CASE REPORT PEER REVIEWED | OPEN ACCESS

Methicillin resistant *Staphylococcus aureus* necrotizing pneumonia and ceftaroline fosamil: An alternative regimen

Fermin López-Rivera, Hernán González Monroig, James Eggert, Hector Cintrón Colón, Jessica Castellanos Díaz, Omar Méndez Meléndez, Fernando Abreu

ABSTRACT

Introduction: Pneumonia is defined as an infection of the parenchyma of the lung and is one of the most common causes of death from infectious diseases in the United States (US). Pneumonia is classified into two groups; community acquired pneumonia (CAP) and hospital acquired pneumonia (HAP). Most CAPs are secondary to bacterial pathogens. Methicillin resistant *Staphylococcus aureus* (MRSA) is identified as a potential pathogen in 8.9% of CAP cases. Community acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) produces a cytotoxin called Panton–Valentine leukocidin (PVL), which causes white blood cell destruction and necrosis, resulting in necrotizing pneumonia when it reaches the lungs. Vancomycin and linezolid are most common recommended antibiotics when treating MRSA necrotizing pneumonia. Ceftaroline fosamil, a fifth-generation cephalosporin, is approved for the treatment of skin and soft tissue infection caused by MRSA and pneumonia, but it has not been approved for MRSA pneumonia. Case Report: A 72-year-old Hispanic male presented with a medical history of hypertension, diabetes mellitus type 2, chronic kidney disease stage 3B, unspecified chronic thrombocytopenia and asthma developed an upper respiratory tract infection that manifested with fever and rhinorrhea and resolved without treatment. Ten days later, the patient arrived at the emergency room due to productive cough of rust colored sputum that started three days before admission. Associated symptoms included malaise, fever, chills and shortness of breath. The patient was admitted to medicine ward with diagnosis of CAP and was initially managed with azithromycin/ceftriaxone. However, persistent fever and tachypnea resulted in the need for reassessment. Sputum culture revealed MRSA and the patient was switched to ceftaroline fosamil for a 21-day course of treatment. Patient was discharged home and has been followed at the outpatient clinic with none of the aforementioned symptoms. Conclusion: Methicillin resistant *Staphylococcus aureus* necrotizing pneumonia is an uncommon cause of CAP, but its incidence has increased during the recent years. This type of CAP has gained notoriety due to the PVL cytotoxin, with its dire results. Vancomycin and linezolid are the most recommended antibiotics; vancomycin is recommended if the bacteria show a minimum inhibitory concentration (MIC) < 2. In this case, the *S. aureus* recovered at sputum culture showed a MIC >2 and since the patient presented with several additional comorbidities management was started with ceftaroline fosamil, a fifth-generation cephalosporin that has no hepatic adjustment and has no problem in thrombocytopenic patients. The ceftaroline fosamil was administered at 400 mg

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intravenously every 12 hours for 21 days. The patient improved clinically and was discharged home and followed the next week then monthly for two months.

Keywords: Ceftaroline fosamil, Methicillin resistant *Staphylococcus aureus* (MRSA), Panton–Valentine leukocidin, Pneumonia

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INTRODUCTION

Pneumonia is defined as an infection of the parenchyma of the lung [1]. As reported by the National Center for Health Statistics in 2014, pneumonia is the eighth cause of mortality in the US [2]. Pneumonia is classified into two groups: community acquired pneumonia (CAP) and hospital acquired pneumonia (HAP). The CAP affects approximately 5.6 million patients every year, and it is ranked as the sixth cause of death in people older than 65 years old [3]. Pneumonia has a bimodal distribution, significantly affecting the very young (< 5 years old) and the elderly (> 65 years old) [4]. The etiological agents of CAPs are most commonly: *Streptococcus pneumoniae, Mycoplasma pneumoniae* and respiratory syncytial virus, while in other cross-sectional study showed most CAP did not recover an etiological agent in 56.7% (Figure 1) [5, 6].

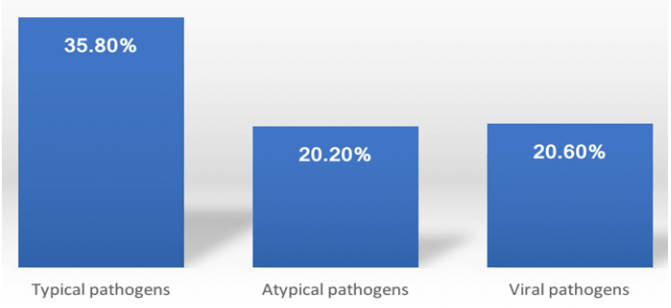

Figure 1: Identified pathogens in community acquired pneumonia.

