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Case Report

Outcome of Cerebral Venous Thrombosis in a Critically Ill CoVID-19 Infected Patient: A Case Report

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Abstract

Human coronavirus disease, a mild to severe pulmonary or respiratory infection caused by the novel SARS-CoV2 or CoVID-19 manifests with other multiple clinical conditions including acute cerebrovascular insults in the form of arterial and venous thrombosis. Here we report a young critical case of CoVID-19 associated cerebral venous thrombosis (CVST), admitted in ICU with ARDS, CoVID-19 positive by PCR and who suddenly developed recurrent seizures. CT-brain revealed extensive acute venous thrombosis involving superior sagittal sinus and adjacent cortical veins, right transverse and sigmoid sinuses and right jugular bulb. Laboratory abnormalities at presentation included considerable elevation of CRP, D-Dimer, ESR, LDH and Ferritin but with no change in activated partial thromboplastin time and prothrombin time. The patient received antibiotics, anticoagulants, and antiviral/steroid therapy that significantly improved his lymphocyte to neutrophil ratio and was discharged after 29-days stay in the hospital. This case highlights the need for awareness about atypical presentation of CVST in CoVID-19 and early intervention with anticoagulants for improved outcome.

Keywords: CoVID-19; Cerebral venous thrombosis; ARDS; Bilateral air space disease

Abbreviations: SARS CoV: Severe Acute Respiratory Syndrome Coronavirus; CT: Computerized Tomography; CVST: Cerebral Venous Sinus Thrombosis; ARDS: Acute Respiratory Distress Syndrome; WHO: World Health Organization; ICU: Intensive Care Unit

Introduction

Human coronavirus disease caused by the novel SARS-CoV2 or CoVID-19 mainly manifests with mild to severe pulmonary or respiratory symptoms [1-3]. However, various other clinical manifestations have been reported that include neurological and cardiovascular events, coagulopathy and systemic inflammatory cytokine storm among others [4-8]. Recent studies have indicated Cerebral Venous Thrombosis (CVST) as a presenting symptom of COVID-19 infection [9-10]. A systematic review by Tu, et al. described 14 patients world-wide from nine studies with a concomitant COVID-19 infection and CVST including four from the USA, two-each from Italy, France and Singapore, and one-each from the UK, Spain, Iran and China [10].

This is the first critical case of CoVID-19 and CVST who was successfully discharged from the hospital free of CoVID-19 disease. A young CoVID-19 positive patient with no known co-morbidities presented to the Emergency Room (ER) with Acute Respiratory Distress Syndrome (ARDS) subsequently developing recurrent seizures. Early CVST detection and immediate therapeutic intervention with anticoagulants, antivirals, and antibiotics resulted in an improved L/N ratio and therefore, a survival outcome.

Clinical Report

The patient is a 35-year old male presented to the ER with history of cough, shortness of breath, and fever. He was tachypnic (50/min) and hypoxic on arrival. He was started on 10L oxygen (face mask). He developed generalized tonic-clonic seizures in ER and received Keppra, was intubated, mechanically ventilated and shifted to ICU. He was managed as per ARDS protocol with low tidal volume (6 mL/kg body weight) and airway pressures (plateau pressure <30 cm H2O) in addition to prone positioning. Additionally, he received antibiotics, antivirals, steroids for suspected CoVID-19 pneumonia. Chest X-ray revealed extensive bilateral air space disease with significant improvement at discharge (Figure 1a, 1b), and a PCR confirmed CoVID-19 infection from a nasopharyngeal swab. CT brain was done during his ICU stay.

Laboratory findings at presentation (day 0), during the course of disease (day 3) and at discharge are shown (Table 1). C-reactive protein (CRP), D-Dimer, Erythrocyte Sedimentation Rate (ESR), Lactate Dehydrogenase (LDH) and ferritin were all elevated while lymphocyte (L) to neutrophil (N) ratio was very low at presentation (Table 1). There was a significant improvement in L/N-ratio and D-dimer at the time of discharge from the hospital (Figure 1c, 1d).

