CASE REPORT

Case Report: Complex parapneumonic effusion and bacteremia secondary to *Granulicatella adiacens* in immunocompetent host [version 1; peer review: 2 approved with reservations]

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Abstract

Granulicatella adiacens is a fastidious Gram-positive streptococcus that is linked with causing a variety of infections in immunocompromised hosts. These include endocarditis, bacteremia, osteomyelitis, and spontaneous bacterial peritonitis. We present a rare incidence of this bacterium causing a complex parapneumonic effusion in an immunocompetent host. An effective antibiotic regimen for treating infections caused by this bacterium includes ampicillin plus penicillin plus gentamicin but resistance to various classes of antibiotics has been reported. In conclusion, this organism can affect different systems in immunocompromised as well as immunocompetent hosts, and a high index of suspicion is required for its diagnosis.

Keywords

granulicatella, adiacens, parapneumonic, pneumonia

Open Peer Review

Approval Status ? ?

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: **Acharya A:** Conceptualization, Methodology, Project Administration; **Sattar Z:** Conceptualization, Data Curation, Investigation; **Ahmad A:** Data Curation, Formal Analysis; **Sattar F:** Investigation, Methodology; **Fiksman A:** Investigation, Methodology, Project Administration

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Introduction

Granulicatella adiacens is a member of the *Granulicatella* genus of the fastidious nutritionally variant group of the Gram-positive streptococci. The most common clinical syndromes associated with this organism are Endocarditis and Bacteremia, but cases of vertebral osteomyelitis and spontaneous bacterial peritonitis have also been reported^{1,2}. To the best of our knowledge, we are presenting the first case of complex parapneumonic effusion with bacteremia secondary to *G. adiacens*.

Case presentation

A 56 year old male with a history of seizure disorder presented to the Emergency Department with shortness of breath for three days. He also reported productive cough with yellow sputum, right sided chest pain, anorexia, night sweats, fatigue and fever for the same duration. The patient denied any hemoptysis, chills, rigors, leg swelling and recent travel, but had an episode of upper respiratory tract infection three months ago due to sick contact. The patient's past surgery history was significant for subdural hematoma treated with frontal craniotomy 20 years ago. In addition, the patient used to take dilantin for his seizure disorder, but stopped taking this medication a long time ago. The patient's mother had a history of breast cancer. The patient is a smoker for 38 years, and smoked half a pack of cigarettes a day. He is a chronic alcoholic and had drunk 3–4 beers every day for many years, but denies any illicit drug use. He lives with his family.

On admission, he was febrile to 100.6 F, tachycardic to 150 bpm, hypertensive to 157/93 and saturating at 91% in room air. In the general examination, the patient was diaphoretic. Respiratory examination revealed mild tachypnea with dullness to percussion on right hemithorax, decreased breath sounds in the same area and crackles but no wheezing. Other than the regular tachycardia, the remainder of the physical examination was unremarkable. Initial labs showed leukocytosis of 36.5 K/uL (normal range, 4.5–11k/uL), hemoglobin of 16.7 g/dl (13.5–17.5 g/dl), platelet of 415 K/uL (130–400 k/uL), blood urea nitrogen of 9mg/dl (6–20mg/dl), creatinine of 0.9mg/dl (0.5–0.90 mg/dl), D-Dimer of 492 ng/ml (<250 ng/ml), lactic acid of 1.8 mmol/L (0.5–2.2 mmol/L), BNP (Brain Natriuretic Peptide) of 10 pg/ml (<100 pg/ml). Other tests, including rapid influenza, urine legionella antigen, urine streptococcus pneumoniae antigen, troponin and HIV were negative. A chest X-ray showed consolidation on the right side (Figure 1).

Computerized tomography (CT) angiography of the chest was negative for pulmonary embolism but showed large volume complex parapneumonic effusion on the right side (Figure 2).

The patient was admitted to the Intensive Care Unit for acute hypoxic respiratory failure and sepsis secondary to right-sided multifocal pneumonia with complex parapneumonic effusion. A chest tube was placed on day 1 with drainage of almost 2.2 L of serosanguinous fluid. Tissue plasminogen activator (10mg every 12 hourly) and deoxyribonuclease therapy (5mg every 12hrly) were given through the chest tube for a total of three days. Pleural fluid was exudative with polymorphonuclear cells. Pleural fluid cultures including mycobacterial cultures, fungal cultures and parasitic exams

Figure 1. Chest X-ray showing right-sided consolidation.

Figure 2. CT scan on admission showing right-sided effusion.

were negative. Blood culture from day 1 grew *G. adiacens* in anaerobic bottles sensitive to Ceftriaxone, Levofloxacin, and Vancomycin. Transesophageal echocardiogram (on day 8) did not show any vegetation.