Methicillin resistant *Staphylococcus aureus* (MRSA), a rare pathogen, its incidence has increased over the last years and nowadays has been identified as a potential pathogen in 8.9% of CAP cases [7]. The MRSA pneumonia is often a post-viral pneumonia, acting as a secondary bacterial infection that commonly affects the lower respiratory tract after a primary viral infection [8]. The MRSA pneumonia can be necrotizing to the lung parenchyma resulting in cavitation due to the pore-forming cytotoxin called Panton–Valentine leukocidin (PVL). This cytotoxin induces cell death by rapid disruption of mitochondrial homeostasis via the activation of caspases (3 and 9) resulting in the lysis of the polymorphonuclear leukocytes and lung cells [9]. This type of pneumonic process usually presents with severe symptoms requiring inpatient management. The most commonly prescribed antibiotics for MRSA pneumonia are vancomycin and linezolid. Vancomycin should be avoided in acute kidney injury and bacterial cultures with minimum inhibitory concentration (MIC) >2. Linezolid is advantageous in MRSA pneumonia as it markedly suppresses PVL protein expression, hindering the progression of the cavitation [10]. The presence of bone marrow (such as thrombocytopenia) problems can impede the implementation of linezolid therapy. Another type of anti-MRSA antibiotic, daptomycin, should not be prescribed in patients with pneumonia because it is inhibited by pulmonary surfactant [11]. Ceftaroline fosamil, a fifth-generation cephalosporin, which has a broad-spectrum activity against gram positive bacteria, working in the penicillin binding protein, that is approved for the treatment CAP's and skin and soft tissue infection caused by MRSA, but its use for the treatment of MRSA pneumonia has not been approved yet.

CASE REPORT

A case of 72-year old Hispanic male presented with a medical history of hypertension, diabetes mellitus type 2, chronic kidney disease stage 3B, unspecified chronic thrombocytopenia and asthma that developed an upper respiratory tract infection that manifested with fever and rhinorrhea and resolved without treatment. Ten days later, the patient arrived at the emergency room due to productive cough of rust colored sputum that started three days before admission. Associated symptoms included malaise, fever, chills and shortness of breath. Triage vital signs showed: blood pressure 149/84 mmHg, heart rate 89 beats per minute, respiratory rate 24/minute, temperature 38.8°C, Sat 89% (room air).

Physical examination was remarkable for an acutely ill patient with non-toxic appearance in mild distress that was talking in words. Trachea was midline, thorax showed symmetric expansion and respiratory system was remarkable for bilateral inspiratory and expiratory crackles, and dullness to percussion was noted at the left lower lobe.

Laboratory studies: White blood cells 26.43x10^9/uL, hemoglobin 9.4 g/dl, hematocrit 27.8%, platelets 74x10^9/L, sodium 146 mmol/L, potassium 3.6 mmol/L, chloride 108.00 mmol/L, carbon dioxide 27.00 mmol/L, blood urea nitrogen 29 mg/dL, creatinine 1.7 mg/dL, glomerular filtration rate by Cockcroft–Gault 34.2 mL/min, BUN/CREA ratio 17.1.

Arterial blood gasses: pH 7.381, pCO_2 44.9 mmHg, pO2 61 mmHg, HCO_3 25.8 mmol/L, O_2 sat 86%, expected A-a gradient 22.0 mmHg, calculated A-a gradient 32.6 mmHg, PaO_2/FiO_2 290.5 mmHg.

Chest X-ray taken at the emergency room showed perihilar thickening, left costophrenic angle effacement and left lower lobe consolidation (Figure 2). Findings were worrisome for abscess formation, therefore, chest CT scan was performed immediately and showed bilateral pulmonary nodules, including several cavitary nodules, in addition to patchy bilateral lower lung airspace disease and small left pleural effusion (Figure 3). CURB-65 and PORT/PSI were calculated showing and found to be: 2 and class IV, respectively (Tables 1, 2) [12]. The patient was admitted to medicine ward with diagnosis of CAP and was initially managed with azithromycin/ceftriaxone. Skin tuberculin test was performed and was determined to be 0 mm. However, persistent fever and tachypnea for 72 hours resulted in the need for reassessment. The follow-up chest X-ray showed worsening of the previous infiltrates/cavities and a second chest CT scan was ordered (Figure 4 and Figure 5). Sputum culture revealed MRSA with a MIC >2 for vancomycin, thus requiring alternative treatment. Infectious disease services were consulted on the use of linezolid, but linezolid use was discouraged due to increased risk of thrombocytopenia. Infectious disease instead recommended the use of ceftaroline fosamil with renal adjustment at 400 mg intravenous every 12 hours as monotherapy. The patient received ceftaroline fosamil as ordered by the infectious disease service and became afebrile within the next 36 hours, completing 21 days of antibiotic. Lung masses were biopsied by interventional radiology and were determined to be negative for malignancy. The patient was discharged home without supplemental oxygen and was followed at the outpatient clinic the next week and monthly for two months and remained afebrile with no shortness of breath.

