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A covid-19 clinical case: Golden lessons and tips for improving clinical practice and outcome

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Abstract

Currently, the management of covid-19 infection remains mostly empirical. We describe the presentation, progress and management outcome of a middle-aged diabetic man with acute Covid-19 infection. His illness was marked by the development of respiratory failure and pulmonary embolism despite guideline-based prophylactic anticoagulation. His illness highlighted the major pathophysiologic manifestations as well as the phasic nature of this novel infection. The patient was discharged well after a 16-days stay in the hospital. At least 10 lessons were learnt from this interesting case.

Keywords

Covid-19 infection; clinical phases; therapy.

Introduction

Since its first case was discovered in Wuhan, China in December 2019 [1], the Covid-19 pandemic has devastated healthcare systems worldwide with an associated significant detrimental impact on populations and societies. More than 115 million people got infected as of March 3, 2021, with at least 2.5 million deaths [2]. The negative impact of this novel infection on healthcare systems has spilled to other systems as well impacting state economies, entertainment industry, transport, education, etc. The management of acutely infected patients remains mostly empirical with few evidence-based interventions [3,4].

In this case report, we are aiming to highlight important pathophysiologic mechanisms determining disease behavior and clinical manifestation and their implications in patient monitoring and treatment. We envisage that lessons learned from this case will empower the readers with the critical domains necessary for transforming the current practice of caring for Covid-19 infected patients (including prevention) as well

as enlighten and galvanize them to employ the current "best available literature evidence" for reducing ICU admissions and death.

Case Report

History: A 65-year-old male, a known case of type 2 Diabetes mellitus (latest A1C 11.8) and dyslipidemia presented to the emergency department with a sore throat, persistent dry cough, recurrent fever and chills, and poor oral intake of 4 days duration. He denied contact with a sick patient. Over the previous 24 hours, fever pattern became continued and was associated with shortness of breath and two episodes of watery diarrhea. He had been a non-smoker and denied alcohol intake or recreational drug use. There was no history of recent travel. His medications consisted of: Degludec and Aspart insulins, Semaglutide, Empagliflozin, Metformin, Rosuvastatin and vitamin B1,B6, and B12 combination. He had no known allergies.

On examination, the patient was alert, oriented to time place and person, and was not in pain or distress. His body mass index was 26.5 Kg/m^2. His had a pulse rate of 86 per minute regular, blood pressure of 111/62 mm Hg, respiration rate of 20 per minute, temperature of 37.9 Celcius, and oxygen saturation of 96% while breathing ambient air. Systemic examination was unremarkable except for bilateral basal crackles.

Investigations: A nasopharangeal sample for SARS-CoV-2 by RT-PCR returned a positive result. A chest x-ray confirmed the presence of bilateral interstitial basal and peripheral lung infiltrates consistent with viral pneumonia (Figure 1).

Complete blood count, differential leucocyte count, liver function, and urinalysis were negative while urine and blood cultures were negative.

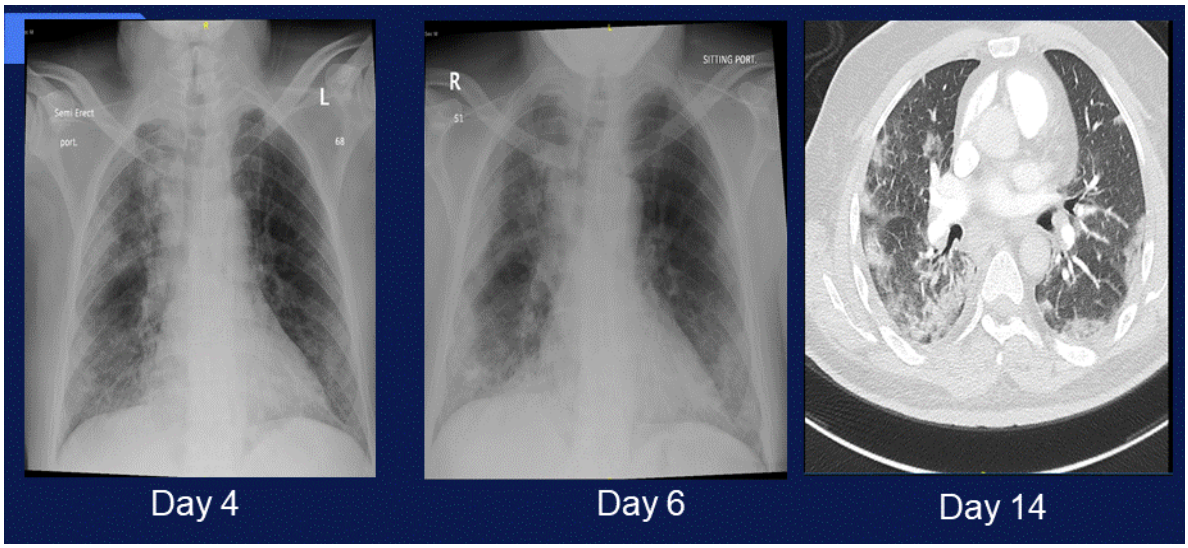

Figure 1: Chest-x-rays and a slice of CT Chest confirming bilateral mainly basal and peripheral interstitial infiltrate.

