); however, it was found that this strain of Streptococcus anginosus was resistant to clindamycin. Previous case studies have reported that SAG are susceptible to penicillin, and that these cases of empyema typically require thoracotomies for complete resolution [10].

Pleural infection rates in adults has increased by 3% per year in adults in the last two decades [1]. In developing countries, empyema represents a major health problem as delay in treatment is common. The prevalence of HIV/AIDS, the widespread use of immunosuppressants and organ transplantation, and the increasing age of population mean that empyema will remain a common and significant illness [11]. Studies from the UK, Canada, Scandinavia and New Zealand all revealed SAG as the most common isolate accounting for 30-50% of adult cases of community-acquired empyema [12-14].

The bacteriology of pleural infection and antimicrobial susceptibility change over time. The most common causes of empyema are Streptococcus pneumoniae, Streptococcus pyogenes, and Staphylococcus aureus; however, SAG are gaining importance as causative organisms [2]. They are known to form abscesses, be rapidly progressive, and demonstrate synergy with oral anaerobes in causing pleural infection [15]. For instance, it is known that anaerobes impair the function of polymorphonuclear leukocytes (PMNL) in the host [4]. In a study comparing the interaction between human PMNL and SAG, it was found that even after being ingested by PMNL, the SAG were killed at only a rate of 3% of that of Staphylococcus aureus. Therefore, SAG are highly resistant to phagocytosis by PMNL, yet the mechanism is still unclear [16]. Due to the lack of reliable in vivo models, the pathophysiology of pleural empyema has yet to be elucidated.

Of note, the bacterial etiology of empyema is not necessarily similar to that of pneumonia; thus, pleural infection requires different treatment [17]. The varied microbial etiology is likely due to the acidic and hypoxic environment of the pleural space in contrast to the high oxygen tension in the lung parenchyma.

The microbial causes of empyema vary by geographic location, source of infection (community vs. nosocomial), and host type (pediatric vs. adult, immunocompetent vs. immunocompromised). Most studies lack detailed characterization, for instance serotyping, of bacteria to identify the cause of empyema. In our case, Gemella morbillorum—a also a Gram-positive, catalase-negative coccus and facultative anaerobe—was the initial report before the thoracotomy. Our microbiology laboratory reported that there was an 86% probability that this could be a different microorganism. Gemella morbillorum is known to cause endocarditis, especially of native valves, septic arthritis, and meningitis [18]. According to the literature, there are only 14 cases of pleural empyema being caused by this microorganism; these patients had predisposing factors such as poor oral hygiene, smoking history, cardiovascular or respiratory disease, drug abuse, alcohol abuse, or malignancies [19]. The most recent case report identified Gemella morbillorum as the cause of pleural empyema via diagnosis with 16S ribosomal RNA gene sequencing [19]. Nevertheless, more studies on this diagnostic technique is required before confirming the true microbiological cause of empyema as Gemella species can be frequently mistaken as Streptococcus species.

Another possibility is mixed infection with other anaerobic bacteria: it is known that SAG bacteria cohabit with other anaerobes of oral origin such as the
Peptostreptococcus, Prevotella, or Fusobacterium species and may demonstrate synergy [15]. However, as noted previously, current diagnostic techniques are limited. For instance, up to 40% of empyema fluid fails to reveal microorganisms by conventional culture [17]. Moreover, the lack of in vivo models is a large contributor to our limited understanding of the pathological causes of empyema [2]. Hence, more research into comprehensive identification of the pathogens that cause severe infections such as empyema is needed.

CONCLUSION

Successful management of empyema includes appropriate antibiotic treatment, pleural fluid culture, antimicrobial susceptibility testing, and thoracostomy or thoracotomy to decrease mortality risk. More research into accurate and comprehensive diagnostic techniques is needed in order to appropriately treat this severe disease with significant morbidity and mortality. Fortunately, both SAG and Gemella species are known to be susceptible to penicillin.

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Author Contributions
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Conflict of Interest
Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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