COVID -19 – For the Hematologist and those who care for SCD patients

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SCD and COVID-19: No mention in the literature

TABLE 5. INFECTIOUS PATHOGENS ISOLATED IN 671 EPISODES OF THE ACUTE CHEST SYNDROME.*

PATHOGEN	NO. OF EPISODES
Chlamydia pneumoniae	71
Mycoplasma pneumoniae	51
Respiratory syncytial virus	26
Coagulase-positive *Staphylococcus aureus*	12
Streptococcus pneumoniae	11
Mycoplasma hominis	10
Parvovirus	10
Rhinovirus	8
Parainfluenzavirus	6
Haemophilus influenzae	5
Cytomegalovirus	4
Influenza A virus	4
Legionella pneumophila	4
Escherichia coli	3
Epstein–Barr virus	3
Herpes simplex virus	3
Pseudomonas species	3
Adenovirus	2
Branhamella species	2
Echovirus	2
Beta-hemolytic streptococcus	2
Mycobacterium tuberculosis	2
Enterobacter species	1
Klebsiella pneumoniae	1
Mycobacterium avium complex	1
Salmonella species	1
Serratia marcescens	1
Total	249

But we know viruses pre-dispose SCD patients to ACS

Vichinsky EP, et al. NEJM 2000; 342(25):1855-65

SCD and Influenza/H1N1

- Influenza in SCD – increased risk for hospitalization and ACS
- H1N1 – Case series suggested an increase in ACS, particularly in adults
- Retrospective chart review of 123 SCD patients with Influenza (94 Influenza A or B, 29 H1N1):

H1N1 influenza: Increased ACS (ACS; 34% vs 13%, *P* = .01), ICU admissions (17% vs 3%, *P* = .02) and mechanical ventilation (10% vs 0%, *P* = .02)

Strouse JJ, et al. Blood 2010; 116(18): 3431–3434.
Bundy DG, et al. Pediatrics 2010;125(2):234-43.

COVID-19: Risk for Severe ACS

- High risk for severe ACS - >50% FiO2, need for intubation
- Multi-organ system failure
- Rapidly progressive ACS: Highest risk in those with PH, multi-lobar disease, and thrombocytopenia

Rapidly Progressive ACS

- Retrospective cohort analysis to try to differentiate those with ACS who developed respiratory failure within 24 hours
- 173 patients – 97 < 20 yrs and 76 were adults
- In adults, those with rapidly progressive ACS:

1) AKI (68.8% vs. 3.3%, $P < 0.001$)
2) Hepatic dysfunction (75.0% vs. 15.0%, $P < 0.001$)
3) Altered mental status (43.8% vs. 11.7%, $P < 0.001$)
4) Multi-organ failure (93.8% vs. 10%, $P < 0.001$)
5) Death (6.3% vs. 0%, $P = 0.05$)

In multi-variate analysis, thrombocytopenia was only predictor of rapidly progressive ACS [odds ratio 4.82 (95% CI 1.20-19.39), $P = 0.027$]

