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TYPHOID FEVER WITH VERY HIGH TRANSAMINASE LEVELS*

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Typhoid fever is endemic in developing countries and may cause very different clinical findings. Although hepatic involvement and abnormal liver function tests may be seen in 50% of the patients, intravascular hemolysis and renal involvement are rare. In this report, a 10-year-old patient with enteric fever presenting with hepatitis, severe intravascular hemolysis and glomerulonephritis is presented. To see all of these findings together in a patient with typhoid fever is very rare and may cause diagnostic difficulties. *Key words: typhoid fever, transaminase level.*

Typhoid fever causes endemics as well as occasional epidemics in developing countries. Enteric fever may sometimes present with completely unexpected clinical findings in adition to its classical signs and symptoms[1]. In this report, a patient with enteric fever presenting with hepatitis, severe intravascular hemolysis and glomerulonephritis is discussed.

Case Report

A 10-year-old male patient was hospitalized with the complaints of apathy and jaundice. The history of his present illness revealed that he had been experiencing anorexia, fever and weight loss during the previous 12 days. He became pale and icteric and had dark urine four days earlier, and he became apathetic two days previously. He had received no drugs or toxic substances, and there was no history of hemolytic anemia or hepatitis in his family or close contacts.

The physical examination revealed a confused and spastic child. His fever was 37.2 °C (axillary), pulse rate 116/min, respiratory rate 38/min, and blood pressure 110/70 mmHg. His skin was very pale, his sclera were icteric, and there was pitting edema in his lower extremities. There was no hepatosplenomegaly.

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The laboratory findings were as follows: hemoglobin 0.82 mmol/L, hematocrit 15% and reticulocyte 16%. Blood smear examination revealed anisocytosis, macrocytosis, and rare spherocytosis with 38% normoblastemia. His white blood cell count was 3.2×10^9/L with 81% polymorphonuclear leukocytes (vacuolization in 5% and severe toxic granulation), 1% monocytes, 5% metamyelocytes and 13% lymphocytes. Mean corpuscular volume was 125 fl and many thrombocytes were noted.

The urine was dark-colored and had a pH of 7 and a specific gravity of 1006. Protein and urobilinogen were (++). Glucose and bilirubin were negative, and 10-15 leukocytes plus 10-15 fine granular casts per field were present on microscopic examination.

The blood chemistry showed the following results: sodium 135 mmol/L, potassium 4.2 mmol/L, blood urea nitrogen 20 mmol/L, creatinine 194.5 µmol/L, alkaline phosphatase 154 IU/L, serum aspartate aminotransferase 2682 IU/L (490 ten days later), serum alanine aminotransferase 7655 IU/L (99 ten days later), total bilirubin 51 µmol/L, conjugated bilirubin 13.8 µmol/L, blood glucose 6.3 mmol/L, total protein 59 g/L, and albumin 34 g/L.

The direct, indirect and complementary Coombs tests were negative. Plasma hemoglobin was 14 µmol/L, and haptoglobulin was 380 mg/L (normal: 700-3790 mg/L). In the hemoglobin electrophoresis, hemoglobin A_2 was found to be 1.3% and hemoglobin F 0.9%. The sickling test and G_6PD were within normal limits. Erythroid hyperplasia and megaloblastic changes were detected on bone marrow aspiration. The G_6PD level and blood smears of both parents were within normal limits. Hepatitis markers including HBsAg, HBeAg, anti-HBs, anti-HBe, anti-HBc IgM and IgG, hepatitis C virus antibody, and hepatitis A virus antibody M and G were negative. Paul-Bunnel test and anti-cytomegalovirus IgM were also negative. Serum copper and ceruloplasmin levels were within normal limits. Cold agglutinin and erythrocyte E antigen were negative. The chest x-ray and the cranial computerized tomography were normal, and there was an increase in the echogenicity of both kidneys on ultrasonographic examination. The level of fibrin degradation products was normal. Salmonella typhi was cultured in blood.

Discussion

There are rare reports in the literature of atypical presentations of typhoid fever[1,2]. Hepatic involvement and especially jaundice in typhoid fever is also rare in childhood. The pathogenesis of typhoid hepatitis is not yet known. It is suggested that a high concentration of endotoxin and bacterial multiplication in the liver may cause a granulomatous and mononuclear inflammatory response, necrotic areas and vacuolar degeneration[3,4]. IgG antibodies against Salmonella typhi O antigen have been demonstrated by Calva and his colleagues[5] in liver biopsy specimens.

The liver function test values may be abnormal in 50 percent of patients with or without hepatomegaly[1,3,4]. The level of transaminases is usually less than 200 IU/L and rarely above 1000 IU/L[2,4]. Our literature search failed to disclose any case with severe jaundice and such high transaminase levels. The high level of SGOT may be partly due to hemolysis, but the rise in SGPT cannot be explained by hemolysis. This condition should be differentiated from other infectious hepatitis. In our case, Salmonella typhi was confirmed by serological tests and the blood culture. After treatment, all the liver function tests returned to normal in a short time.

Intravascular hemolysis is also rare in typhoid fever. It is seen particularly in patients with G_6PD deficiency[6]. It may be due to both antimicrobial therapy and a direct effect of the infection[6,7]. G_6PD levels were normal in our patient and his parents, and there was no history of drug intake or exposure to other hemolytic agents. Therefore, hemolysis was considered to be a direct effect of typhoid fever.

During the course of typhoid fever, glomerulonephritis, IgA nephropathy and pyelonephritis can be seen as a direct effect of Salmonella typhi with or without clinical findings and abnormal kidney functions[8,9]. Hemolytic uremic syndrome has also been reported[10]. The disturbance in renal function tests was explained by glomerulonephritis. Deposition of salmonella Vi antigen C_3 and immunoglobulin have been shown in the glomerular capillary wall[9]. The clinical and laboratory findings of our case were not compatible with disseminated intravascular coagulation or hemolytic uremic syndrome.

These findings are very rare in typhoid fever and can cause diagnostic difficulties.

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