

A CASE OF TYPHOID FEVER PRESENTING WITH MULTIPLE COMPLICATIONS

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An 18- year old female patient was admitted to the Emergency Department with complaints of fever and fatigue beginning 15 days ago associated with headache, weakness, palpitation, abdominal pain, and diarrhea a week later. The patient who apathic confused and discordant was transferred to the Department of Infectious Diseases. There was also hypocalcemia, hypopotassemia, pancytopenia, intestinal hemorrhage, and hepatic involvement. *S. typhi* was grown in the blood culture. The patient was discharged with full recovery after ciprofloxacin treatment in addition to electrolyte replacement. Typhoid fever is a widespread infectious disease in our country and should be taken into consideration in differential diagnosis of many diseases because it may involve a number of systems and may present with a variety of complications.

Key words: Salmonella, salmonellosis, typhoid fever, hypocalcemia, hypopotassemia, pancytopenia, intestinal hemorrhage, and hepatitis.

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INTRODUCTION

Typhoid fever, an acute systemic infectious disease seen only in humans, is a classical example of enteric fever caused by *Salmonella enterica serovar typhi* (1). The etiologic agent of the disease characterized by prolonged fever, is a gram negative rod with capacity of living and growing in mononuclear phagocytic cells of the reticuloendothelial tissue (2). The spread to a healthy and susceptible person occurs usually from patients with typhoid fever or carriers by oral-fecal route. It is an endemic disease in Turkey and sometimes causes epidemics (1,3).

Here we would like to present a case of typhoid fever in a female patient presenting with hypocalcemia, hypopotassemia, pancytopenia, intestinal hemorrhage, and hepatitis as complications and discussed in the light of literature.

CASE

An 18-year-old female patient applied to Patnos and then Van State Hospital with complaints of fever and fatigue beginning 15

days ago accompanied by headache, weakness, palpitation, abdominal pain, and diarrhea a week later. The patient was transferred to the Infectious Diseases Department of the Medical Faculty of Yüzüncü Yıl University. On her physical examination, temperature was 39°C, pulse rate: 92/min, rhythmic, breath rate: 24/min, blood pressure: 100/60 mmHg. She had apathic confusion, her sclerae were subicteric, her skin and conjunctivae pale, her lips and tongue dry and tongue rusty. She had a painful hepatomegaly which exceeds the costal ridge 1 cm and she had no lymphadenopathy.

In laboratory examinations: leukocytes 2.500/mm³, (with differential: 47% lymphocytes, 43% polymorphonuclear leukocytes, and 10% monocytes), erythrocytes: 3.360.000/mm³, Hb: 9.9 gr/dl, Htc: 27.8%, platelets: 31.000/mm³, ESR: 30 mm/h, PT: 16.3 sc (INR: 1.36), PTT: 32 sc, CRP: 75 mg/dl. In blood biochemistry: AST: 161 U/L, ALT: 67 U/L, total bilirubin: 2.05 mg/dl, direct bilirubin: 1.65 mg/dl, LDH: 1250 U/L, CK: 898 U/L, BUN: 19 mg/dl, creatinine: 0.8

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mg/dl, Na: 131 mEq/l, K: 2.52 mEq/l, Ca: 6.1 mg/dl, Mg: 1.51 mg/dl. G6PD deficiency was not determined. Occult blood in stool was ++ positive, there were sparse leukocytes and erythrocytes in stool examination. Thyroid hormones were in normal range. In abdominal ultrasonography, only pathological finding was hepatomegaly (liver size: 160 mm). The patient was hospitalized with a preliminary diagnosis of typhoid fever with complications such as hypocalcemia, hypopotassemia, pancytopenia, intestinal hemorrhage, and hepatitis. After samples were taken for microbiological analyses, oral treatment of ciprofloxacin 2x500 mg was initiated by means of nasogastric tube and electrolyte replacement was maintained. After 8 hours of her admission, discordance between pulse and fever disappeared and pulse rate increased to 116/min while fever was 38°C. Tachycardia was attributed to hypopotassemia. In Gruber-Widal test, TO antibody was 1:200 and TH antibody 1:100. After 2 days of admission, *S. typhi* was grown in blood culture. Salmonella did not grow on urine and stool cultures. In antibiotic susceptibility testing of the isolated strain, there was only moderate resistance to ceftriaxone, but sensitive to ciprofloxacin, chloramphenicol and co-trimoxazole. Fever disappeared at the third day of her admission and electrolytes came to normal at the fifth day. Repeated Gruber-Widal test revealed that TO antibodies increased to 1:800 and TH antibodies to 1:200 one week later. Her platelets came to 199.000 and also her leukopenia improved. Hb level gradually reduced to 7.6 gr/dl after admission and remained at that level. She was given 2 units of whole blood, occult blood positivity in stool disappeared after 10 days of admission. After 2 weeks of antibiotic treatment, the patient was discharged with full recovery.

