ORIGINAL RESEARCH PAPER

General Medicine

A CASE REPORT OF SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN A POST-COVID-19 : AN EMERGING COMPLICATION

KEY WORDS:

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ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a disease that can affect both children and adults. HLH can be categorized as primary or secondary. Secondary HLH (sHLH) may be secondary to various viral infections. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection is a pandemic with multi- system involvement. HLH in COVID-19 positive patients is a recognized entity. However, in post-COVID-19 patients who have recovered and are negative by serological tests and reverse transcription-polymerase chain reaction test may present with sHLH due to dysregulation of the immune system. We highlight this unusual finding of post-COVID-19 sHLH in this case, who was diagnosed by the new revised H-score.

Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a lethal disorder of varying etiology and encompasses a wide range of diseases. Familial HLH (FHLH) and immune-related HLH constitute the primary HLH spectrum whereas HLH secondary to infections, drug exposure, transplantation, malignancies and macrophage activation syndrome(MAS) constitute the secondary HLH (sHLH) spectrum[1]. Laboratory parameters like elevated cytokines, marked cytopenia, increased ferritin levels, hypertriglyceridemia, and hypofibrinogenemia along with clinical findings of splenomegaly, lymphadenopathy, multiorgan dysfunction and fever predominate in HLH patients [2]. Various viral, bacterial, fungal, and protozoan organisms have been implicated in the etiopathogenesis of sHLH [1,2]. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus has been implicated as a causative agent of sHLH in patients with active Covid-19 disease; however, cases of sHLH in patients who have recovered from active COVID-19 are rare. We are reporting here a case of post-COVID-19 patient presenting with sHLH.

Case Presentation

Case

A 48-year-old male with background history of T2DM on regular medication was tested positive for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) and the degree of illness was severe for which he was hospitalized for a period of 18 days and discharged. Four days later he started developing intermittent fever, dry cough, loss of appetite and pain abdomen which lasted for a month before he presented to our institute. At the time of presentation, the patient was conscious, alert, and oriented. His blood pressure was 160/70 mmHg, pulse rate was 138 beats per minute, respiratory rate was 28/min and SPO2 was 93% on RA, and the temperature was 101.7 F. On examination bilateral cervical and axillary lymphadenopathy were present, hepatomegaly was present and spleen was palpable four fingers below the left costal margin. Crackles were present in bilateral infrascapular regions in respiratory system auscultation. The cardiovascular system and central nervous system were unremarkable. USG whole abdomen revealed hepatosplenomegaly. HRCT Thorax showed multiple inter and intralobular septal thickening with ground glass opacities, which were appreciated in bilateral peripheral lung fields with CT Severity Score of 12/25.

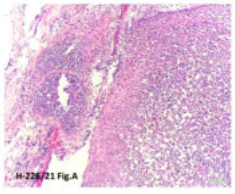

Fig A shows partially effaced architecture, expansion of sinuses and involvement of the perinodal tissue

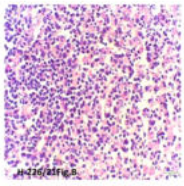

Fig B shows numerous histiocytes with phagocytosed hemic cells and debris

Laboratory findings

Hemoglobin (Hb) was 11.2 g% on presentation and reduced to 8.3g% on 3rd day of presentation

Total leukocyte count (TLC) was 2.3x103 /μL with ANC of 950
Platelet was markedly reduced ($27x10^3$/μL).
Renal parameters were within normal Limits.
Procalcitonin was elevated (3.09 ng/ml)
(AST) was elevated (209 IU/L)
Rest of the liver parameters were within normal limit
Fibrinogen level was mildly on lower side (2.0 g/L),
Ferritin was markedly elevated (>2000ng/ml)
C-reactive protein was elevated (1.8mg/dl)
All viral markers, anti-nuclear antibody (ANA) was negative
Scrub typhus, Malarial parasite and widal were negative
Triglyceride was mildly elevated (201mg/dl)

The H-score estimated as per the H-score of 2014 was 276 points with a probability of sHLH to be >99% (Table 1).

