Nusantara Medical Science Journal
Volume 9 Issue 1, January – June 2024
P-ISSN: 2460-9757, E-ISSN: 2597-7288
Nationally Accredited Journal, Decree No. 230/E/KPT/2022.

Case Report

A Rare Case of Aplastic Anemia in Toxic Typhoid Fever

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ARTICLE INFO

Keywords:
Typhoid fever ;
Pancytopenia;

How to cite:

DOI:

ABSTRACT

Introduction and importance: *Typhoid fever is one of the representative febrile diseases in the tropics, with unhygienic environmental conditions and poor public health systems. Pancytopenia from hemophagocytic lymphohistiocytosis is a rare complication of typhoid fever, which may be fatal if untreated.* ***Presentation of case:*** *A 20-year-old woman presented to our tertiary care center with high-grade fever, body pain, and slurring of speech. Investigations showed pancytopenia, TUBEX IgM Salmonella test positive, lymphadenopathy, and peripheral blood smear showed aplastic anemia after ruling out other possibilities and diagnostics. The patient responded to culture-sensitive antibiotics, steroids, and supportive care.* ***Discussion:*** *Pancytopenia in typhoid fever patients is linked to the mechanism of HLH (Hemophagocytic lymphohistiocytosis).* ***Conclusion:*** *It is essential to diagnose and treat toxic typhoid fever with an appropriate antibiotic to prevent complications.*

1. INTRODUCTION

Typhoid fever is one of the most representative febrile diseases in the tropics, with unhygienic environmental conditions and poor public health systems. Typhoid fever is a systemic disease caused by *Salmonella enterica typhi*. World Health Organization (WHO) reports an increase in confirmed cases, more than 25 million cases during one year. Children under 15 years old and young adults have a higher risk of typhoid fever.[1] Symptoms of Typhoid fever such as constipation, body aches, diarrhea, and fever. Clinical deterioration may occur

in untreated typhoid fever after a few days.[2] We report a previously healthy Indonesian female with severe typhoid fever complicated by unconsciousness with multiple organ dysfunction syndrome and pancytopenia.

2. CASE PRESENTATION

A 20-year-old woman came to the Emergency Room, Dr. Loekmono Hadi Hospital, on March 28, 2023, with complaints of fever from three weeks before. Fever appears suddenly and increases slowly. The patient's consciousness began to decline approximately one week before hospital admission. The patient did not respond to or answer questions from family members. Other complaints were bone pain and decreased appetite. The patient's clinical manifestations were fever (38.7 C), GCS E4V3M5 (apathy), and weakness.

Laboratory examination results on March 28, 2023, showed Hemoglobin 9.8 g/dL, Total Erythocyte Count 3.38 million/µL, Total leucocyte count (TLC) 2.7 thousand/µL (Neturophil 75%, Lymphocyte 20.9%, Monocyte 3.7%, Eosinophil 0.0%, Basophil 0.4%), Platelets 29 thousand/ul, urea 16.4 mg/dL, HBsAG rapid negative, Anti-HIV negative, Anti-HCV negative, Calcium 1.92 mmol/L, Sodium 125 mmol/L, and Chloride 88 mmol/L. The peripheral blood smear showed normochromic normocytic anemia; the leukocyte count decreased without morphological abnormalities, the platelet count decreased without morphological abnormalities, and the impression on examination was aplastic anemia (pancytopenia). The TUBEX Anti-Salmonella IgM examination showed a positive result of 8 (a strong indication of active typhoid fever infection). Immunological examination ANA Test ELISA method obtained a 0.3 (negative) result. Abdominal ultrasonography examination on March 28, 2023, showed lymphadenopathy in the ileocaecal region measuring (± 0.78 x 0.65 cm), suspicious for an inflammatory process, and sonography of other solid abdominal organs within normal limits. A non-contrast CT-Scan examination on March 30, 2023, showed no intracranial bleeding and no signs of increased intracranial pressure. Based on the results of the patient's examination, the patient's diagnosis was typhoid fever followed by aplastic anemia. The patient's family was explained the examination results, diagnosis, prognosis, and complications that can occur. After listening to the explanation, the parents were given informed consent to refer the patient but refused to be referred for further treatment and agreed to be hospitalized for typhoid fever. The patient was given antibiotic therapy of Ceftriaxone 1 gram intravenously, Paracetamol 1 gram intravenously, Prednisone 5 mg orally, and Ringer lactate intravenously. Treatment was carried out for 5 days; the patient had no fever, and the patient's consciousness had increased. The patient returned to the Internal Medicine Polyclinic Dr. Loekmono Hadi Hospital Kudus after 2 weeks with an increase in platelet count to 269 thousand/ul, an increase in TLC of 10.4 thousand/ul, and Hemoglobin of 11.7 g/dL.