On day 1 of hospitalization, the patient was started on vancomycin (1250mg every 12 hourly; goal trough of 15–20 mcg/ml), Piperacillin/Tazobactam (3.375 gm every 8 hourly) and azithromycin (500mg daily empirically), which was continued until day 5. On day 6, antibiotics were switched to Ceftriaxone (2 gram IV every 24 hourly), Ampicillin (2 gram IV every 4 hourly), Gentamicin (80mg IV every 8 hourly; goal trough <1 mcg/ml and goal peak 3–4 mcg/ml) and Metronidazole (500mg IV every 8 hourly) for complex parapneumonic effusion with bacteremia secondary to *G. adiacens*, as per recommendations from the Infectious Disease team, which was continued up to day 21.

The patient started feeling better with resolution of his fever, cough, chest pain, fatigue and anorexia on day 7. By day 10 his shortness of breath resolved, and he was discharged on day 21.

baseline. His leukocytosis improved from 35.6 k/uL on day 1 to 16.7 k/uL on day 9 and resolved to 9.14 k/uL on day 17. Follow up CT scan chest on day 15 showed small loculated effusion, which had improved from admission (Figure 3).

The CT surgery team evaluated the patient and deferred video-assisted thoracoscopic surgery decortication. On day 21, the patient left against the medical advice. The patient completed one more week of Ceftriaxone (2 gram every 24 hourly) and Metronidazole (500mg every 8 hourly) as an outpatient with sustained remission of symptoms on follow-up. A follow-up CT scan of the chest two months later showed a near complete resolution of the residual effusion (Figure 4).

Discussion

A new type of Viridans group Streptococci was discovered in 1961 by Frenkle and Hirsch. This was termed as NVS

(Nutritionally Variant Streptococci) and the discovery was based on prolonged incubation period, characteristic growth requirement, variable gram stain findings and satellite promoting phenomenon around colonies of other bacteria. The growth of NVS is not supported by routinely used blood culture media unless they are supplemented with pyridoxal. That is why NVS are usually considered to be very fastidious³. Identification of *Granulicatella* isolates are performed by either biochemical testing such as API Strep or bioMerieux or molecular confirmation. Identification was delayed in several cases, as isolates were thought to be poorly growing streptococci before consideration of pyridoxal dependence⁴. Though it is a normal commensal in the oral cavity, the spectrum of infections with *Granulicatella* species seems to be expanding, and infections are associated with significant morbidity and mortality. The clinical course is more severe than Viridans streptococci. A high index of suspicion and vigilance is needed because of its fastidious nature, slow growth rate, difficulty in isolation on culture media, and multiple antibiotic resistance. Microbial communities that have any kind of impact on tumor progression and microorganisms associated with tumors have been defined as oncobiome. The detailed analysis of microbiome in lung cancer patients documents the presence of *G. adiacens*, which is not a normal commensal in healthy lungs and further research into this area is warranted⁵.

There are reports of *G. adiacens* as a rare cause of neonatal pneumonia^{6,7}. We could not find any reported cases of pneumonia caused by *G. adiacens* in immunocompetent adults; however, it has been reported in patients suffering from pulmonary tuberculosis and concurrent HIV infection⁸. To the best of our knowledge, our case could be the first case of a parapneumonic effusion caused by infection with *G. adiacens*. Patients at risk of developing *Granulicatella* species infections are usually immunocompromised in contrast to our patient who was immunocompetent^{2,9}.

Both *G. adiacens* (susceptibility rates of 0–63% to ceftriaxone, 81% to amoxicillin, 55–67% to penicillin and 96% to meropenem) and *G. elegans* (susceptibility rates of 0% to cefuroxime, 100% to penicillin and 33% to ceftriaxone) were reported to have the resistance to β -lactam antibiotics. Resistance was also reported to tetracycline, clindamycin, ciprofloxacin, erythromycin, but not to rifampicin or vancomycin^{10,11}. The infection is usually treated with the antibiotic regimen used for enterococcal endocarditis usually consisting of a combination of ampicillin or penicillin plus gentamicin. Ceftriaxone plus gentamicin or vancomycin monotherapy are reasonable alternatives¹².

Conclusions

Granulicatella adiacens is a fastidious organism that has the potential to infect multiple systems in both immunocompetent and immunocompromised patients.

Given our case of *G. adiacens* complex parapneumonic effusion/pneumonia and bacteremia in an otherwise immunocompetent adult and the difficulty to diagnose, a high index of suspicion is required to catch and treat it early on.

Figure 3. Post-drainage CT showing improvement in right-sided effusion.

Figure 4. Follow-up CT scan chest after two months showing near complete resolution of effusion.

