

Hepatic Sinusoidal Obstruction Syndrome (Veno-Occlusive Disease) Mimicking Hemophagocytic Lymphohistiocytosis in a Post-COVID Patient: A Diagnostic Challenge and Holistic Approach

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INTRODUCTION

Hepatic sinusoidal obstruction syndrome (SOS), also known as veno-occlusive disease (VOD), is a systemic endothelial disorder that typically manifests in the days or weeks following bone marrow transplantation¹, characterized by refractory thrombocytopenia, coagulopathy, hepatomegaly, ascites, and jaundice. It can swiftly progress to multiorgan dysfunction and mortality in 50% of patients. Hemophagocytic syndrome (HLH) in Liver⁴ with other systemic manifestations can also Mimics with similar clinical spectrum at the outset. Rarely, SOS may develop after other liver injuries, necessitating a high index of suspicion for diagnosis and prompt management to mitigate morbidity and mortality. In this case report, we present a unique and challenging case of hepatic SOS in a 48-year-old male following a recent COVID-19 infection such manifestations of COVID induced endothelitis² and VOD were only reported during autopsies of COVID patients as per literature.

CASE REPORT

A 48-year-old male with a history of hypothyroidism was discharged from the hospital after receiving treatment for severe COVID-19 pneumonia, which included tapering steroids and Continued on oral anticoagulants³. Two weeks post-discharge, he presented with persistent fever spikes and tachycardia. Laboratory investigations revealed pancytopenia (Hb 9.8 g/dl, WBC 1400 10³/mm³, platelets 87,000 10³/mm³) along with elevated ferritin of 35,000 (Normal range 23- 336 ng/ml), LDH of 4,320 (Normal range 135 – 225 u/l), AST (281 u/l), ALT (461

u/l), ALP (81 u/l), bilirubin (0.43 mg/dl), and D-dimer of 7,272 (Normal Reference range <250 ng/ml D-DU).

Based on these findings, which included fever, splenomegaly, pancytopenia, high ferritin, and abnormal liver functions, Hemophagocytic Lymphohistiocytosis (HLH) was initially suspected. The patient was promptly transferred to haematology care for further evaluation. Bone marrow aspiration and biopsy showed occasional macrophage activation but less than 10% hence does not qualify for definitive diagnosis of HLH.

Despite this, the patient's liver function deteriorated rapidly within 24 hrs prompting a triphasic CT scan, which revealed hepatomegaly (20 cm) without evidence of obstruction or hepatic lesions. Viral hepatitis panel results were negative.

The sudden enlargement of the liver within 48 hours raised suspicion of possible veno-occlusive disease (VOD). The patient underwent a Trans jugular Liver biopsy after correcting coagulopathy and platelet levels, confirming the diagnosis of VOD likely triggered by recent COVID-19 sequelae. His hospitalization was marked by two stressful weeks in the intensive care unit, necessitating a multidisciplinary approach to manage acute Liver decompensation, ascites, and coagulation abnormalities. The patient received transfusion support, therapeutic doses of enoxaparin, steroids, N-Acetyl Cysteine, and antibiotics.

