Secondary hemophagocytic lymphohistiocytosis: an unusual complication in disseminated Mycobacterium tuberculosis

Authors: Shan Kai Ing, Grace Wan Chieng Lee, Tze Shin Leong, Yih Hoong Lee, George Yew Liang Lau, Nur Nazihah Yusof, Andrew Kean Wei Chang and Kelly Kee Yung Wong

Introduction
Hemophagocytic lymphohistiocytosis (HLH) is a rare hematologic disorder characterized by uncontrolled immune response resulting in multiorgan damage. HLH can be primary due to genetic disorder or secondary due to an acquired condition such as neoplastic or infectious diseases. TB is still a public health problem in Malaysia. We report a case of HLH associated with disseminated TB in an immunocompetent healthy man. This case highlights the importance of an aggressive diagnostic approach, high clinical suspicions, and early therapeutic intervention for successful outcomes.

Case report
A 53-year-old man of Melanau ethnic origin, from Sibu, Sarawak, presented to us with a 1-week history of fever and abdominal discomfort. He was an active smoker with underlying hypertension who worked as an ambulance driver. Physical examination revealed a healthy man with normal vital parameters, except for tachycardia and fever. Dull percussion was noted on Traube's space with mild tenderness over the bilateral hypochondriac area. He was treated with multiple courses of antibiotics for infection, but there was no clinical improvement. Cultures, including blood, urine, and sputum, were all sterile. Initial chest X-ray (CXR) and pulmonary tuberculosis workups were all unremarkable. However, he continued to be febrile and eventually developed multiorgan failure, acute respiratory distress syndrome (ARDS), transaminitis and bone marrow dysfunction. The clinical course and simultaneous increase in serum ferritin raised the suspicion of HLH. His Hscore was 254, indicating a high probability of hemophagocytic syndrome. TB diagnosis was confirmed by positive endotracheal TB GeneXpert and bone marrow aspiration (BMA) which detected acid-fast bacilli organisms. The patient was promptly started on anti-TB, dexamethasone and IVIG. The patient responded well to treatment and made a full recovery without any lasting complications. This case highlights the importance of promptly recognising HLH and identifying the underlying cause. In critically ill patients, it is crucial not to delay HLH-specific treatment while working up for differential diagnosis.

KEYWORDS: tuberculosis, hemophagocytic lymphohistiocytosis, dexamethasone, intravenous immunoglobulin

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Tuberculosis associated hemophagocytic lymphohistiocytosis

poor. Studies have reported a mortality rate of 50–70%, regardless of its underlying cause.

2 HLH can be classified into primary and secondary forms, with the latter resulting from various underlying conditions including infections, malignancies and autoimmune disorders.

3 HLH presents as fever of unknown origin with elevated ferritin levels and multi-organ involvement. The HScore has been developed as a tool to aid in diagnosis.

Hyperferritinemia and marrow failure are the key indicators in the diagnosis of HLH. A BMA demonstrating hemophagocytosis is essential for diagnosis and to rule out secondary causes of HLH such as underlying malignant disorders. Fasting hypertriglyceridemia and/or hypofibrinogenemia can also be detected in HLH. Diagnosing HLH is challenging due to variable clinical presentations and lack of specificity of clinical and laboratory findings.

4 HLH is associated with various infections, including viral, fungal and parasitic infections. 5 TB-HLH is most often seen in immunocompromised patients. In Malaysia, where TB prevalence is high, TB-HLH should be considered, especially among healthcare workers. TB-HLH has a high mortality rate as immunosuppressive treatments can exacerbate the course of TB. Combination therapy with etoposide and corticosteroids is often used to treat HLH, and the addition of intravenous immunoglobulin (IVIG) may also be considered due to its anti-inflammatory potential.

The patient in our case demonstrated significant improvement in CXR, respiratory function and biochemical markers following treatment with a combination of steroids, IVIG and anti-TB drugs. Dexamethasone was tapered off during his stay and he was discharged home well after 68 days of admission. Anti-TB treatment was planned for a total duration of 9 months.

Discussion

HLH is a rare syndrome characterised by intense immune and inflammatory system activity and the prognosis of this disease is poor. Studies have reported a mortality rate of 50–70%, regardless of its underlying cause. 2 HLH can be classified into primary and secondary forms, with the latter resulting from various underlying conditions including infections, malignancies and autoimmune disorders. 3 HLH presents as fever of unknown origin with elevated ferritin levels and multi-organ involvement. The HScore has been developed as a tool to aid in diagnosis. Hyperferritinemia and marrow failure are the key indicators in the diagnosis of HLH. A BMA demonstrating hemophagocytosis is essential for diagnosis and to rule out secondary causes of HLH such as underlying malignant disorders. Fasting hypertriglyceridemia and/or hypofibrinogenemia can also be detected in HLH. Diagnosing HLH is challenging due to variable clinical presentations and lack of specificity of clinical and laboratory findings. 4

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This case highlights the importance of early initiation of HLH treatment as well as treating the underlying cause of HLH. Clinicians should be aware that HLH can be a potential complication of TB.

References


Address for correspondence: Shan Kai Ing, Sibu General Hospital, Batu 5 1/2, Jalan Ulu Oya, Sibu, Sarawak 96000, Malaysia.

Email: shankai1992@gmail.com

Twitter: @shankai_26