3. DISCUSSION

Typhoid fever caused by Salmonella Typhii can cause complications of various severity in 10-15% of patients, the most common of which are gastrointestinal bleeding, intestinal perforation, and typhoid encephalopathy (toxic typhoid). Intermittent confusion, insomnia, and dizziness are reported in 3-10% of cases.[3] These symptoms are associated with high mortality, such as hemophagocytic syndrome with blood disorders similar to those of aplastic anemia.[4] Typhoid fever and pancytopenia have been described in several reports from Asia during the last two decades. Typhoid fever can affect the bone marrow, resulting in a decrease in the volume of packed cells and an increase in neutrophils[5]. There was a

significant decrease in the number of erythrocytes and platelets in patients positive for typhoid fever. These changes occur due to the body's metabolic response process in the form of hemophagocytosis to the release of toxins from Salmonella enterica typhi. This mechanism involves hematopoiesis organs such as lymph nodes, bone marrow, and spleen[2]. Salmonella Typhii stimulates macrophages to engulf blood cells, and infected macrophages engulf more erythrocytes, potentially transitioning to chronic infection.[6]

Pancytopenia in typhoid fever patients is linked to the mechanism of Hemophagocytic lymphohistiocytosis (HLH).[7,8] The incidence of HLH as a complication of typhus is rarely reported—the pathophysiology of HLH due to the hypersecretion of cytokines by lymphocyte.[8] HLH is diagnosed using clinical and molecular criteria. This patient has four diagnoses from five clinical findings: fever, splenomegaly, hypofibrinogenemia/hemophagocytosis, and cytopenia; the other was hypertriglyceridemia, which was not diagnosed. Demonstration of hemophagocytosis in lymph nodes was also diagnosed in this patient, but decreased natural killer cell function and an elevated soluble CD25 or IL-2Rα chain ≥ 2,400 IU/mL were not diagnosed[9]. The TUBEX Anti-Salmonella IgM examination was the only basis for diagnosis in this patient.[10] Though the TUBEX test and Widal test have often been used controversially to diagnose typhoid fever in developing countries, we presumptively treated her as such. Typhoid fever should be included in the differential diagnosis of pancytopenia in unconscious kids with fever. It should be managed with an appropriate antibiotic and adequate hydration to prevent complications.

4. CONCLUSION

An unconscious patient with fever should be suspected of toxic typhoid fever complicated by pancytopenia, which could be HLH. Recognition is essential for diagnosis and treatment with an appropriate antibiotic to prevent complications and decrease mortality.

CONSENT FOR PUBLICATION

All contributing authors are requested to indicate that they have read and accepted the final version of this manuscript, that they have made all necessary statements at the time of acceptance, and to provide their agreement.

ACKNOWLEDGMENTS

The author would like to thank all clinical colleagues at the Department of Interna Medicine, Faculty of Medicine, Sultan Agung Islamic University, and Interna Medicine of Loekmono Hadi Hospital Kudus for their assistance throughout this work. The author also acknowledges Loekmono Hadi Hospital Kudus for providing clinical patients for this case report.

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Conflict of Interest Statement:

The author declares that the case report was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.