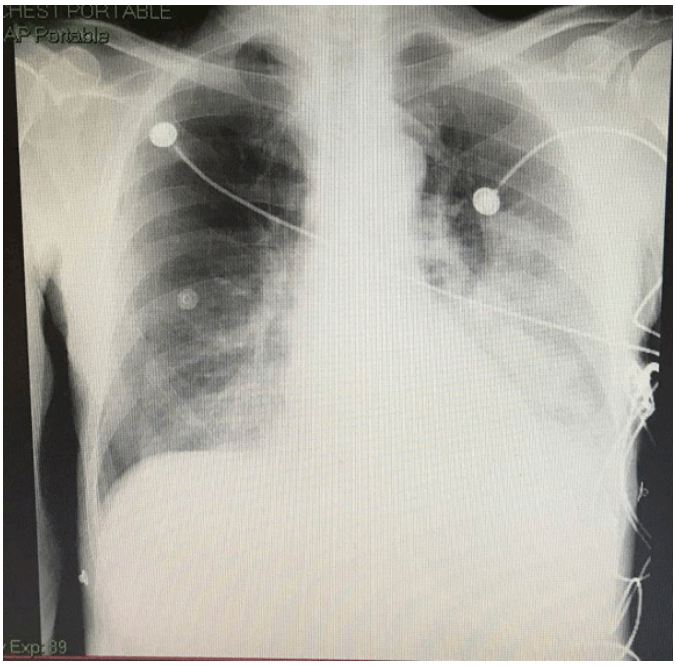

Figure 2: Chest X-ray showing perihilar thickening, left costophrenic angle effacement and left lower lobe consolidation.

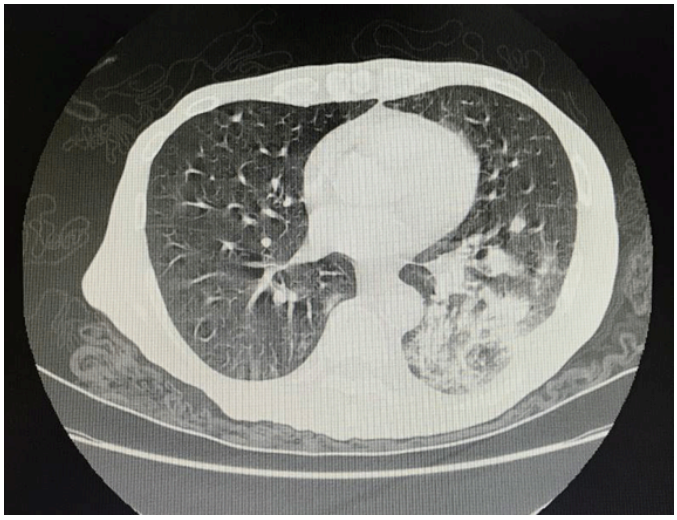

Figure 3: Chest computed tomography scan showing bilateral pulmonary nodules, a few of which were seen to be cavitary in addition to patchy bilateral lower lung zones airspace disease and small left pleural effusion.

Table 1: PORT/PSI: Estimates mortality for adult patient with community-acquired pneumonia

Risk class	Risk	Points value	Mortality	Management
I	Low	No comorbidities	0.1%	Outpatient
II	Low	< 70	0.6%	
III	Low	71–90	0.9%	
IV	Moderate	91–130	9.3%	Inpatient
V	High	> 131 points	27%	

Table 2: CURB-65: Estimates mortality of community acquired-pneumonia to help determine inpatient versus outpatient treatment

CURB-65 score	Mortality risk	Recommendation
0	0.6%	Consider home treatment
1	2.70%	Consider home treatment
2	6.80%	Short inpatient hospitalization
3	14.0%	Consider ICU admission
4–5	27.8%	Consider ICU admission