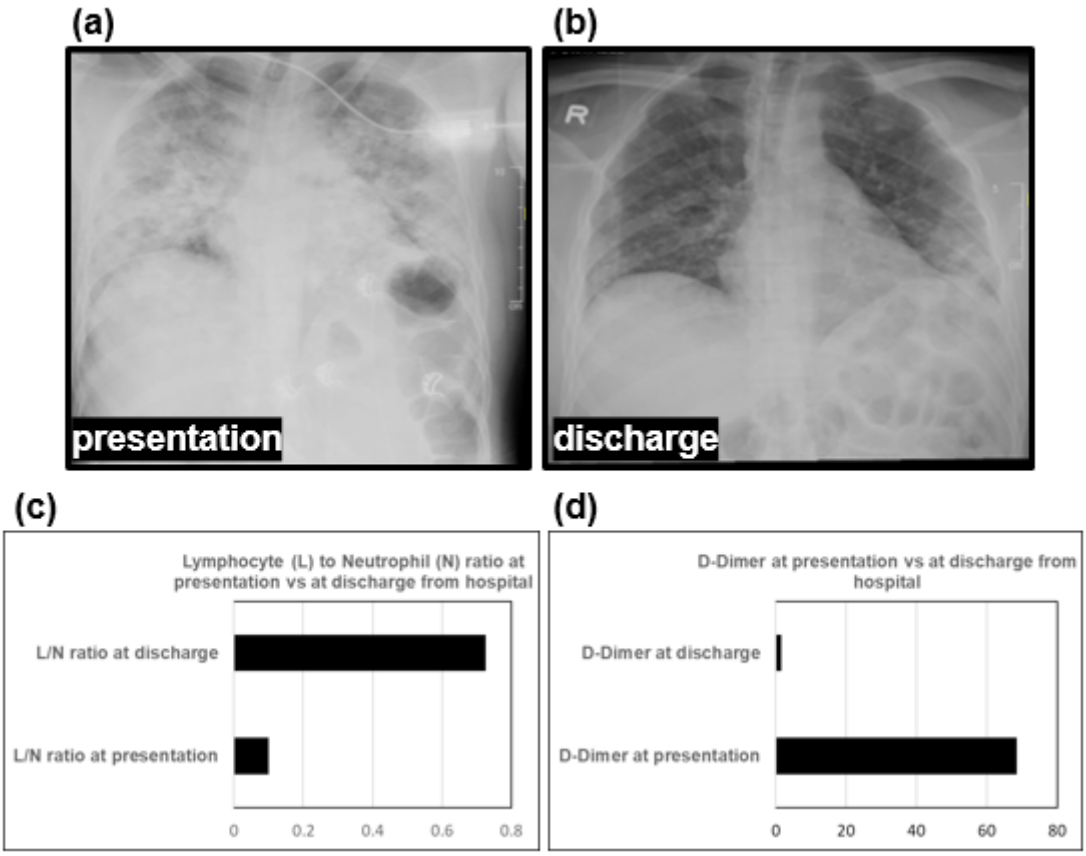

Figure 1: Chest X-ray and laboratory investigations (neutrophils, lymphocytes and D-Dimer) at presentation vs at discharge from hospital: a) Portable chest X-ray images at presentation showing extensive bilateral air space disease vs b) significant improvement at discharge. c) laboratory investigations for lymphocyte (L) and neutrophil (N) showing a very low ratio indicating severity of the disease at presentation vs high ratio indicating clinical improvement at discharge d) laboratory investigations for D-Dimer showing very high level at presentation vs a very low level at discharge.

Laboratory investigation (reference range)	At presentation (day 0)	During infection (day 3)	At Discharge
WBC (4.3-11.3 x 10^9/L)	11.97	16.51	10.69
Neutrophils (30-70%)	**84.5***	89.2	**47****
Lymphocytes (23-60%)	**8.5***	1.5	**34.1****
Eosinophils (1-12%)	0	0	7.1
Hb (11-15 g/dl)	13.8	11.4	12.3
Platelets (155-435 x 10^9/L)	123	156	475
CRP 0 (1-3 mg/L)	**68***	20.8	24.3
APTT (25.3-38.3 s)	32.4	37.3	57.9
D-Dimer (0-0.5 µg/mL)	**68.56***	31.29	**1.59****
Fibrinogen (1.61-4.39 g/L)	3.05	ND	3.65
ESR (0-20)	**41***	70	ND
LDH-(125-220 U/L)	**567***	744	301
Ferritin serum (10-204 ng/mL)	**594.4***	911.3	557.9

WBC: White Blood Cell count; Hb: Hemoglobin; CRP: C-Reactive Protein; APTT: Activated Partial Thromboplastin Time; ESR: Erythrocyte Sedimentation Rate; LDH: Lactate Dehydrogenase; ND: Not Determined.

