CASE REPORTS

TYPHOID FEVER WITH SEVERE PANCYTOPENIA

AĞIR PANSİTOPENİ İLE BİRLİKTE TİFO ATEŞİ

Nevin UZUNER M.D., Ahmet ARICI, M.D., Ebru YILMAZ, M.D.,
Hale ÖREN, M.D., Salih KAVUKÇU, M.D.

Dokuz Eylül University, Faculty of Medicine, Department of Pediatrics, İzmir-Turkey
Gazi Medical Journal 2002; 13: 191-193

SUMMARY: Typhoid fever (TF), a systemic prolonged febrile illness, continues to be a worldwide health problem, especially in developing countries where there is poor sanitation and low standards of personal hygiene. In this case report we describe a 14-year-old girl who had high fever with severe pancytopenia and whose blood culture grew Salmonella typhi. We wish to emphasize that TF must be kept in mind during the differential diagnosis of pancytopenic patients.

Key Words: *Pancytopenia, Typhoid Fever.*

ÖZET: Tifo ateşi, kişisel hijyenik koşulları zayıf ve sanitizasyonu kötü olan, gelişmekteki ülkelerde dünya sağlığını tehdit etmeye devam eden ateşli sistemik bir hastalıktır. Bu vaka takdiminde 14 yaşında bir kız çocuğundan kan kültüründe solmonella typli üreyen ve pansitopeni ile seyreden yüksek ateşli bir olgu pansitopenik hastalarda ayrırıcı tanı açısından tifo ateşininde akılda tutulması için sunulmaktadır.

Anahtar Kelimeler: *Pansitopeni, Tifo Ateşi.*

INTRODUCTION

The worldwide incidence of typhoid fever (TF) is estimated to be approximately 16 million cases annually (1). Most infections are caused by the ingestion of contaminated food or water. Salmonella infection occurs when ingested organisms bypass gastric defenses, multiply within the intestinal lumen, penetrate the intestinal mucosa, and multiply within macrophages of the reticuloendothelial system. from where they may then disseminate via the systemic circulation. Several virulence factors have been identified. The wide range of pathologic and clinical manifestations are subdivided into four syndromes, each requiring a distinct diagnostic and therapeutic approach: 1- gastroenteritis, 2- bacteremia with or without metastatic disease, 3- asymptomatic carriage, and 4- typhoid (enteric) fever (2). In recent years, significant issues have been raised about patients suffering from TF with severe pancytopenia whose bone marrow examination revealed extensive hemophagocytosis, known as infection-associated hemophagocytic syndrome (IAHS), that possibly contributed to the pancytopenia (3).

CASE PRESENTATION

A 14-year-old girl was brought to the pediatric outpatients department with a 1-week history of fever, headache and fatigue. She had no symptoms of diarrhea or vomiting. Although she had received an oral antibiotic, sulbactam-ampicillin, for 4 days prescribed by the referring physician with a presumed diagnosis of upper respiratory tract infection, her complaints had not improved. She was living in an urban area and her past and family history were uneventful.

On physical examination she was alert, her weight and height were 52 kg (50-75p) and 150

cm (75-90p) respectively, axillary temperature was 42°C, heart rate was 112 beats/min and regular, respiratory rate was 28/min and blood pressure was 110/70 mm Hg. She was pale and fatigued. Her oropharnyx was diffusely reddened without any lymph node enlargement. On cardiac auscultation, a 1/6 grade systolic ejection murmur was audible at the left sternal border. The liver was palpable 1 cm below the right costal margin. The rest of her physical examination was unremarkable.

Laboratory evaluation on admission revealed a white blood cell count of 1.6x109/l, a hemoglobin level of 11.6 g/dl, a hematocrit rate of 34.7%, platelet count of 56x109/l, and a erythrocyte sedimentation rate of 10 mm/h. Her peripheral blood smear showed 72% segmented neutrophils with toxic granulation, 20% lymphocytes, and 8% monocytes with few schistocytes and fragmented erythrocytes. Her reticulocyte count was 3%. Although the results of urinalysis, stool analysis, chest radiography, levels of serum electrolytes, serum proteins, creatinine and blood urine nitrogen levels were normal, her alanine amino transferase, aspartate amino transferase, gamma glutamyltranspeptidase, alkaline phosphatase and lactate dehydrogenase levels were elevated and they were 50 IU/l, 102 IU/l, 172 IU/l, 542 IU/l, and 1605 IU/l respectively. The results of serologic tests for Epstein-Barr virus, Human Immunodeficiency Virus, Hepatitis A-B-C viruses, Cytomegalovirus, Lyme disease and Brucella were negative. A Direct Coomb's test and anti-nuclear antibody test were negative. Blood coagulation tests revealed prolonged bleeding time, with elevated activated partial prothrombin time and prothrombin time. Her fibrinogen level was 2.25 g/l and D-dimer level >2 µg/ml. Because of pancytopenia, bone marrow aspiration was done primarily to exclude leukemia and aplastic anemia. A bone marrow aspiration smear revealed mildly hypocellular bone marrow with a predominance of myeloid cells, suppressed erythroid precursors, and an increased number of plasma cell and histiocytes. Hemaphogocytosis was present in rare areas.