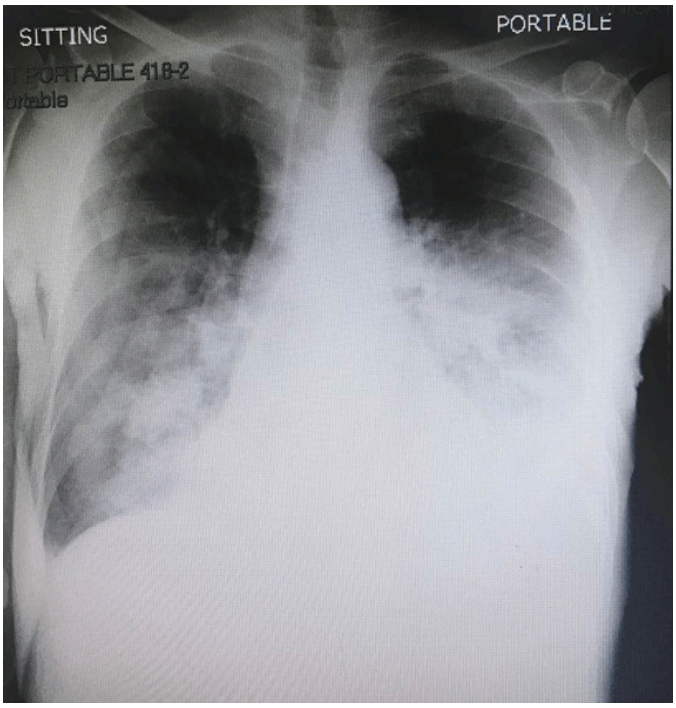

Figure 4: Chest X-ray showing worsening of bilateral airspace disease.

DISCUSSION

Our patient was admitted with diagnosis of CAP and was initially managed with azithromycin/ceftriaxone, a regimen that covers most common pathogens. The current history of upper respiratory symptoms had resolved, and MRSA pneumonia was not initially considered, primarily because of a lack of a bilateral pattern on chest X-ray. However, the patient's chest X-ray findings were not related to a specific etiologic agent [13]. After 72 hours of antibiotic treatment, the patient's persistent fever warranted a reassessment of the medical treatment. Although X-rays are no pathognomonic for a specific pathogen, new imaging studies showed suspicious findings of MRSA necrotizing pneumonia and the suspicion was confirmed with sputum culture [14]. An anti-MRSA drug should be prescribed but vancomycin was not recommended due to high MIC (>2) and linezolid was discouraged in view of thrombocytopenia. ID service recommended ceftaroline fosamil, a fifth-generation cephalosporin with spectrum that cover MRSA. Our patient received ceftaroline fosamil 400 mg IV every 12 hour for 21 days as monotherapy with a great outcome, finally being discharge home with no supplemental oxygen. The follow-up chest X-ray was requested for two months later in view of delayed imaging clearance due to *Staphylococcus aureus* pneumonia (Table 3) [15].

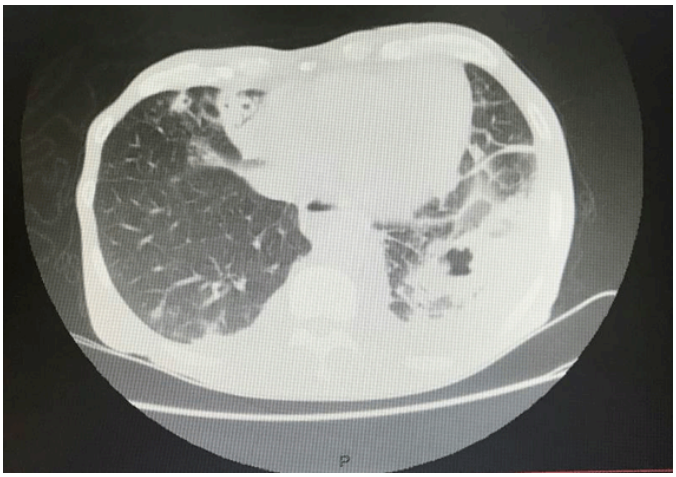

Figure 5: Chest computed tomography scan showing worsening of cavitary lesions with patchy infiltrates.

