CASE REPORT

Uncommon Presentation of a Common Infection

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ABSTRACT

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a clinical syndrome resulting from the immunological hyperactivation of macrophages. The condition can be triggered by an infection, malignancy, or autoimmune disease. Though the current literatures demonstrated a significant portion of sepsis patients are probably suffering from HLH.

Case description: Here, we present a case who presented like features of gram-negative sepsis but prompt diagnosis of HLH and treatment saved the patient’s life.

Conclusion: Hemophagocytic lymphohistiocytosis should be anticipated and recognized in fulminating sepsis-like conditions and promptly treated with steroids.

Keywords: Ferritin, Hemophagocytic lymphohistiocytosis, Salmonella, Sepsis.

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INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a clinical syndrome resulting from the immunological hyperactivation of macrophages. It causes the release of various proinflammatory cytokines like IL-1, IL-6, IL-8, and more.1,2 The histological feature of this condition is activated macrophages phagocytosing other immune cells. The condition can be triggered by an infection, malignancy, or autoimmune disease. In 1984, Risdall reported this condition which often mimics sepsis.3 But for decades, and probably till today, this was believed to be extremely rare. Though the current literatures demonstrated a significant portion of sepsis patients are probably suffering from HLH.4,5 Here, we present a case who presented like features of gram-negative sepsis but prompt diagnosis of HLH and treatment saved the patient’s life.

CASE DESCRIPTION

This 27-year-old man was admitted with a history of fever and dry cough for 6 days along with diffuse pain abdomen and constipation. Initial evaluation revealed a right hypochondriac tenderness and dry coated tongue, the vital signs were normal except for the fever. He was COVID-19 negative. Initial investigations showed raised CRP, SGOT, SGPT, and the total leukocyte count was 5,000. After admission, the patient developed loose motion and IV saline was given. The initial working diagnosis was enteric fever and injection ceftriaxone was started. The next day an ultrasound abdomen was performed and revealed hepatosplenomegaly, gallbladder sludge, and distended bowel loops. But patient developed a very high spike of fever (104°F) and tachycardia with diffuse pain in the abdomen; the procalcitonin level was much raised. So, meropenem and teicoplanin were stopped and shifted to sensitive antibiotics. C3 and C4 complement levels were raised and Epstein–Barr virus (EBV) serology was negative. Interestingly, LDH, ferritin (32,095 ng/mL), and triglyceride (662 mg/dL) levels were way beyond normal. He had also features of rhabdomyolysis with elevated CPK (18,856 IU/L). The patient was reviewed by a hematologist and HLH was suspected.

The patient was given parenteral dexamethasone. By that night, the patient had lower temperature and tachycardia and for the first time since admission he felt well, and his mental function improved remarkably. The blood culture showed growth of Salmonella typhi sensitive to ceftriaxone and ofloxacin. So, meropenem and teicoplanin were stopped and shifted to sensitive antibiotics. C3 and C4 complement levels were raised and Epstein–Barr virus (EBV) serology was negative. The patient gradually became well with this regimen and blood parameters started improving. He was discharged 16 days after admission with tapering steroid doses. His final diagnosis was secondary HLH due to Salmonella typhi infection.

DISCUSSION

Sepsis and HLH share many features like fever, cytopenias, hepatic involvement, disseminated intravascular coagulation

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(DIC). But like HLH which is often triggered by viral infections, sepsis is caused by bacterial or fungal infections. The most common infectious trigger of HLH is—EBV, cytomegalovirus (CMV), parvovirus, herpes simplex virus, varicella-zoster virus, measles virus, human herpesvirus 6, H1N1, HIV, SARS-CoV2. Occasionally bacterial infections like Brucella, gram-negative bacteria like Salmonella or Mycobacterium tuberculosis or parasites like leishmaniasis, malaria or fungus may also give rise to HLH. The following modified criteria are sufficient to diagnose HLH: three of four clinical findings (fever, splenomegaly, cytopenias, hepatitis) plus abnormality of one of four immune markers (hemophagocytosis, increased ferritin, hypofibrinogenemia, absent or very decreased NK cell function). Unfortunately, there are no laboratory tests to distinguish between sepsis and HLH, but extremely high ferritin and elevated LDH are more common in HLH. Bone marrow examination to demonstrate hemophagocytosis in HLH is not often feasible in acutely ill patients nor is required to diagnose HLH. Treatment of underlying condition and prompt treatment with steroid are life-saving in this condition.

Salmonella as a cause of HLH is not common, but some case reports are there in the medical literature. The uniqueness of the current case lies here; where the patient presented as a case of fulminating gram-negative sepsis, but not responding to antibiotics alone. A timely administration of steroids, after quick anticipation of HLH, helped to save a precious life. Another important aspect was the presence of rhabdomyolysis in Salmonella infection. This was not a part of HLH criteria and was thought to be a separate complication of invasive Salmonella infection.

**Conclusion**

Hemophagocytic lymphohistiocytosis can closely mimic sepsis and is not uncommon. This disease should be anticipated and recognized in fulminating sepsis-like conditions and promptly treated with steroids (Table 1).

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**Table 1:** Investigations as per days

| Day | WBC  | Platelet | CRP | ALT  | AST  | Ferritin | CPK |
|-----|------|----------|-----|------|------|----------|-----|
| D1  | 5,000| 80,000   | 79  | 100  | 144  | 32,095   | 1095|
| D2  | 2,300| 69,000   | 280 | 160  | 644  | 37,301   | 37,301|
| D3  | 4,100| 90,000   | 312 | 168  | 926  | 1,101    | 1,101|
| D5  | 6,300| 201      | 195 | 196  | 1,321| 721      | 721|
| D8  | 6,300| 187      | 196 | 201  | 1,101| 64       | 64|
| D9  |      |          | 51  |      |      |          |     |
| D14 |      |          | 1   |      |      |          |     |