Since the patient was leukopenic, in bad condition and had a high fever, empiric intravenous antibiotic treatment (meropenem and amikacin) was initiated before hematologic malignancy was excluded. According to the hematologic features of disseminated intravascular coagulation (DIC), fresh frozen plasma 10 ml/kg/dose, once every 8 to 12 h was started until the features of DIC disappeared. At the same time, she was evaluated to determine the primary infection site and the reasons for DIC. When the results of her serologic tests and cultures were obtained, her serum Salmonella titers were TO-1/164, TH-1/164. There was no growth on urine, stool or pharyngeal cultures, but her blood culture yielded Salmonella typhi, which was susceptible to amikacin, cefazolin, gentamicin, trimethoprim-sulfamethoxazole, meropenem, aztreonam, amoxicillin-clavulanate, and ampicillin-sulbactam. Therefore, her final diagnosis was enteric fever and meropenem and amikacin therapy was continued according to her blood culture antibiogram results. At the end of 10 days she was in good condition, without any complaints, and displayed normal hematologic features.

DISCUSSION

Typhoid fever remains a disease of major importance worldwide, despite improvements in public health. Salmonellosis has several clinical manifestations, ranging from gastroenteritis to typhoid fever and bacteremia. Patients can be suspected of having enteric fever when they are seen with fever, leukopenia and relative bradycardia (4). Rose spots may also appear and can be diagnostic. Final diagnosis is based on organism cultures from appropriate sites. Serologic tests are also helpful in the diagnosis of TF, although as many as one third of patients may show insignificant titers. A single titer value of ≥1:320 for the O antibody, especially in a child, should alert the physician to consider TF. However, it is sometimes difficult to diagnose TF, because of atypical clinical presentation. Our patients had high fever, mild hepatomegaly, pancytopenia and DIC features on admission.

In our case, bone marrow aspiration smear revealed mild hypocellularity with a predominance of myeloid cells and suppressed erythroid precursors, and an increased number of plasma cells and histiocytes. Hemaphagocytosis was not evident, though it was present in a few areas. Hemophagocytosis, suppression of bone marrow cells due to systemic infection and peripheral destruction due to DIC were the

probable reasons for pancytopenia in our case. TF usually produces discernable leukopenia and neutropenia early in the course of the illness, which is often associated with thrombocytopenia and anemia (4-6). The occurrence of DIC in TF is rare; however, awareness of such a potential complication and early diagnosis and treatment may be life saving (6). In patients with Salmonellosis, pancytopenia is mostly due to histiocytic hyperplasia in bone marrow, with marked phagocytosis of platelets, leukocytes, and red blood cells, which is also called IAHS (7).

The first line therapy in TF, chloramphenicol, ampicillin, amoxicillin, ß lactam antibiotics and trimethoprim-sulfamethoxazole, have demonstrated good clinical efficacy. Resistant strains are usually susceptible to third-generation cephalosporins. Fluoroquinolones are efficient, but are not approved for children (4-8). According to the culture antibiogram of our patient we used meropenem and amikacin. The response was very good and clinical and laboratory improvement were significant after 10 days.

In conclusion, this case illustrates once more that TF must be included in the differential diagnosis of pancytopenia.

Correspondence to: Nevin UZUNER, M.D.
Vali Hüseyin Öğütçen cad.
Yavuz apt. No: 17 daire: 6
Balçova
35330 İZMİR - TÜRKİYE
Phone: 232 - 277 95 15
Fax: 232 - 231 26 10
E-mail: www.nuzuner.deü.edü.tr.

REFERENCES

1. Goldberg MB, Rubin RH. The spectrum of Salmonella infection, Infect. Dis Clin North. AM 1988; 2: 571-598.
2. Merican I. Typhoid fever: present and future. Med J Malaysia 1997; 52: 299-308.
3. Sood R, Roy S, Kaushik P. Typhoid fever with severe pancytopenia. Postgrad Med J 1997; 73: 41-42.
4. Miller SI, Hohmann EL, Peques DA. Salmonella (including salmonella typhi). In: Mandell GL, Bennet DE, Dolin R (eds.), Principles and Practice of Infectious Diseases (4th ed.), Vol 2, Churchill Livingstone, New York, 1995; 2013-2032.
5. Shin BM, Paik IK, Cho HI. Bone marrow pathology of culture proven typhoid fever. J Korean Med Sci 1994; 9: 57-63.
6. Nasrallah SM, Nassar VH Enteric fever: a clinicopathologic study of 104 cases. Am J Gastroenterol 1978; 69: 63-93.
7. Udden MM, Banez E, Sears DA. Bone marrow histiocytic hyperplasia and hemophagocytosis with pancytopenia in typhoid fever. Am J Med Sci 1986; 291: 396-400.
8. Clearly TG. Salmonella. In: Behrman RE, Kliegman RM, Jenson HB (eds.). Textbook of Pediatrics (16th ed). WB Saunders Company, Philadelphia, 2000: 842-848.