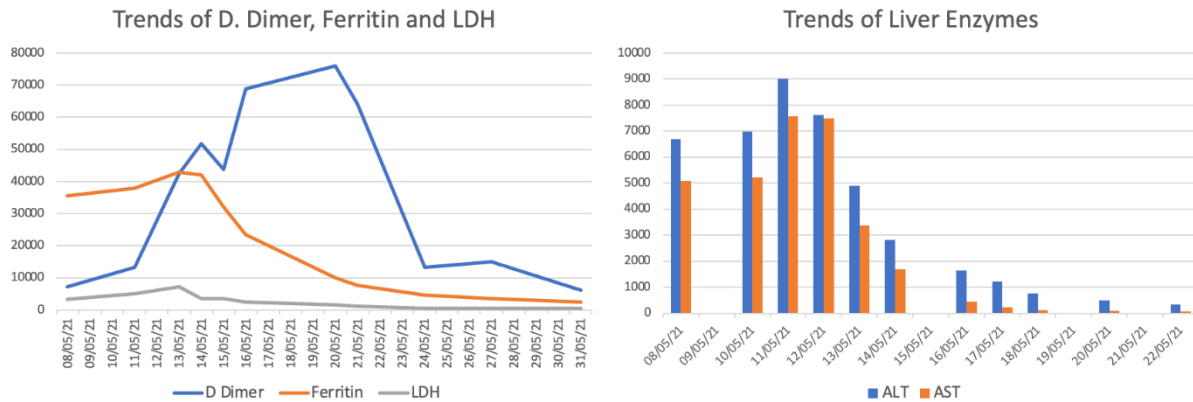
Specialist teams, including Pulmonology, Infectious Disease, and Gastroenterology, were involved in the patient's care. Due to elevated levels of TNF-alpha (165) and IL-6 (101.5), the patient was treated with infliximab and underwent cytokine filtration.

Liver biopsy showed coagulative necrosis and microvascular thrombi, confirming VOD. Subsequently, liver enzymes and D-dimer surged (AST 7,580, ALT 9,010, LDH 7,210, D-dimer 13,238 ng/ml). Defibrotide treatment led to gradual improvement, with D-dimer peaking at 75,991 ng/ml as pre-existing clots degraded during therapy. After 21 days of defibrotide, D-dimer decreased alongside resolution of thrombocytopenia and inflammation.

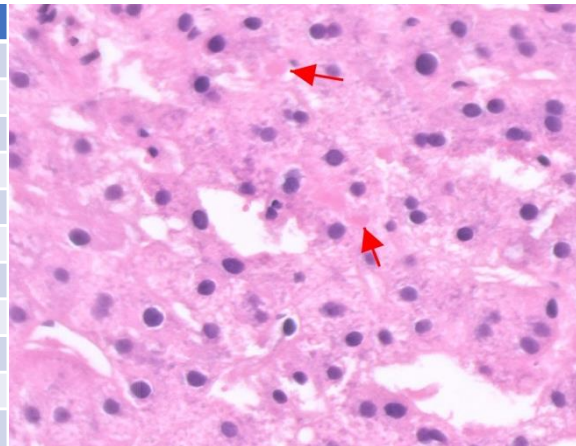
Post-defibrotide, anticoagulation was maintained for a year. Now two years post-episode, no recurrence underscores VOD as a rare post-COVID complication. With an 80% mortality rate, this case highlights the value of a holistic diagnostic approach, supported by clinical, pathological, and radiological data.

DISCUSSION

This case highlights the diagnostic challenges posed by hepatic SOS, which can mimic other severe systemic conditions like HLH, especially in post-COVID patients. A multidisciplinary team approach, accurate diagnostic evaluation, and timely intervention, including defibrotide therapy, were pivotal in achieving a favourable outcome for this patient. The unique presentation and successful management of this case emphasize the need for heightened awareness of VOD as a potential post-COVID complication and mimicker of HLH.



Date	D Dimer	Ferritin	LDH	ALT	AST
08/05/21	7272	35433	3280	6700	5090
11/05/21	13238	38000	5120	6980	5220
13/05/21	42468	42800	7210	9010	7580
14/05/21	51729	42000	3468	7630	7480
15/05/21	43824	32000	3454	4900	3380
16/05/21	68904	23500	2468	2824	1708
20/05/21	75991	10000	1560	1648	438
21/05/21	64030	7668	1200	1212	233
24/05/21	13177	4670	586	757	123
27/05/21	15000	3554	430	497	100
31/05/21	6120	2460	400	331	81



References

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4. Hemophagocytic Syndrome Associated with Fatal VenoOcclusive Disease in the Liver Atsuko Nakatsuka 1, Jun Wada 1, Ryo Nagase 1, Masaya Takeda 1, Tadashi Yoshino 2 and Hirofumi Makino 1 (DOI: 10.2169/internalmedicine.46.6294)