

Brain abscess caused by *Salmonella enterica* subspecies *houtenae* in a patient with chronic granulomatous disease

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A 44-month-old boy with chronic granulomatous disease has been suffering from fever and skin rash for 7 days prior to admission. The blood culture obtained on admission revealed *Salmonella enterica* subspecies *houtenae*. He received intravenous ceftriaxone therapy during his hospital stay and oral cefixime after discharge. Unfortunately, the same symptoms recurred 2 weeks after discontinuing cefixime and the culture from the aspirate of a skin nodule yielded the same microorganism again. He received intravenous ceftriaxone therapy after readmission and became afebrile 3 days later. However, focal seizure was noted on the 14th day of hospitalization. Brain magnetic resonance imaging revealed multiple brain abscesses, and electroencephalogram showed epileptiform activity. The intravenous antimicrobial agents were continued for a total of 84 days and interferon-gamma was administered as adjunctive therapy. Finally, he recovered from brain abscesses without any neurologic sequel. It is suggested that an extended course of antimicrobial treatment is necessary for chronic granulomatous disease with pyogenic infection because of the defective intracellular killing ability.

Key words: Brain abscess, chronic granulomatous disease, *Salmonella enterica* subspecies *houtenae*

Salmonella species are common pathogens of pyogenic infections in the patients with chronic granulomatous disease (CGD) [1]. Brain abscess is a rare complication of extraintestinal manifestations of nontyphoidal *Salmonella* infections [2]. It has been observed in patients with stroke, brain tumor, meningitis, cerebral toxoplasmosis, skull osteomyelitis, head trauma, recent neurosurgery, prolonged lymphadenopathy, and human immunodeficiency virus (HIV) infection [3-5]. It has also been reported in immunocompetent patients and in a neonate due to perinatal infection [3,6].

Salmonella enterica subspecies *houtenae* was first isolated by Phillip *et al* from a cockatiel in 1978 [7]. It is very rarely encountered in clinical practice [8]. Herein we report a child with CGD who presented with prolonged fever and skin rash on admission. Cultures of the blood and the skin nodule aspirate revealed *S. enterica* subsp. *houtenae*. Focal seizure developed during intravenous antimicrobial therapy and brain MRI showed multiple brain abscesses. To our knowledge, this is the first description of brain abscesses caused by *S. enterica* subsp. *houtenae*.

Case Report

A 44-month-old boy with CGD was admitted to the Taichung Veterans General Hospital after 7 days of pyrexia. Maculopapular rash was found on his lower extremities. Neither vomiting nor diarrhea was noted before this episode. The white blood cell count (WBC) was 8700 /mm³ with 50% neutrophils, 46% lymphocytes, and 4% monocytes. C-reactive protein (CRP) level was 9.7 mg/dL (normal <0.8 mg/dL). Intravenous ceftriaxone (100 mg/kg/day, in 2 divided doses) was administered as empirical therapy. Three days later, the blood culture yielded *Salmonella* species that were susceptible to ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole (TMP-SMX), ciprofloxacin, and ceftriaxone. With phase induction method, this organism was further identified as *Salmonella enterica* group O44 subsp. *houtenae* by the Center for Disease Control in Taiwan. He received intravenous ceftriaxone therapy for 12 days, and was discharged with oral cefixime for another one week.

The boy remained relatively well until 3 weeks after discharge when fever recurred. Several hard skin nodules were found on his face and upper extremities. Percutaneous aspiration of a skin lesion was done and a little aspirate was obtained for bacterial culture. The WBC count was 9800 /mm³ with 34% neutrophils, 58% lymphocytes, and 8% monocytes, and CRP level was 3