Table 1: Initial Investigations

Test	Result (Reference Range)
COVID-19 PCR	POSITIVE
AGAP	25 (7-15 mmol/L)
Creatinine	116 (64-110 umol/L)
BUN	5.6 (3-9.2 umol/L)
HCO3-	13 (23-31 mmol/L)
eGFR	58
Glucose	7.4 (3.9-7.7 mmol/L)
Zinc Level	10.43 (10-16 umol/L)
UA Glucose	>=1.000 mg/dL
UA Ketones	Negative
VIT-D 25 OH	36.8 (50-125 nmol/L)
Adjusted Calcium	2.07 (2.2-2.5 mmol/L)
PTH	11.830 (1.5-7.2 pmol/L)
ESR	89 mm/hr (0-20)
Ferritin	566.6 (21.8-274.6 ug/L)
LDH	351 (125-220 U/L)
PCT	0.15 (<0.08ng/ml)
CRP	98 (< 7 mg/L)
Lactic Acid	2.94 (0.5-2.2 mmol/L)
Fibrinogen	5.47 (1.5-4.1 gm/L)
D-Dimer	0.47 (0-0.5 mg/L)

Table 2: Diagnostic Labelling and the Immediate Therapeutic Plan.

1. Bedside-Clinical Diagnosis	Community-Acquired Pneumonia
2. Etiology	Covid-19
3. Severity	CURB-65= 1, 4C Mortality Score: 8 (intermediate risk, 9.1-9.9% in-hospital mortality) https://www.mdcalc.com/4c-mortality-score-covid-19
4. Problem List	Vitamin D Deficiency, Increased Inflammatory Markers, Lactic Acidosis, Renal Impairment, Poorly Controlled Diabetes Mellitus
5. Site of Care	General Ward (Negative Pressure Room)
6. Symptomatic	Anti-pyretic (Acetaminophen) Antitussive (Dextromethorphan)
7. Supportive	Anti-pyretic (Acetaminophen) Antitussive (Dextromethorphan) Intravenous Fluids Enoxaparin 40 mg Subcut OD Aspirin 81 mg OD Vitamin C 100 mg daily, Vitamin D 50,000 units weekly, and Zinc 100 mg daily
8. Specific	Antibiotics: Ceftriaxone and Azithromycin
9. Specialty Referral	Infection Control Team Infectious Diseases Consult

Diagnosis and immediate treatment

Using an evidence-based approach that will facilitate a comprehensive management plan [5], a diagnostic label and important therapeutic interventions were documented as per Table 2.

Community-acquired pneumonia cover was started as per the hospital's clinical pathway. Vitamins C and D were prescribed as immunostimulants together with Zinc.

Prophylactic Enoxaparin and Aspirin were started because of the known hypercoagulability associated with Covid-19.

Progress

Over the ensuing 4 days, the patient continued to spike temperature. Additionally, a repeat chest x-ray confirmed a progressive increase in his pulmonary shadowing (Figure 1). His saturation on room air ranged between 93-95%. His major symptom was a troublesome dry cough which was helped by Dextromethorphan. On direct questioning, he denied any breathlessness. Clinically, his auscultatory findings were unchanged. An arterial blood gas analysis confirmed Type 1 respiratory failure with PaO_2 of 57.4 mmHg, $PaCO_2$ 31.2 mmHg, pH 7.45, bicarbonate 21 mmol/L, base excess (BE) 1.4, and P/F Ratio (PaO_2/

FIO_2) of 273.5.

Furthermore, his procalcitonin, CRP, and d-Dimer continued to increase (Table 3, Graph 1). Dexamethasone was started and antibiotics were changed to Tazocin (Piperacillin/Tazobactam 4.5 gm 8 hourly) and PO Doxycycline 100 mg twice per day. On Dexamethasone, his glucose readings were uncontrolled. These were managed employing the hospitals, Bolus Basal Insulin regime.

By day 14, CRP and procalcitonin had almost normalized. Surprisingly, his d-Dimer continued to increase (Graph 1). Ultrasound doppler of both lower limbs was negative for deep venous thrombosis. However, a computerised pulmonary angiogram confirmed the presence of a sub-segmental pulmonary embolism. He was shifted to therapeutic dose Enoxaparin that was later converted to Apixaban, a novel oral anticoagulant. Anti-cardiolipin antibody (Antiphospholipid Antibody) ACA IgM was POSITIVE!
He was discharged home well on day 16 of admission.

