Antibiotic Stewardship During A Viral Pandemic

What is a co-infection, secondary infection or superinfection?

- A co-infection is an infection concurrent with the initial infection whereas a superinfection/secondary infection occurs following a previous infection especially when caused by microorganisms that are resistant or have become resistant to the antibiotics used earlier. The difference is temporal.
- Studies have shown that up to 65% of laboratory-confirmed cases of influenza infection are complicated by bacterial co/superinfections with the majority ranging between 11% and 35% in a meta-analysis. Secondary infections following respiratory viral illnesses most commonly involve the lower respiratory tract, with Streptococcus pneumoniae, Haemophilus influenzae, and Staphylococcus aureus being the most frequently reported pathogens.
- Superinfections and coinfections can augment pathogenesis, increasing the morbidity and mortality of viral infections. In fact, the majority of deaths associated with the Spanish influenza pandemic of 1918 were not thought to be caused by the H1N1 virus itself, but rather by secondary bacterial pneumonia. The relatively high incidence of severe infection and mortality in COVID-19 is thought in part due to secondary infections, alongside lack of natural immunity and viral replication in the lower respiratory tract leading to severe lung injury and acute respiratory distress syndrome.

What are the rates of co-infection/superinfection with COVID-19?

- Very difficult to discern from the emerging data due to variable population data as well as testing and diagnostic capabilities. Notably, there is a desire to avoid invasive diagnostic procedures such as bronchoscopy and

radiologic imaging such as computed tomography (CT), in order to minimize aerosol-generating procedures and healthcare worker exposure. This has created a somewhat unique diagnostic challenge in assessing and managing secondary infections relative to other respiratory viral illnesses.

- *Co-infection rates appear to range from around 8% to just over 20%.*
- Secondary infections are reportedly common in hospitalized, severely ill COVID-19 patients, encompassing between 10%-30% of cases with much greater frequency in the ICU setting.
- Patients with severe illness are much more likely (10x) to have bacterial/fungal secondary infections than viral (2x).
- ICU patients with prolonged illness/intubation have more frequent detection of multidrug-resistant Gram-negative pathogens, likely reflecting hospital-acquired infection.
- Recent limited observations suggest that coinfections in COVID-19 patients are more frequently viral than bacterial, and rates of viral coinfections in COVID-19 illness are consistent with what is seen with other respiratory viral illnesses. The difference is with severe COVID-19 infections where the likelihood of a bacterial superinfection is 10x higher than with non-severe infections.

What about antibiotic use during the COVID-19 pandemic?

- Among patients hospitalized in metropolitan New York with COVID-19, treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality.
- A recent review of COVID-19 studies published since the pandemic began found that while 8% to 21% of COVID-19 patients had documented bacterial co-infections, 72% had received antibiotic therapy.
- While the use of Azithromycin and other antibiotics has gone up significantly in hospitalized patients with respiratory symptoms, the overall use of antibiotics is down because of the temporary halt in elective procedures.

Clinical Pearls:

- Just as any other time:
    - Viral pneumonia - insidious onset, normal WBC count with a higher lymphocyte fraction, more rhinorrhea, lower serum creatinine, procalcitonin <0.25, ground-glass appearance and/or bilateral lung findings on CXR
    - Bacterial pneumonia - leukocytosis, elevated procalcitonin, rapid onset of symptoms, more often with a fever, unilateral lung findings
- If someone is COVID-19 positive or presumed positive consider keeping them in the nursing home under isolation precautions as this will reduce their risk of bacterial superinfections. As always this needs to be in line with their goals of care.
- For nursing home patients, regimens for HCAP pneumonia with COVID-19 to consider are: azithromycin and a cephalosporin such as cefuroxime. Doxycycline plus amoxicillin/clavulanate or levofloxacin alone, taking into account side effect profile and individualized patient care.
- Finally, one of the hardest things to do in medicine is nothing, even when nothing is the right thing. We all want to help so the impulse to treat with antibiotics is understandable, but remember that multidrug resistant organisms are growing while the antibiotic pipeline is shrinking and a recent task force from the CDC revealed this problem is getting worse, not better. The feeling you have when treating a COVID-19 patient and there is nothing you can do is a feeling we may all feel more often with bacterial infections if we don't continue to be diligent with our stewardship efforts.

References:

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