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mg/dL. Intravenous ceftriaxone (100 mg/kg/day, in 2 divided doses) was initiated again after readmission. The fever subsided on the 4th day, and the culture of the aspirate revealed *S. enterica* subsp. *houtenae*, with the same antibiogram as the previous isolate. Unfortunately, focal seizure developed on the 14th day of hospitalization. Electroencephalogram showed epileptiform activity over bilateral fronto-centro-parietal areas. Multiple brain abscesses over the right parieto-temporal area were detected on brain magnetic resonance imaging (Fig. 1). His parents refused further invasive procedures, including lumbar puncture, percutaneous brain biopsy, and craniotomy. Two weeks later, he was transferred to another medical center for second opinion and interferon therapy. He received subcutaneous interferon-gamma (IFN- γ , 50 $\mu\text{g}/\text{m}^2/\text{day}$, in single daily dose) injections 3 times per week. Intravenous ceftriaxone was replaced by ceftazidime (150 mg/kg/day, in 3 divided doses) due to an allergic reaction to the former drug. The follow-up brain MRI revealed successive regression of the brain abscesses. Totally, intravenous antimicrobial therapy was continued for 84 days and IFN- γ for 53 days. He was finally discharged in stable condition and has remained well without any neurologic sequel. Brain MRI showed only mild scarring of the brain parenchyma on the 3rd week of his discharge (Fig. 2).

Discussion

More than 2000 serotypes are included in the genus *Salmonella* and new serotypes are continuously being identified. With modern taxonomic techniques, all serotypes belong to 2 species: *S. enterica* and *Salmonella bongori*. *S. enterica* comprises 6 subspecies, including *S. enterica* subsp. *enterica*, *salamae*, *arizonae*,



Fig. 1. Brain MRI (T1WI) revealed multiple brain abscesses with mild perifocal edema over the right parieto-temporal area (arrow).



Fig. 2. Brain MRI (T1WI) showed mild scarring of the brain parenchyma over the right parieto-temporal area (arrow) of the same patient 3 months later.

diarizonae, *houtenae*, and *indica*. *S. enterica* subsp. *enterica* includes most of the serotypes responsible for diseases in mammals, including humans. The other subspecies are commonly found in the intestinal tract of cold-blooded animals and in the natural environment; however, in rare instances, they can become real pathogens in immunocompromised patients [8,9].

Chronic granulomatous disease is the most common inherited disorder of phagocyte dysfunction. In patients with this disorder, phagocytes display a deficient intracellular microbial killing ability. Recurrent pyogenic infections usually develop in the first years and involve lung, skin, lymph nodes, liver, spleen, bone and intestine. Central nervous system infection is an extremely rare complication of CGD [10]. Although we did not obtain an adequate specimen for bacteriologic study in this case, the concurrent infection of *S. enterica* subsp. *houtenae* and the good clinical response convinced us that brain abscess was caused by the same organism. From a search of the English literature on Medline, we believe that this is the first description of human infection with *S. enterica* subsp. *houtenae*.

Brain abscess caused by *Salmonella* is rare in pediatric patients. Lu *et al* reported that most patients with brain abscess caused by *Salmonella* were young male infants without preceding enterocolitis, and concurrent meningitis occurred at a rate of 41.7% [11]. Extended-spectrum cephalosporins usually result in more favorable outcomes than ampicillin or chloramphenicol [12]. Although not officially licensed for use in children, fluoroquinolones have excellent intracellular bactericidal activity and should be considered as an alternative therapy for patients with unsatisfactory response to extended-spectrum

cephalosporins [6]. Surgical intervention plays an important role in the treatment of *Salmonella* brain abscess [11,13]. However, Bonvin *et al* has reported a patient who recovered from brain abscess caused by *Salmonella* serovar Enteritidis without surgical drainage.

There are at least 2 probable reasons accounting for recurrent *Salmonella* infections in the present case. One is the inadequate duration of antimicrobial treatment due to underlying immunodeficiency. The duration of 10 to 14 days of antimicrobial therapy is adequate for immunocompetent children with nontyphoidal *Salmonella* bacteremia. However, a more extended course of treatment may be required for the CGD patients because of their defective intracellular killing ability. The second is persistence of the infection sources, which may be related to contamination of the surrounding environment or the diet [14]. Patients with CGD are more vulnerable to *Salmonella* infections. We reasoned that incomplete treatment resulted in the recurrent *Salmonella* infection in this patient.

In summary, we suggest that CGD patients should avoid risky eating habits. A prolonged course of antimicrobial agents with high intracellular concentrations is helpful to control pyogenic infections in such patients. Interferon-gamma is an effective adjunctive therapy for serious infections in patients with CGD [15-17]. This case report demonstrates a successful treatment of *Salmonella* brain abscesses with long-term antimicrobial therapy without surgery; however, experience from more cases is required to confirm this observation.

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