Salmonella meningitis in a 16-month-old child with AIDS

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Impairment of cellular immunity related to human immunodeficiency virus (HIV) infection predisposes patients to opportunistic infections. In this report, we describe a 16-month-old boy with salmonella meningitis and acquired immunodeficiency syndrome (AIDS). The patient was referred to the Infectious Diseases Ward with a history of prolonged fever and refractory vomiting. In direct smear of the cerebrospinal fluid (CSF), gram-negative bacillus was observed. Glucose and protein levels in CSF were 2 mg/dl and 890 mg/dl, respectively. Salmonella spp. was isolated from CSF and blood culture. HIV antibody titer by ELISA, western blot analysis, and HIV polymerase chain reaction (PCR) test were performed and were positive for HIV. Despite the treatment, the patient did not respond and died one month later.

Key words: child, human immunodeficiency virus, salmonella meningitis.

Bacterial meningitis is a widespread infectious disease in developing countries[1]. It is about 10 times more common in these countries than in developed countries[2]. It is highly prevalent among infants and young children[1], and is associated with a high fatality rate in this group, and among the elderly and immunosuppressed, or in chronic medical conditions such as human immunodeficiency virus (HIV) infection or diabetes[2,3].

Approximately 20% of acquired immunodeficiency syndrome (AIDS)-defining illnesses in children are recurrent bacterial infection caused primarily by encapsulated organisms such as *Streptococcus pneumoniae* and salmonella, with a high rate of mortality and recurrent infection [1,2]. The most common serious infections are bacteremia, sepsis and pneumonia, accounting for 75% of infections in HIV-infected children. Meningitis, urinary tract infections, deep-seated abscesses, and bone/joint infections occur less frequently. In these patients, it should be noted that less common etiologic agents and unusual complications occur[1,4]. Salmonella meningitis is one of these unusual complications in individuals with impaired cellular immunosuppression[1], which has poorer outcome compared with other pyogenic meningitis, with a high mortality rate[5].

Case Report

A 16-month-old boy was referred to the Infectious Ward of the Children's Medical Center, the referral pediatric center in Tehran, Iran, with a history of fever and intermittent vomiting for the past one month as well as developmental regression for the past three months. He was admitted to the hospital for one week before, and abdominal sonography and computed tomography (CT) scan revealed multiple lymphadenopathies in his abdomen; thus, he referred to our hospital with suspicion of malignancy and was also treated with ceftriaxone for his fever and ill appearance. In the first admission in his hometown, the blood and urine cultures were negative. Brain CT result was also normal. The family history revealed that his father was an intravenous (IV) drug user, and his parents had died in a car accident. On admission to our ward, the child appeared ill and had low-grade fever (38°C axillary) and refractory vomiting. On physical examination, he had a pulse rate (PR) of 110/min, respiratory rate (RR) of 38/min and blood pressure (BP) of 95/65.

The patient was pale and non-icteric, auscultation of heart and lung was normal, and the abdomen was distended, without tenderness, with spleen enlargement (4 cm below costal margin). Meningeal sign (Kernig, Brudzinski and neck stiffness) was negative.

A blood sample was taken for full blood count, plasma glucose and electrolytes, liver function tests, direct agglutination test (DAT) and K39, Wright, Widal, peripheral blood smear (PBS) for malaria, and blood culture. Tuberculin skin test (TST) was done. Lumbar puncture was done due to his prolonged fever and vomiting and his ill appearance. The cerebrospinal fluid (CSF) appeared purulent. Therefore, ceftriaxone with meningeal doses and vancomycin were started with suspicion of meningitis.

Results of initial laboratory tests were as follows: white blood cells (WBC): 8050/mm^3, neutrophils: 60%, lymphocytes: 34%, basophils: 0.1%, monocytes: 5.5%, and eosinophils: 0.3%.

Platelet counts were 464,000/mm^3. His hemoglobin level was 8.5 g/dl, erythrocyte sedimentation rate (ESR) 57 mm/h, C-reactive protein (CRP): 3+, aspartate aminotransferase (AST): 60 U/L, alanine aminotransferase (ALT): 58 u/L, alkaline phosphatase (ALP): 421 U/L, lactate dehydrogenase (LDH): 658 IU/L, and blood glucose 97 mg/dl.

The CSF was examined microscopically for total cell count and white cell differential count, and results were as follows: cloudy appearance, WBC: 16000 cells/ml (poly= 95%, lymph = 5%) and red blood cells (RBC): 0. In direct smear of the CSF, gram-negative bacillus was observed. Glucose and protein levels of CSF were 2 mg/dl and 890 mg/dl, respectively.