Table 3: Radiographic resolution of community acquire pneumonia [15]

Agent	Resolution time	Residual X-ray findings
Streptococcus pneumoniae	3–5 months	30%
Haemophilus influenzae	1–5 months	Rare
Legionella pneumophila	2–6 months	17%
Mycoplasma pneumoniae	1 month	Rare
Chlamydia pneumoniae	2 months	15%
Staphylococcus aureus	3–5 months	Common
Moraxella catarrhalis	2 months	Rare

CONCLUSION

With each diagnosis of CAP, the physician must inquire about any recent history of upper respiratory symptoms that occurred in the last 8–14 days. Antibiotic regimens should not be based solely on imaging studies but also correlate with the past medical history. Ceftaroline fosamil, a fifth-generation cephalosporin that works in the PBP (penicillin binding protein), is approved for CAP and skin and soft tissue infection and is characterized by its coverage against MRSA. However, it is not FDA approved for MRSA-CAP. When common anti-MRSA pneumonia antibiotics, such as vancomycin and linezolid, are contraindicated due to MIC >2 or additional comorbidities, as in the case of our patient, ceftaroline fosamil could be considered. This novel antibiotic poses the benefit that need modification only in renal impairment, does not need modification in liver disease including Child-Pugh B or B and finally does not need to be followed with peaks or trough. Our patient was managed with an anti-MRSA cephalosporin for 21

days as a salvage therapy with a positive outcome. The authors suggest that a large multicenter clinical trial can be performed to assess the efficacy of this drug in treating MRSA-CAPs.

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Hernán González Monroig – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Omar Méndez Meléndez – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

REFERENCES

1. Ebert MD, Sheth S, Fishman EK. Necrotizing pneumonia caused by community-acquired methicillin-resistant *Staphylococcus aureus*: An increasing cause of “mayhem in the lung”. Emerg Radiol 2009 Mar;16(2):159–62.
2. Murphy SL, Kochanek KD, Xu J, Arias E. Mortality in the United States, 2014. NCHS Data Brief 2015 Dec;(229):1–8.
3. Brar NK, Niederman MS. Management of community-acquired pneumonia: A review and update. Ther Adv Respir Dis 2011 Feb;5(1):61–78.
4. Polverino E, Torres Marti A. Community-acquired pneumonia. Minerva Anestesiol 2011 Feb;77(2):196–211.
5. Köksal I, Ozlü T, Bayraktar O, et al. Etiological agents of community-acquired pneumonia in adult patients in Turkey: A multicentric, cross-sectional study. Tuberk Toraks 2010;58(2):119–27.
6. Xiao K, Su LX, Han BC, et al. Analysis of the severity and prognosis assessment of aged patients with community-acquired pneumonia: A retrospective study. J Thorac Dis 2013 Oct;5(5):626–33.
7. Rubinstein E, Kollef MH, Nathwani D. Pneumonia caused by methicillin-resistant *Staphylococcus aureus*. Clin Infect Dis 2008 Jun 1;46 Suppl 5:S378–85.
8. van der Sluijs KF, van der Poll T, Lutter R, Juffermans NP, Schultz MJ. Bench-to-bedside review: Bacterial pneumonia with influenza— pathogenesis and clinical implications. Crit Care 2010;14(2):219.
9. Genestier AL, Michallet MC, Prévost G, et al. *Staphylococcus aureus* Panton–Valentine leukocidin directly targets mitochondria and induces Bax-independent apoptosis of human neutrophils. J Clin Invest 2005 Nov;115(11):3117–27.
10. Diep BA, Equils O, Huang DB, Gladue R. Linezolid effects on bacterial toxin production and host immune response: Review of the evidence. Curr Ther Res Clin Exp 2012 Jun;73(3):86–102.
11. Silverman JA, Mortin LI, Vanpraagh AD, Li T, Alder J. Inhibition of daptomycin by pulmonary surfactant: In vitro modeling and clinical impact. J Infect Dis 2005 Jun 15;191(12):2149–52.
12. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997 Jan 23;336(4):243–50.
13. Moncada DC, Rueda ZV, Macías A, Suárez T, Ortega H, Vélez LA. Reading and interpretation of chest X-ray in adults with community-acquired pneumonia. Braz J Infect Dis 2011 Nov–Dec;15(6):540–6.
14. Nguyen ET, Kanne JP, Hoang LM, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* pneumonia: Radiographic and computed tomography findings. J Thorac Imaging 2008 Feb;23(1):13–9.
15. El Solh AA, Aquilina AT, Gunen H, Ramadan F. Radiographic resolution of community-acquired bacterial pneumonia in the elderly. J Am Geriatr Soc 2004 Feb;52(2):224–9.