Table 3: In-patient Progress.

Day 1	Day 5	Day 6	Day 7	Day 14	Day 16
• Admission • Enoxaparin 40 mg Subcut OD • Aspirin 81 mg OD • Vitamin C 1000 mg OD, Vitamin D 50,000 units weekly, and Zinc Sulphate 100 mg OD • Ceftriaxone 1 gm OD and Azithromycin 500 mg OD • Serial CRP, d-Dimer, Procalcitonin • CRP 98 on admission	Worsening Chest x-ray Sats RA 93-95% ABG Type 1 Respiratory Failure	Increasing CRP, Ferritin, D-Dimer, and Procalcitonin Fever subsided.	Significant improvement of CRP, Procalcitonin, and d-Dimer	Significant improvement /normalization of CRP, Procalcitonin but increasing d-Dimer PE on CTPA	Improved d-Dimer. Steroids stopped.
	Dexamethasone Started	Shifted to Tazocin 4.5 gm 6 hourly & Doxycycline 100 mg orally 12 hourly Both given for 7 days.		Shifted to Therapeutic Dose Enoxaparin	Discharged
	CRP 143 on Day 5 Procalcitonin 241.7	CRP 152 on Day 6 Procalcitonin 99.1	CRP 76 on Day 7 Procalcitonin 41.0	CRP 6 on Day 14 Procalcitonin 0.35	CRP 5, Procalcitonin 0.19 on Day of discharge (Shifted to Apixaban in OPD)
	Minimal clinical issues (No dyspnea, Chest pains, or Fever). Major issues were troublesome dry cough– managed with dextromethorphan -and later on, steroid-induced hyperglycemia.				

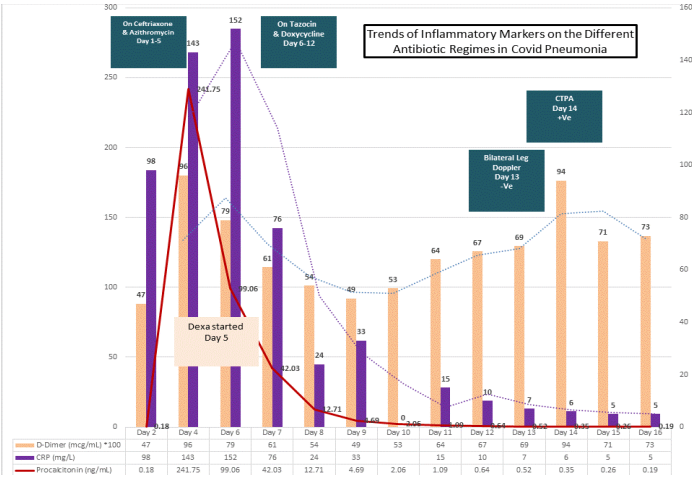

Figure 2: Trends of Inflammatory Markers on the Different Antibiotic Regimes in Covid-19 Pneumonia. Case.

Discussion & Lessions

This fairly common presentation and progress of a Covid-19 case allowed us to learn at least 10 lessons.

1. Curb-65 Score for community-acquired pneumonia does not apply to Covid-19 pneumonia! According to this scoring tool, this patient would have been managed at home! Instead, new scoring tools for severity assessment are needed. An example is the one we used: 4C Mortality Score: 8 (intermediate risk, 9.1-9.9% in-hospital mortality) https://www.mdcalc.com/4c-mortality-score-covid-19 ISARIC Coronavirus Clinical Characterization Consortium (ISARIC-4C).

His mortality score was worryingly high but thankfully he recovered from his illness.

2. Azithromycin (with Ceftriaxone) is not a useful agent for COVID-19. This patient's inflammatory markers continued to worsen on this regime. Azithromycin ineffectiveness was recently confirmed in a randomized study [6].

3. Pulse Oximetry may be misleading as a sole tool for assessing for hypoxemia especially at saturations above 92% [7]. This is not a new fact and overreliance on pulse oximetry may delay the initiation of steroids in these patients. "Pulse oximetry should not replace analysis of an arterial blood gas sample in the clinical evaluation of oxygenation in emergency patients" [7].

4. Covid-19 pneumonia has this peculiar phenomenon of " Silent Hypoxia" i.e. severe hypoxia with no increased work of breathing or symptoms especially in the older patient [8]!

5. Regular dose prophylactic anticoagulation is not always enough in Covid-19 infection! Several papers and authorities recommend higher or doubling the prophylactic dosing in these patients taking into consideration the patient's risk of bleeding [9].