Table 1: Summary of laboratory investigations at presentation, during hospital stay and at discharge: this table summarizes hematological, biochemical, infectious serology and coagulation factors laboratory at various time intervals. Abnormal values are highlighted bold with asterisk (*) and improved values as double asterisk (**).

Brain CT scan (Figure 2, compare i, iii, v and vii) showed extensive acute venous thrombosis involving superior sagittal sinus and adjacent cortical veins, right transverse and sigmoid sinuses and right jugular bulb suggestive of acute Cerebral Venous Sinus Thrombosis (CVST). Venous infarcts in the parietal and occipital lobes were observed. Brain CT scan at discharge (Figure 2, compare ii, iv, vi and viii) showed partial recanalization of thrombosis and stability of venous thrombosis.

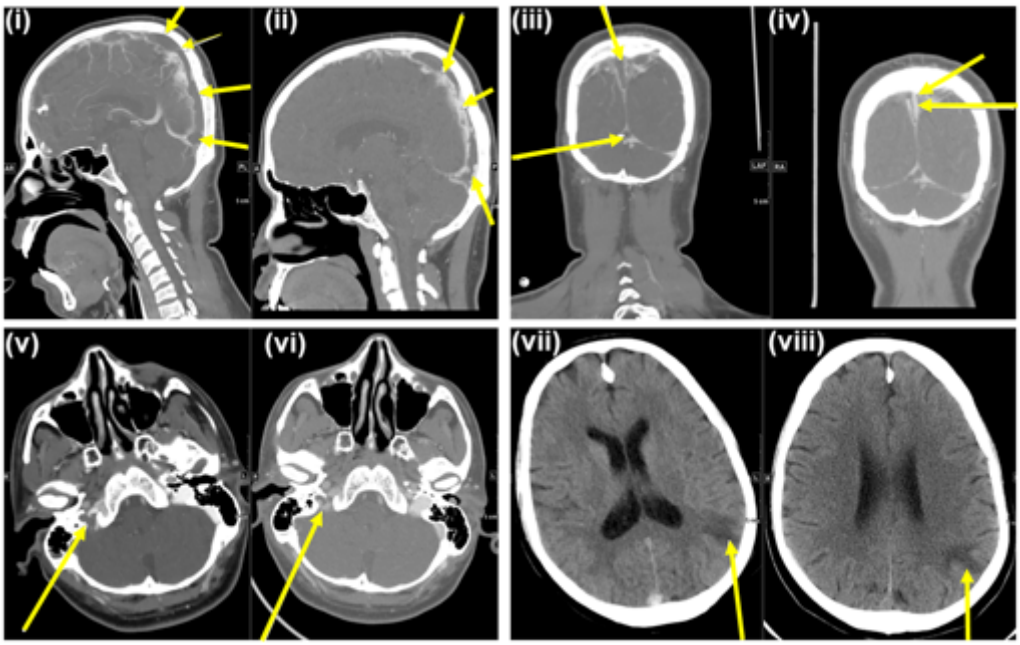

Figure 2: CT brain showing CVST at presentation (i, iii, v and vii arrows) vs no CVST at discharge (ii, iv, vi and viii arrows)d: i) and iii) brain CT scan showing superior sagittal sinus and confluence of sinuses thrombosis with collaterals suggestive of CVST vs ii) and iv) improved CT scan at discharge; v) and vi) brain CT scan showing right jugular bulb thrombosis at presentation vs with partial recanalization at discharge; vii) and viii) left parietal venous infarct at presentation vs at discharge.

Discussion

CoVID-19 infection is a global pandemic that is known to cause ARDS with pulmonary manifestations in the form of bilateral pneumonia and other symptoms. There has been an increase in the number of cases, albeit a few with CVST as a presenting symptom of COVID-19 infection [10]. We describe here a critical case with a concomitant CoVID-19 infection and CVST who was successfully discharged after 29-days of the hospital stay free of disease. This case points to the importance of considering thromboembolic events in CoVID-19 infection by the attending physician, its early detection, and therapeutic intervention for improved outcome.