Consent

Written informed consent was obtained from the patient for the publication of this case report and any associated images.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

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Version 1

Reviewer Report 23 January 2023

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Werner C Albrich

Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St. Gallen, Rorschacherstrasse, Switzerland

In this case report the authors describe a patient with bacteremia and a pneumonia with a parapneumonic effusion caused by *Granulicatella adiacens*.

Major comments:

- The diagnosis (in title, abstract and main text) should include pneumonia. There was a description of consolidation supporting the diagnosis of pneumonia on chest X-ray. Was this also seen on the chest CT scan, prior to or after drainage of the pleural effusion? If so, this should be added. The text described it as multifocal pneumonia. Common pneumonia classifications use rather multilobar (if this was the case). Which lobe was affected as this might give a clue towards aspiration?
- In addition, the case report does not contain information which allows to confirm that it is a complex parapneumonic effusion versus a pleural empyema. Was there septation or inhomogeneity on chest CT? Were pH, LDH, protein/albumin measured? Were pleural cultures obtained prior to or after start of antibiotics?
- Given the reported data, the patient was not septic according to the Sepsis-3 definition, in fact, he was hypertensive.
- The patient is a chronic alcoholic and smoker and may differ therefore from a healthy person. Therefore, it seems more accurate to state this rather than to call him an immunocompetent host (in title, abstract, case presentation and discussion). Was there any clue for aspiration pneumonia?
- Was there continuous bacteremia, i.e. follow-up blood cultures?
- Was there susceptibility testing for penicillin/ampicillin and gentamicin or other aminoglycosides?
- I cannot follow the rational to combine ampicillin with penicillin (as stated in the abstract) and would reformulate "ampicillin or penicillin plus gentamicin".
- The antibiotic regimen is unusual in several aspects:
 - Was there a loading dose for vancomycin?

- The piperacillin dosage is rather low if there was normal renal function.
- Given concerns for acute renal failure with the combination of vancomycin with piperacillin/tazobactam, this combination is falling out of favour and is very broad for a patient not at risk for resistant pathogens and not in septic shock.
- The targeted quadruple therapy is not explained by the susceptibility testing. Why was ceftriaxone combined with ampicillin? And if ceftriaxone is used why was gentamicin added and why 3x/d rather than the less nephrotoxic once daily dose? Also, the addition of metronidazole can be viewed critically if there is no evidence of empyema or aspiration.
- If there was no empyema (and no sign of endocarditis), the treatment duration of 4 weeks is much longer than currently recommended in guidelines for pneumonia.
- In view of the threat of antibiotic resistance and to support antibiotic stewardship, this therapy should be critically discussed.

Minor comments:

Abstract:

- *Granulicatella adiacens* is not formally any more a streptococcus but belongs a separate genus (https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=962037#null).

Introduction:

- The pathogen should be more properly described as “the fastidious *Granulicatella* genus previously considered as nutritionally variant group streptococci”.

Case presentation:

- I am not sure if previous phenytoin use is important. Should use the name of the drug rather than the trade name.
- If known, should add the actual number of breaths per second to characterize the tachypnea.
- Was sputum cultured? Was there testing for SARS-CoV-2 or was this prior to the pandemic?
- Purohit et al¹ also describe a case of empyema with *Granulicatella adiacens*, so this is likely not the first case.

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Is the background of the case's history and progression described in sufficient detail?

Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious Diseases; respiratory tract infections; antibiotic therapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 10 November 2022

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Motoi Ugajin

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The authors intend to show *G.adiacens* can cause complicated parapneumonic effusion with bacteremia through this case report. However, I feel there are several flaws on the current report. Now I will mention my concerns for this report:

- 1) Please show the detailed information about right pleural effusion. The definition of complicated parapneumonic effusion requires lactate dehydrogenase level and glucose level.
- 2) In this case, blood culture showed the growth of *G.adiacens*, while pleural effusion could not reveal the growth of this bacteria. In the discussion section, the authors mention routinely used blood culture media does not support the growth of *G.adiacens*. Nevertheless, the case could obtain the growth of *G.adiacens* on blood culture. The authors should describe the reasons why the authors could obtain the growth of this bacteria on blood cultures and why the authors could not reveal the growth of this bacteria on pleural effusion.
- 3) In the discussion section, the authors mention the clinical course of infection due to *G.adiacens* is more severe than *Viridans streptococcus*. Please show the concrete information which can support your opinion.
- 4) The authors mention this patient is immunocompetent. However, this patient is reported to be a chronic alcoholic. Some previous literature has shown alcoholic patients are susceptible to respiratory infections^{1,2}. Indeed, the definition of immunocompromised is unclear, but I think it is difficult to categorize this patient as immunocompetent.

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Is the background of the case's history and progression described in sufficient detail?

Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory infections, lung malignancies, and interstitial pneumonia.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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