DISCUSSION

The definite diagnosis of typhoid fever is achieved by culture of blood and bone marrow. Positive blood cultures is seen in 60-80% of the cases. Possibility of blood culture positivity decreases after the first week and becomes negative in the fourth week. Although our patient was in the third week of her illness, her blood culture gave positive result. The fact that the patient had not used antibiotics prior to hospitalization is a good chance in order to grow the etiologic agent. Microorganisms can be grown from stool and urine cultures in later periods of the disease. Cultures can also be performed from

intestinal secretions and from contents of rose spots in the skin (4). Gruber Widal test five positive results at the end of the first week. Agglutinins may not be developed in some patients. The diagnostic value of Gruber Widal test is controversial because its sensitivity, specificity, and titer values taken into account are varied according to geographic regions (2,5). TO antibodies were found positive first in 1:200 titer and one week later increased to 1:800 and TH antibodies to 1:200 titers.

Clinical presentation and severity of the disease is varied. Fever, headache, flu-like symptoms, fatigue, nonproductive cough, lack of appetite, nausea, and myalgia are the most frequent symptoms (2,6). Classical disease duration is 4 weeks and high fever, toxemia, and constipation occur in the first week, diarrhea in the second week, and splenomegaly, bone marrow findings as well as complications such as encephalopathy, intestinal hemorrhage and perforation are typical findings seen in the third week (6,7). Also our patient had diarrhea, apathic confusion state, pancytopenia, and intestinal hemorrhage.

Most of the complications of typhoid fever develops in the third and fourth weeks of the infection in untreated patients (1). Although almost all systems may be involved, intestinal hemorrhage and perforation, toxic myocarditis, bronchitis and toxic confusion are the most common complications (1). Complication rate may be 10-15% and gastrointestinal bleeding, perforation, and typhoid encephalopathy are the most important complications (2). Confusion was present in our case in the third week of her illness and intestinal bleeding developed, but recovered after the treatment.

Complications in gastrointestinal system in typhoid fever may vary from a simple glossitis or esophagial ulcer to fatal perforation or intestinal bleeding. The most common complication is gastrointestinal bleeding seen in 10% of patients. 2% of gastrointestinal bleedings is clinically apparent and blood transfusions are required in such cases (2,8,9). Also in our case, there was gastrointestinal bleeding and whole blood transfusion of 2 units has been required. A clinical presentation as acute gastroenteritis may be seen in typhoid fever cases most frequently in children but also in adults (10) as in our case.

Intestinal bleeding usually occurs in the third week by ulceration of necrosis in the small bowels. Occult blood in stool is found at 20% during the disease. Gross bleeding

is seen in 10% of the patients and massive bleeding in fewer. Sudden decreases in blood pressure and body temperature are the first signs of bleeding. Arterial pressure decreases to 80-90 mmHg or even less than this, and shock may follow this. Perforation rate was higher in patients with typhoid fever before chloramphenicol (2,8,9). Although perforation occurs most frequently in distal part of ileum in the third week, perforation cases with fulminant prognosis in the first two weeks are not rare (10,11).

Abnormal liver biochemical tests are frequent in typhoid fever; transaminases may increase up to 2-3 times of normal range (2,12,13). Jaundice develops usually in the first two weeks of infection. Hepatitis seen in typhoid fever is generally of nonspecific reactive hepatitis. But rarely severe hepatic involvement as acute hepatitis is encountered. These cases of typhoid hepatitis have been reported at frequencies ranging from 1% to 26%. Bacterial virulence, delay in treatment and severity of general state of the patient are predisposing factors for typhoid hepatitis. ALT values were approximately 2 times higher than normal and AST values 4 times in our patient with minimal rise in bilirubin values. In differential diagnosis with acute viral infections, the severity of jaundice and the extent of elevation of transaminase levels are much greater than those observed in typhoid fever. The cause of the increase in transaminases in typhoid fever may also be hepatic granulomas or hepatic abscesses formation (14). But in our case, there was no such a space-occupying lesion. Splenomegaly rate is varied, having been reported in approximately half of the cases (1,15). Sometimes splenic rupture, and abscess or granuloma may be seen (16,17).

Hematological complications vary from hemolytic anemia to hemolytic uremic syndrome and DIC (2,12). Hemoglobin may be normal or low, platelets in the same manner, and leukocytes may be low, normal or increased. Eosinopenia is generally present, and prothrombin time is prolonged (2,16). Although various complications seen in our patient, leukocytosis did not occur, and the patient had leukopenic, neutropenic and thrombocytopenic course. Hb level in our patient decreased and required whole blood transfusion of 2 units required. LDH levels were 3-4 times of the normal.

The most common complication after intestinal bleeding is the neuropsychiatric complication, being in the first range in some

regions (2,17). Neurologic complication rates are varied (5-35%) according to geographic regions and drug resistance (18). Meningismus and acute confusion are the most frequent states (19). Confusion may have intermittent character and appears as apathy in many patients (6). Apathy was present in our case too, but intermittent character was absent. The presence of hypopotassemia and hypocalcemia together with diarrhea in our patient with apathy is striking. The agent was sensitive to antibiotics except moderate resistance to ceftriaxone. She was discharged with full recovery.

The clinical picture of typhoid fever is not pathognomonic, although it has characteristic features. Many diseases causing fever, eruption and abdominal complaints should be taken into consideration in differential diagnosis (1). Subclinical cases of typhoid fever with mild course are frequent and most of them have been taking treatment in outpatient clinics (20). Because of the diversity of complications and difference in the course of the disease, occurrence of complications in the second and third weeks of the illness even under treatment, one should be careful in the follow up of the patients and multidisciplinary approach should be exhibited.

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