According to the protocols of our institute, the patient was managed with broad spectrum iv antibiotics, oxygen support and other supportive measures. Patient clinical condition detoriated over a period of next 48 hrs. Patient developed Septic shock during the hospital stay and inotrope support were initiated. Cervical Lymph node biopsy was done and sent for HPE. IV steroid (methyl Prednisolone 80mg/day) was initiated as soon as sample was taken but patient did not

responded to treatment, Patient had to be intubated and mechanically ventilated in view of poor GCS, In spite of all earnest measures patient succumbed to death on 4th day of admission. HPE report of Cervical LN arrived on next day which showed features of florid Hemophagocytosis.

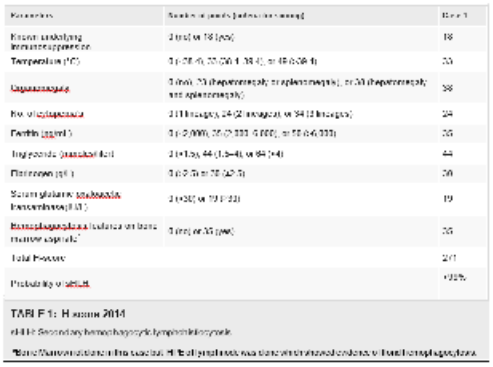

TABLE 1: H score 2014

Discussion

HLH was first described by Farquhar and Claireaux in the year 1952 [3]. Primary HLH is a genetic disorder manifesting mainly in children whereas sHLH is a disease primarily of the adult with multiple etiologies [4]. sHLH may occasionally be a complication of various infections and viral infections are one of the common culprits for sHLH [5]. The recent pandemic of the SARS-CoV-2 virus has highlighted that sHLH in COVID-19 positive patients may result in a considerable increase in mortality [5]. Although cases of sHLH in patient with active COVID-19 are increasingly recognized, sHLH in post COVID-19 patients is sparse in the literature[4].

HLH is a relatively underdiagnosed entity with an absence of definitive clinical, laboratory, or histopathological criteria [6]. Hemophagocytic activity in the bone marrow aspirate is considered to be a sign of HLH; however other specimen like lypmhnode biopsy was also considered for diagnosing HLH [6-8].

The HLH-1994 criteria included various clinical (fever, splenomegaly), laboratory (cytopenia's, hypertriglyceridemia, and/or hypofibrinogenemia) and histological parameters (hemophagocytosis in bone marrow or spleen or lymph nodes with no evidence of malignancy) which was modified in 2004 [8].

The H-score devised by Fard et al. was a modification of the previous systems and gave simplified numerical values to the various clinical, laboratory and histological parameters which is comparatively easier and helps in prompt diagnosis of sHLH patients [9].

The optimal cut-off for a diagnosis of HLH was considered to be 169 by Fardet et al. with 93% sensitivity and 86% specificity [10]. In our case, the H-score was 276 points which predict >99% probability of hemophagocytic syndrome. Thus, a diagnosis of sHLH was considered in this case in view of the high revised H-score, clinical, laboratory and histological findings.

Conclusions

SARS-CoV-2 infection is a recent pandemic with important complications inherent to its multisystemic affections. Recent information about etiopathogenesis, clinical signs and symptoms and treatment protocols are getting highlighted. sHLH is a condition primarily occurring in COVID-19 positive patients; however, sHLH in post-COVID-19 patients is rare. Immune dysregulation following infection by the SARS- CoV-2 virus may be the prime reason for sHLH in such patients. We highlighted such post-COVID-19 patient who was negative for COVID-19 at the time of presentation but were diagnosed as cases of sHLH based on the H-score. sHLH is always to be kept as a differential diagnosis for fever associated with hepatosplenomegaly with or without hepatosplenomegaly in post-COVID-19 patients.

Disclosures

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