The organisms isolated from the CSF and blood culture were identified as salmonella by conventional biochemical tests and serotyped as salmonella group D by slide agglutination with specific polyvalent and monovalent antisera. Antibiotic susceptibilities were determined by disc diffusion on Mueller-Hinton agar, and the isolate was susceptible to cotrimoxazole, gentamicin, cefepime, and cefixime; therefore, because he had taken ceftriaxone for at least 10 days without any improvement, his antibiotic was changed to intravenous cotrimoxazole.

According to ultrasound result, bone marrow aspiration (BMA) to exclude malignancy was done and showed no evidence of malignancy. Salmonella group D was isolated from BMA culture. According to antibiogram, the isolate was susceptible to cotrimoxazole and cefixime.

Wright test for brucellosis and DAT and K39 test for kala-azar were negative, and the result of Widal test was OD=1:80, OB=1:80 and HB=1:640. PBS for malaria was negative. After 72 hours, TST showed 6 mm induration.

Abdominal ultrasound and chest X-ray were performed, and abdominal ultrasound showed multiple lymph nodes in porta hepatis, spleen, around the pancreas, and paraaortic and mesenteric region. After 72 hours, his fever resolved.

Due to salmonella meningitis, immunity assessment was done, and the result of immunity for immunoglobulin (Ig)G, IgM, and IgA were 2485, 247, and 246 mg/dl, respectively, and IgE titer was more than 500 ng/ml. Nitro-blue tetrazolium (NBT) test was 100%. HIV antibody titer by ELISA and western blot tests was positive, which was confirmed with the HIV polymerase chain reaction (PCR) test; his viral load was 6,650,000 and CD4 and CD8 were 13.11% and 64.20%, respectively.

Because of positive TST, isoniazid was also started, and 72 hours after treatment, a second CSF examination was done with the following results: glucose: 19 mg/dl, protein: 980 mg/dl, WBC: 700/mm^3 (PMN=80%, lymph=20%), and negative CSF culture. Brain CT scan was performed due to refractory vomiting that showed mild communicative hydrocephalus. No evidence of SOL (space occupying lesion) or gross structural abnormality was observed. Ventricles had normal size and configuration, and posterior fossa structures seemed unremarkable.

After one week, the second abdominal sonography was performed and showed disappearance of lymph nodes. His general appearance was good and the vomiting had stopped.

Anti-retroviral agents (zidovudine, lamivudine and nevirapine) were started for the patient after three weeks, when his infection was under control as decided by the Pediatric HIV Center, and he was prescribed cotrimoxazole for six weeks due to completing treatment for salmonella meningitis. Because it was

difficult for his grandmother to remain in the city, he was referred to a hospital in his hometown (Ahwaz) at his grandmother's request. Unfortunately, he did not respond to the treatment and died one month later.

Discussion

Salmonella is a motile gram-negative bacillus that infects or colonizes many mammalian hosts. According to data, bacterial meningitis is a rare presentation of salmonella infection, and when it does occur, it is common in infancy[1].

In the literature, the first case of salmonella meningitis was reported by Ghon in 1907[6]. The incidence of salmonella meningitis is low, but it is a common reason for gram-negative meningitis in newborns. As reports reveal, salmonella causes bacterial meningitis in 5-6% of two-month infants and in 16% of neonates in endemic regions[5].

The incidence of salmonellosis in AIDS patients is 20-100-fold more than in the general population. In some endemic regions, no cases of salmonella meningitis were reported until 1990 [4]. The incidence of non-typhi Salmonella spp. bacteremia is increased in patients with HIV infection. Among 73 HIV-positive children with bacterial meningitis studied by Nansera[7] in Uganda, six of them had Salmonella spp. pathogen. In northern Tanzania, Crump[8] studied 467 admitted children. Of those patients, 12.2% were HIV-infected. Blood culture was positive in 5.8%. Of these, 25.9% were salmonella, including 6 S. *typhi*, but they did not have CSF samples. In McCormick's study[9] in Malawi among 559 HIV-seropositive children, 37 (6.7%) had Salmonella spp. meningitis. This study revealed that HIV infection is a risk factor for death and severe sequelae in bacterial meningitis. Despite the high incidence of bacteremia, the occurrence of focal Salmonella spp. infection, such as meningitis, in AIDS is uncommon[1].

In HIV-positive patients, with impaired cell-mediated immunity, less common causes of bacterial meningitis become a frequent cause. On the other hand, the outcome of salmonella meningitis is poorer in this group compared to other pyogenic meningitis[5]. The most important known risk factors that make a person susceptible to salmonella infection are bacterial virulence, the infectious dose, genetics, and the host immunological condition[6]. In this case, the greatest predisposing factor seems to be defective cell-mediated immunity. The recurrence rate of salmonella infection is high in these patients, despite the appropriate treatment[1]. When salmonella infection is detected in a child, he should be investigated for immune deficiency such as HIV/AIDS. This kind of information is useful for planning in both curative and preventive medical fields and also for making quick medical decisions in the hospital environment.

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