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A Review of: Nosocomial K. pneumoniae, A. baumannii, and Elizabethkingia meningoseptica Septicemia in a Patient of COVID-19

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Secondary bacterial infections are known to be a destructive complication of coronavirus disease 2019 (COVID-19) infection. Despite corticosteroids, anti-IL6 and other anti-viral medications such as remdesivir, nirmatrelvir and ritonavir were initiated for immunomodulation, aggressive supportive care such as mechanical ventilation and extracorporeal membrane oxygenation may be needed for those with respiratory failure and hemodynamic instability. These invasive procedures and immune modulators render these patients vulnerable to nosocomial infections, negatively impacting treatment outcomes. It could be a dilemma whether antibiotics should be used for those with deteriorating multiorgan dysfunctions. We reported a patient of COVID-19 associated acute hypoxemic respiratory failure who was initially treated with broad-spectrum antibiotics, corticosteroids, tocilizumab, and remdesivir and was successfully liberated from mechanical ventilation. Yet, bacteremia and osteomyelitis of multidrug-resistant nosocomial pathogens ensued, leading to a protracted course of hospitalization.

This is a case of 65-year-old man visited the emergency room due to a productive cough, lightheadedness, weakness, and shortness of breath for one week during an outbreak of domestic COVID-19. He has a past medical history of alcoholic liver cirrhosis.

He was febrile, tachypneic, and cyanotic (SpO2 87%). Initial laboratory test revealed abnormal liver function tests, elevated infection parameters, lactic acidosis, and incidentally noticed high hemoglobin A1c% (Table 1). SARS-CoV-2 PCR was positive and a chest X-ray showed bilateral ground-glass opacities.

After admission, he was empirically treated with ertapenem and levofloxacin (Table 2). Dexamethasone, remdesivir, and tocilizumab were given per treatment guidelines. Enoxaparin 40 mg QD was prescribed to prevent thromboembolism.

Table 1: Patient's Initial Laboratory Data.

Liver Function	AST 119 U/l	ALT 89 U/l	Total Bilirubin 2.4 mg/dl	
Infection Parameters	CRP 3.1 mg/dl	Procalcitonin 1.07 ng/ml	D-dimer 1.02 mcg/ml	Ferritin 4298 ng/ml
Lactic Acidosis	pH 7.308	HCO3 19.1 mmol/l	Lactate 8.7 mmol/l	
Hemoglobin A1c (9.0%)				

Table 2:

Time (day)	Event	Antibiotics	Culture
-7	Cough, shortness of breath		
1	Admission, dexamethasone given	Ertapenem, levofloxacin	Sputum: normal flora Blood: negative
3	Tocilizumab and remdesivir used	Ertapenem, levofloxacin	
6	Mechanical ventilation (MV)	Doripenem, levofloxacin, teicoplanin	Sputum: normal flora and *Candida albicans* Blood: negative
9	Liberation from MV		
19	Jaundice, sepsis	Meropenem, fluconazole	Blood: *A. baumannii*, *K. pneumoniae*, *Elizabethkingia meningoseptica*
22		Cefoperazone/sulbactam, tigecycline	
23	Spiking fever jaundice progressed	Ceftazidime/avibactam, amikacin	Blood: *E. meningoseptica*
26		Piperacillin/tazobactam, tigecycline	Blood: *E. meningoseptica*
31			Blood: *E. meningoseptica*
44	Spine MRI: osteomyelitis	Cefoperazone/sulbactam, tigecycline	Blood: negative
58	Discharge	Minocycline, sulfamethoxazole/trimethoprim	Blood: negative

He developed severe hypoxemia on the 6th day of admission (PaO2/FiO2 = 170 mmHg). Invasive mechanical ventilation and empirical antibiotics were applied. He improved promptly and was liberated from mechanical ventilation three days later. Antibiotics were adjusted throughout his admission course according to his microbiology studies and clinical conditions of recurring spiking fever and jaundice. Elizabethkingia meningoseptica bacteremia ensued on the 23rd day of admission and remained positive until the 31st day.

He complained about lower back pain and abnormal ALP ranging from 110-220 U/l persisted. It raised the doubt about unresolved infection foci. A spine MRI revealed an abnormal enhancement in T2-weighted images, suggestive of osteomyelitis, at L3-4 endplates. A 14-day course of cefoperazone/sulbactam and tigecycline was administered. Subsequent blood cultures yielded no positive results. The antibiotics were changed to oral minocycline and sulfamethoxazole/trimethoprim, and he was discharged. The oral antibiotics were continued for four months in the outpatient department until the erythrocyte sedimentation rate declined to be within normal limits.

E. meningoseptica septicemia and osteomyelitis, although uncommon, is highly resistant to antibiotics and carries a high mortality risk. Imprudent use of broad-spectrum antibiotics expands multi-drug resistant strains and predisposes the patients to secondary bacterial infections. The usefulness of procalcitonin as an indicator for bacterial septicemia to guide antibiotics therapy was compromised in cytokine storms of severe COVID-19. Judicious use of antibiotics is suggested to avoid the expansion of multi-drug resistant pathogens, and agile microbiological study is advised if clinical clues of sepsis arise.