Chaturvedi S, et al. Am J Hematol. **2016** Dec;91(12):1185-1190

Diagnosing Fat Emboli Syndrome

Major Criteria

- **Respiratory Distress**
- **Cerebral involvement**
- **Petechial Rash**

Diagnosis: 2 major criteria or 1 major criteria and 4 minor criteria

Minor Criteria

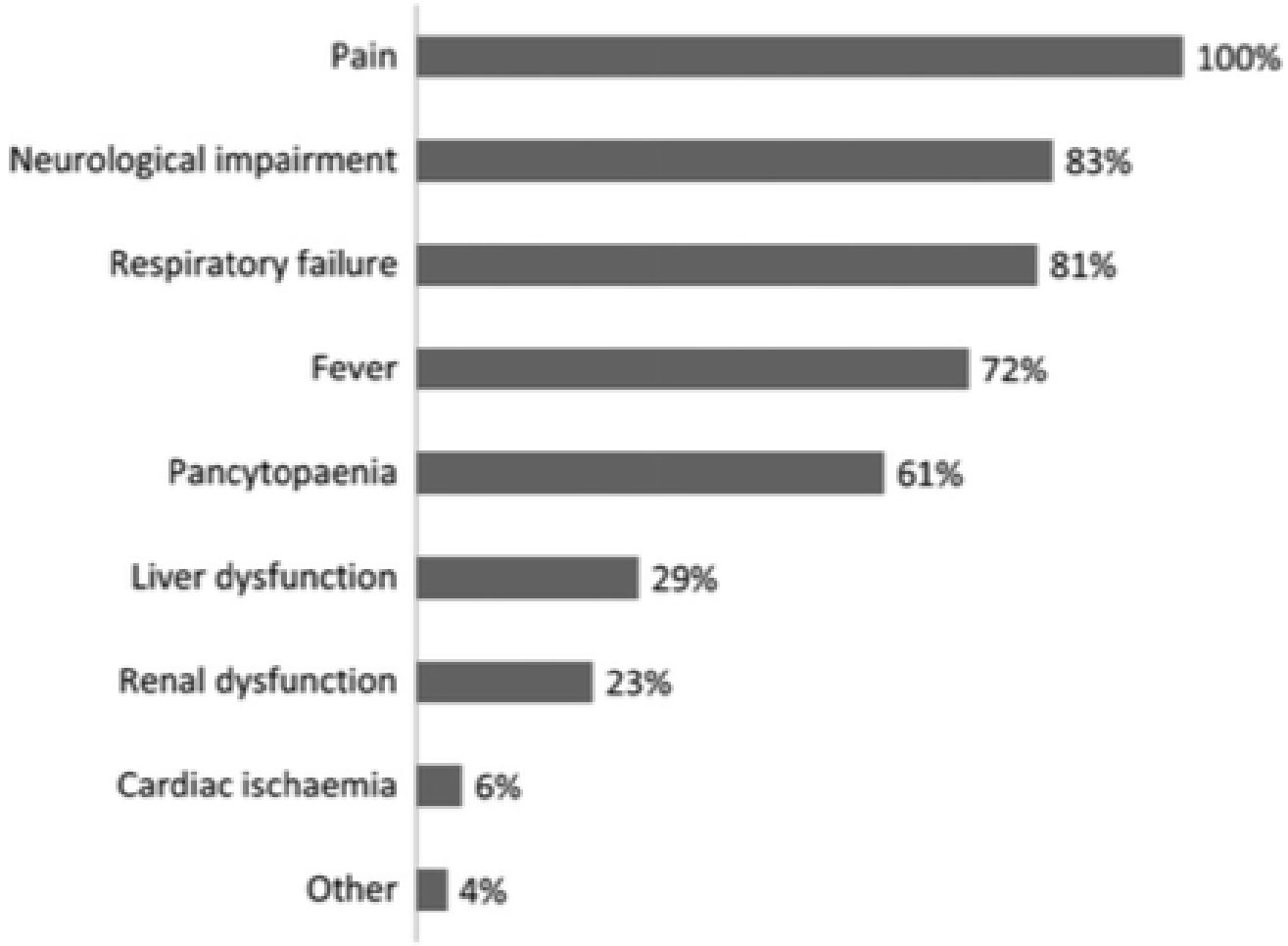
- Tachycardia (HR > 110 bpm)
- Fever (>38.5 C)
- Jaundice
- Renal Changes
- Retinal changes
- Drop in hemoglobin (> 20%)
- New onset thrombocytopenia (> 50%)
- Elevated ESR (> 71 mm/h)
- Fat macroglobulinemia

Fat Emboli Syndrome

- Rare, most of what is known is limited to small case series
- Pathophysiology – unclear
- Breakdown of fat within pulmonary vasculature leads to release of FFAs – sepsis, acute lung injury/pulmonary edema and hypoalbuminemia
- More common in HbSC than HbSS – Higher Hb is a risk factor
- Labs – None specific – worsening anemia, hemolysis, thrombocytopenia, hypoalbuminemia
- BAL – Fat laden macrophages >30%

Greaves P, et al. Clin Case Reports 2017; 5:39-43.
Bailey K, et al. J Intensive Care Med 2017 doi: 10.1177/0885066617712676

Clinical Characteristics of Fat Emboli Syndrome



Tsitsikas DA, et al. Blood Rev 2014; 28:23-30.

