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AN INTERESTING CASE OF PERSISTENT DIARRHEA

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Abstract:
Hemophagocytic Lymphohistiocytosis(HLH) is the second major alarm in infections. HLH is due to hyper-immune activity, leading to a variety of Hemato-immunological abnormalities. The disease can be fatal if left untreated. We report a 42-year-old male who has been admitted in our teritiary hospital with presenting complaints of loose stools, fever, and shortness of breath. The blood investigations showed a decline in cell count with pancytopenia, Hyperferritinemia, Hypofibrinogenemia, and hypertriglyceridemia. Blood culture revealed Salmonella typhyi growth. On overt exclusion of further possibilities, we made a diagnosis of HLH in accordance with HLH-2004 diagnostic criteria. This patient responded well with the traditional antibiotics, corticosteroids and on supportive management. There by we discuss the clinical course of this Hemato immunological condition and strive to raise the awareness of complications like secondary Hemophagocytic Lymphohistiocytosis caused by common diseases, such as a typhoid fever.

Keywords:Hemophagocytic Lymphohistiocytosis, Salmonella Typhi, Hyperferritinemia, Hypofibrinogenemia, Hypertriglyceridemia

Introduction

Enteric fever is one of the predominant causes of fever in developing country like India.A gram-negative bacterium, Salmonella enterica serotype typhi that has plagued impoverished countries for millennia causing Typhoid fever. After identifying distinctive lesions in the abdominal lymph nodes of individuals who had died from "gastric fever" Pierre Louis was the first to coin the name "typhoid fever" in 1829 [1,2]. The derived term "typhus" comes from the Greek literature "typhus," which means "smoky," and was originally used to describe the delirium that patients would experience as a result of the sickness [3].

This infection, caused by Salmonella typhi and para typhi is typically accompanied by a history of outside food consumption. The only known reservoir of this bacteria are humans. The gram-negative Salmonella enterica, spreads from Peyer's patches through the lymphatic system and the bloodstream[4].The disease's hallmark is cellular multiplication within the reticuloendothelial system, which eventually leads to the systemic symptoms that a doctor may notice. After replication, organisms will remain in the liver, spleen, and bone marrow macrophages [5,6].
The typhoid fever and paratyphoid fever are both referred as enteric fever as they are clinically indistinguishable, the terms enteric and typhoid fever are interchangeable. Salmonella serovars that cause human infection can evolve over time and in different environments [7].
It usually presents as a gradually increasing or continuous fever with or without abdominal symptoms. The course of the illness can range from a simple febrile illness to a complicated deadly infection [8,9]. Here, we report to you a case of previously healthy Indian male with severe enteric fever complicated by HemophagocyticLymphohistiocytosis.

Case report

An over-weighted 42-year male came to the casualty with the history of loose stools and fever (high grade) associated with rigors and chills for 5 days. Patient also gives history of breathlessness since morning. History of abdominal pain and history of outside food consumption. Patient denied history of abdominal distention, vomiting, blood in vomitus, stool, urine or dark colored stools. Patient also gives history of taking siddha medication for fatty liver and no history of any recent travel.
On examination, he was conscious, febrile, tachypneic, dyspneic and dehydrated; however, no features of pallor, icterus, lymphadenopathy, or edema were noted. His vital signs showed respiratory rate-28 per min, temperature-104 F, pulse rate-121 per minute, blood pressure-130/90 mm of mercury and oxygen saturation-92%. Abdominal examination-showed no obvious finding /organomegaly, and other systems were normal. All necessary investigations and samples for cultures were sent, patient was started on IV Fluids and intravenous empirical antibiotics. ABG analysis showed respiratory alkalosis with raised lactate levels. Routine investigations on day 1, blood picture showed Hb% 12.1 gm/dl, and platelet 82,000/cubic mm, with leukocyte count 5070/cubic mm, with liver enzymes serum total bilirubin - 2.3 mg/dL, serum direct bilirubin - 1.6 mg/dL, Alkaline phosphatase - 329, SGPT - 85 U/L, SGOT - 126 U/L, GGT-552

and renal function with BUN - 17 mg/dL, and serum creatinine - 1.0 mg/dL. Ultrasonography of abdomen showed fatty liver with mild splenomegaly. Blood samples were obtained and sent for rapid diagnostic tests for COVID-19, malaria, dengue, scrub and leptospirosis were negative. Pro-calcitonin levels were mildly elevated to 3.6, chest X ray showed normal study without any infiltrates. Patient had no symptomatic improvement till day 3, Blood culture showed Salmonella typhi growth and antibiotics were escalated as per sensitivity. Patient persistently had high grade fever along with the loose stools more than 5 episodes/day and respiratory distress for next 48hours. Chest X ray showed bilateral infiltrates suggestive of ARDS, Lactate levels were persistently high.

Serial blood counts were suggestive of Pancytopenia, involving all three cell lineages as in the table below (Table 1). Patientbegan to mutter to himself about past events while he was conscious and oriented to time, place and person, he occasionally had these episodes of muttering. On further evaluation, he has dramatically elevated levels of serum ferritin levels (>2000ng/mL), serum triglycerides 564 mg/dL (150–200 mg/dL). Hence a provisional diagnosis of HLH was made. Based on the above, the diagnosis of hemophagocyticlymphohistiocytosis (HLH) was established, as our patient fulfilled 5 out of the 8 criteria from HLH- 2004 diagnostic criteria, without any familial history. His condition improved following corticosteroids administration, patient became afebrile and tachypnea began to settle in the next 24 hours. His stools frequency reduced and consistency improved. His blood parameters began to improve and his vitals were stable. In view of elevated GGT on repeated liver function tests, MRCP was done which did not show any obstructive or inflammatory pathology. As per the treatment protocol the patient was discharged and followed up regularly.

Parameters	Day 1	Day 3	Day 5
Hemoglobin	12.1	10.6	9.3
WBC	5070	4570	3970
Platelet	82000	67000	45000

Table 1: Serial Blood Counts from Day 1 to Day 5

DISCUSSION

HLH seen with viral fevers like Epstein-Barr virus has been encountered commonly in last decade and less common in bacterial infections, rarely reported as a complication of typhoid fever [10,11]. Incidence of HLH with typhoid fever is not clearly known. HLH is an aggressive and life-threatening syndrome of excessive immune activation due to dysregulated activation and proliferation of T cells, lymphocytes and natural killer cells [11]. 10-15% of patients with typhoid fever caused by salmonella typhi can have multiple systemic involvement such as Muttering delirium, Guillain- barre syndrome, pancreatitis, hepatitis, myocarditis, pneumonia, arthritis, endophthalmitis, abscess, HUS, DIC and HLH like complications [12]. Around 60-70% of patients with HLH respond to supportive therapy and antibiotics, but severe life-threatening cases associated with Ebsteinbarr virus have required chemotherapy [13]. Our patient who has HLH with typhoid did not require any chemotherapy.

Conclusion

The diagnostic criteria may not be always be fulfilled as some features may develop late in the disease, hence it is prudent to start treatment based on clinical picture.HLH resulting from immune activation is fatal if untreated, however proper supportive care and treatment brings down mortality by 40-60%.

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