CoVID-19 infection follows a course ranging from mild to severe to a one that is fatal [3]. The presentation of our case as ARDS in hypoxic state requiring oxygen support with chest X-ray showing extensive bilateral air space disease indicated critical disease in line with the World Health Organization (WHO) disease severity category [11]. Most of the patients with CoVID-19 infection develop either mild or moderate disease with only 15% and 5% presenting with severe and critical disease, respectively [11]. Some of the complications reported for critical patients with CoVID-19 infection include acute cardiac and kidney injury, thromboembolic events and hypercoagulable state [12,13].

Laboratory investigations in patients with COVID-19 infection have revealed multiple abnormalities in hematological, inflammatory, biochemical profiles including liver enzyme and cardiac markers in addition to coagulation profiles [3,7,12,14,15]. Our case showed abnormal laboratory profile with lymphopenia, neutrophilia, elevated CRP, LDH, ferritin and a very high D-Dimer (Table 1) at presentation. Approximately 65% of the patients with CoVID-19 infection show lymphopenia that is reported to correlate with a severe disease course [3,11,16]. It is interesting to note that L/N ratio in our case is significantly low with a concomitant very high D-Dimer at presentation (Figure 1d). A higher N/L (or alternatively low L/N) ratio is associated with an increased risk of venous thromboembolism and increased mortality [16,17].

CoVID-19 infection may induce a pro-thrombotic state such as elevated D-Dimer levels (as in our case) that is a risk factor for CVST [9,10]. CT brain revealed extensive acute venous thrombosis involving superior sagittal sinus and adjacent cortical veins, right transverse and sigmoid sinuses and right jugular bulb suggestive of acute venous sinus thrombosis in our case. CVST is a rare neurovascular and potentially fatal condition with the common symptoms including nausea, seizures, severe focal neurological deficits, coma, and headache [18,19]. Apart from the clinical presentation, the current diagnosis of CVST is mainly

based on the neuro-radiological findings and anticoagulation is the mainstay of treatment for CVST [19].

In the context of CoVID-19, only a few sporadic reports have been published across the globe showing association between CoVID-19 and CVST [10]. This is the first such case from a single center in Saudi Arabia. In a systematic review by Tu, MT et al., the authors have described a series of 14 cases till date with patient demographics, clinical characteristics, pro-thrombotic workup, neuroimaging findings, treatment and outcomes of COVID-19 patients with CVST. The data revealed similar clinical and laboratory characteristics of the reported patients and our case such as middle age group (median 43 years' vs ours 35 years), fever, dyspnea, acute respiratory infection and neurological symptoms viz seizures in addition to raised D-Dimer and CRP levels. However, the clinical outcome of all the critical patients reported with CoVID-19 infection and CVST was death in contrast with our case, who was successfully discharged from the hospital with significantly improved N/L ratio and D-Dimer free of CoVID-19 disease. This improved outcome in our case could be attributed to many factors such as absence of any significant co-morbidities, early detection and early start of anticoagulation/antiviral/steroid therapy, administration route and dosage of the anticoagulants. The two critical cases reported had associated comorbidities, one with autism spectrum disorder [20] and the other with CA prostate and CLL [21] while the third case without any comorbidity did not receive any therapy. The mortality associated with CoVID-19 is higher in patients with comorbidities although more than half of the patients do not have significant comorbidities [16]. Additionally, there is a growing evidence that initial anticoagulant therapy in CVST is beneficial in improving outcome in patients with CVST by facilitating recanalization and preventing thromboembolism [19].

In conclusion, the attending physicians need to be aware about atypical presentation of CVST in CoVID-19 and take appropriate measures for its early detection so that appropriate therapeutic intervention with anticoagulants could be planned for improved outcome of the patients. A more in-depth understanding of CoVID-19 and CVST manifestation, severity, and outcome will become increasingly evident in future reports.

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Authorship List

SM, FA, AW and HS are physicians involved in the clinical management of patients, edited clinical part of the manuscript. Peer-Zada AA performed laboratory data analyses, writing and editing of the manuscript.

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