Fat Emboli Syndrome in SCD

- 1st described by Wade and Stevenson in 1941
- Bone Marrow necrosis, mobilization of BM – pulmonary vasculature
- Fat emboli – pulmonary micro-circulation, systemic vasculature
- No definitive way to make diagnosis – Classic triad: petechial rash, pulmonary edema and CNS depression – but all 3 don't need to be present
- Usually presents with a rapidly progressive course – mortality rates >60% in 1st 48 hours

Targueta EP, et al. Autopsy Case Rep 2017;7:42-50
Bailey K, et al. J Intensive Care Med 2017 doi: 10.1177/0885066617712676.

Treatment of Fat Emboli Syndrome

- Treatment is supportive
- Exchange transfusion associated with reduced mortality – 29% vs 91% in non-transfused
- Traditional treatment for ACS – antibiotics, bronchodilators
- Use of steroids – controversial

Protocol version 2020_3_14

COVID treatment protocol

- **No steroids for mild/moderate sickness**
- **Avoid Nebs**
- **Steroid use should be a discussion between ID and Pulmonary/Critical Care**

All Persons Under Investigation

Contact/Droplet Precautions
Comprehensive Respiratory Panel *
COVID-19 PCR*
Sputum Cultures*
MRSA Nares*
Procalcitonin
G6PD
Imaging: CXR, EKG
Continuous Pulse OX

***NOTE: N95 respirator specimen collection. Collect all at same time to minimize exposure**

Temp > 101F AND O2 sat <90%

Start Hydroxychloroquine
Trend QTc qD
Trend Glucose qD

COVID PCR Negative AND Alternative Diagnosis

Stop Hydroxychloroquine

COVID PCR Positive

Call Infectious Diseases
Continue Hydroxychloroquine
Request Remdesivir through online portal:

https://rdvcu.gilead.com

BOSTON MEDICAL CENTER
EXCEPTIONAL CARE. WITHOUT EXCEPTION.

Hydroxychloroquine dosing:
400mg BID first day then
200mg BID for 4 days (total 5d)

Remdesivir dosing:
200mg first day then
100mg daily for 4 days (total 5d)

How to approach the SCD patient hospitalized with COVID-19 symptoms?

- Test everyone if possible
- Depending on where you are at, results may take several days to return
- CXR on admission for everyone with VOC or symptoms of COVID-19
- At BMC, we are going to repeat CXR 48 hours post-admission if test is positive or not back yet

Things to consider in management

- General respiratory measures for infected patients are to avoid aerosol-based interventions.
- Nebulizers should not be used in a non-negative pressure room, instead use
- metered-dose inhaler for Albuterol
- No non-invasive ventilation or high flow oxygen, or bronchoscopy on the general floors; should only be done in negative pressure rooms
- Non-invasive oxygen therapy should progress to intubation to limit aerosolization and infection risk.

ACS Management in COVID-19

- Early exchange transfusion
- Echocardiograms – Likely will have RV dysfunction/elevated PA pressures, can be transient. Inhaled NO helpful?
- Broad spectrum antibiotics – include MRSA coverage, atypicals, pneumococcus
- May be some benefit of plasmapheresis
- Stop L-glutamine in critically ill patients

- Randomized placebo controlled trial of 1223 patients with multi-organ system failure treated with L-glutamine (0.35 mg/kg), anti-oxidants or placebo
- Trend toward increased mortality at 28 days among patients who received glutamine as compared with those who did not receive glutamine (32.4% vs. 27.2%; adjusted odds ratio, 1.28; 95% confidence interval [CI], 1.00 to 1.64; P=0.05). In-hospital mortality and mortality at 6 months were significantly higher among those who received glutamine than among those who did not. Glutamine had no effect on rates of organ failure or infectious complications

Heyland D, et al. NEJM 2013 Apr 18;368(16):1489-97.

Medical ICU Management of COVID-19 at BMC

- Centralization of ICU care – 1 of the 3 MICU teams will have the majority of patients until census is too high
- Patients will be in negative pressure rooms
- No BiPAP, no nebulizers, early intubation for all
- May need inhaled NO to improve oxygenation
- ARDS Management – low VT ventilation, proning, fluid management (keep patients dry)
- ECMO

Final Thoughts

- Landscape is constantly changing
- What I say today may be wrong next week
- Things we don’t know- NSAIDs, ACE inhibitors/ARBs, does exchange transfusion do anything