Initial Investigations:
- CT chest R/O PE
- Sputum, blood cultures and others as appropriate
- Consider TTE (MIS-A, CHF)
- Consider CT abdo (bowel perforation related to toc/corticosteroids)

Note: inflammatory markers (CRP/ESR) and possibly procalcitonin may be suppressed by tocilizumab and similar drugs for several weeks

Assessment for Uncommon Causes:
- Consider overall degree of immunosuppression, including COVID-19 therapies (tocilizumab, steroids)
- Travel history, risk of tropical illness/TB exposure
- Ensure HIV status documented

Treat Common Causes if Found:
- PE --> anticoagulation
- Pneumothorax or effusion --> chest tube
- Volume overload or CHF --> Diuresis
- HAP/VAP --> antibiotics

At Risk for or Clinical Imaging Features Suggestive of Less Common Secondary Causes/Infections,/*/**: including:
- Immunosuppression outside of therapies for COVID (e.g., transplant status, extended immunosuppression)
- Latent parasitic infections: eosinophilia may be masked by steroids
- Polymicrobial bacteremia may be suggestive of Strongyloides hyperinfection
- Previous radiologic evidence of TB infection, or clinical/social history suggests increased risk TB exposure
- Strongyloides serology
- Stool tests for strongyloides

Further Investigations for Uncommon Secondary Infections/ Initial Investigations Inconclusive +/- Consultation with ID/ Respiratory
- Sputum for AFB/mycobacterial culture
- Bronchoscopy – BAL for bacterial culture, PJP PCR, BAL galactomannan, mycobacterial culture, fungal culture, cytology
- Strongyloides serology

Many patients may simply be observed with continued supportive care if the treating team has determined the likelihood of a less common secondary cause to be low probability.

Potential Empiric Therapies Pending or Inconclusive Results in Consultation with Appropriate Services:
- Reinstitution/escalation of steroids for COP
- Reduction of immunosuppression (e.g. transplant, suspected secondary infection)
- Empiric antifungals (CAPA) or ivermectin (strongyloides)

Differential Diagnosis

Common:
- Ongoing/unresolved COVID pneumonia/cryptogenic organizing pneumonia (COP) - similar clinical and radiographic findings
- Pulmonary embolism (PE)
- Hospital or ventilator acquired pneumonia (HAP/VAP)
- Pleural effusion, pneumothorax
- Congestive heart failure (CHF)

Less Common:
- Multisystem Inflammatory Syndrome (MIS-A)/cardiac involvement
- Progressive pulmonary fibrosis or necrosis
- CAPA (COVID associated pulmonary aspergillosis)*
- Pneumocystis jiroveci (PJP)
- Tuberculosis (TB)
- Strongyloides hyperinfection**
- Pulmonary hemorrhage

Rare:
- Drug-related lung injury
- *Confronting and mitigating the risk of COVID-19 associated pulmonary aspergillosis (CAPA) https://erj.ersjournals.com/content/early/2020/07/09/13993003.02554-2020
- **COVID-19 and Dexamethasone: A Potential Strategy to Avoid Steroid-Related Strongyloides Hyperinfection https://jamanetwork.com/journals/jama/fullarticle/2769100

Created by the B.C. COVID-19 Therapeutics Committee and reviewed by expert clinicians. This is meant as a diagnostic aid based on expert opinion. Empiric therapies for suspected secondary causes should be guided by appropriate service consultation and shared decision making when possible.