6. Serial d-Dimer (and CRP) tests are essential for inpatient monitoring [10]! In our patient, monitoring his d-Dimer enabled us to discover the development of thromboembolism (despite his prophylactic enoxaparin). He remained well despite pulmonary embolism. His repeat arterial blood gas was actually improved to PaO_2 of 70 mmHg! The clinical team must have a high index of suspicion for the presence of deep venous or pulmonary embolism and investigate urgently e.g. if a sudden worsening in gas exchange occurs, or if D-dimers remain elevated (if unexplained) or show a progressive rise. A rising d-Dimer with improving CRP is an indication/ marker of active thrombosis! In our patient his Immunoglobulin M anticardiolipin antibody was positive Development of the Antiphospholipid antibodies is a recognized complication of Covid-19 infection [11].

7. Covid-19 infection is a "Phasic Disease" [3,12]: Close monitoring and stage-specific interventions are mandatory! The acute infection phase is usually followed by a hyperinflammatory phase followed or accompanied by a hypercoagulable phase (Figure 3). Non-timely or delayed stage-specific therapeutic interventions worsen the outcome: e.g. early steroid therapy or delayed antiviral therapy.

8. Current evidence suggests that Vitamin D [13,14] and Doxycycline [15-17] have antiviral and anti-inflammatory properties that may enhance patient recovery. Vitamin D in daily high-dose was shown to reduce viral shedding, improve outcome and may reduce intensive care admissions [18-20]. Vitamin D deficiency (as seen in our patient) predisposes to Covid-19 infection and pre-exposure replacement may be a reasonable preventative strategy [21].

9. In addition to steroids [22] and vitamin D specially if given in regular daily dosing [18-20], Aspirin therapy [23] may also reduce intensive care admissions, a very important aim of any Covid-19-directed intervention especially in resource-poor countries where intensive care beds are a luxury.

10. A final and important lesson we learned from our Covid-19 case is to have a very open-mind in caring for these patients. It is crucial, with this novel infection, to apply interventions based on the important principle of evidence-based practice and that is "using the best available research evidence and not delaying interventions awaiting results of randomized studies."

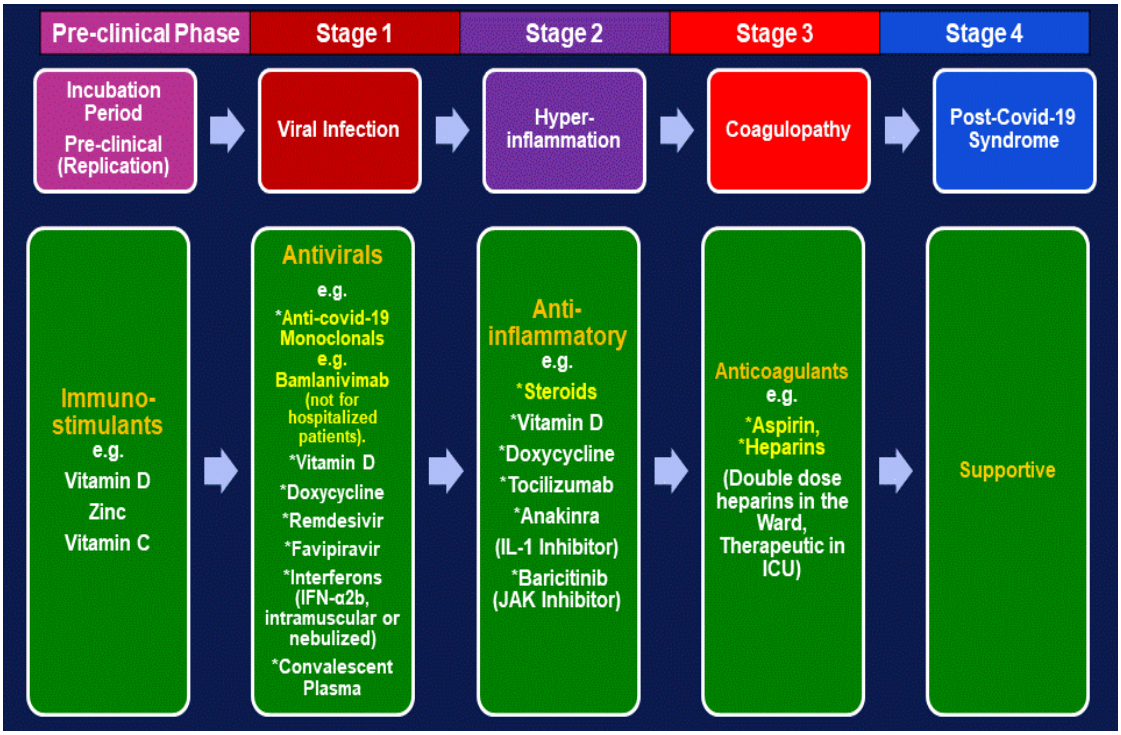

Figure 3: The different Phases of Covid-19 Infection and Proposed Interventions. [3,4,24].

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