CASE REPORT
AN UNUSUAL CASE OF LISTERIA MENINGITIS

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Human infection with *Listeria monocytogenes* was first reported in 1929 (Nyfeldt, 1929). The disease is known as being worldwide (Armstrong, 1990), however, it does not appear to have been recorded in Thailand. We report a case of human listeriosis with an unusual presentation and clinical course, which occurred in the country where listeriosis had never been diagnosed and remains the only case reported in Thailand until now. Difficulties in diagnosis and management of this patient are presented.

An 11 year-old Thai boy was admitted to a hospital in Ubon Ratchathani Province in the northeast of Thailand, on January 16, 1982 because of fever, headache and stiffness of neck for 6 days. He had been treated in a local health center without improvement. No other abnormal physical finding was detected. A lumbar puncture revealed turbid cerebrospinal fluid (CSF) containing about 3,000 white blood cells (WBC)/mm^3, 80% of which were polymorphs (PMN), and low sugar concentration. No micro-organism was seen on Gram stain. He was treated with penicillin G 0.2 million units/kg/day and chloramphenicol 100 mg/kg/day. Fever and stiff neck persisted. Repeated lumbar puncture on day 5 after the treatment revealed the same abnormalities of CSF plus numerous organisms which were described as Gram-positive cocci. Routine cultures of CSF specimens did not grow any bacteria. His condition remained unchanged for 10 days so that penicillin G was increased to 0.4 million units/kg/day. His temperature decreased to be normal within 5 days and this antibiotic regimen was continued for 21 days. CSF findings also improved and contained only 50 lymphocytes (L)/mm^3 when the antibiotics were discontinued. He started having fever again, after one day of antibiotic discontinuation, without any other abnormal clinical signs and symptoms. Three days later, his CSF contained 1,300 WBC/mm^3 with 90% PMN, low sugar, and no organism revealed on Gram stain. Intravenous trimethoprim/sulfamethoxazole (TMP/SMX) of 10 mg TMP/kg/day was started. Fever decreased but persisted at about 38°C. On day 12 after TMP/SMX treatment his CSF contained 920 WBC/mm^3, 90% of which were PMN. Cefuroxime 200 mg/kg/day was added for 2 weeks without satisfactory improvement of fever and CSF findings although he was clinically doing well. Roentgenograms of his paranasal sinuses and carotid angiogram were performed to exclude localized source of infection They revealed normal findings. None of his CSF specimens grew bacteria. Tests for evidence of tuberculosis and cryptococcosis were all negative.

On March 8, 1982 (about 2 months after onset of illness) he was referred to Ramathibodi Hospital, a tertiary referral hospital in Bangkok. On admission, he was afebrile without neck stiffness or other abnormal findings. A Gram-stained smear of his CSF from the previous hospital was re-examined and revealed numerous Gram-positive cocci and coccobacilli. Since listeriosis had never been diagnosed in Thailand, therefore, the probability that he had listeric meningitis was very low. His CSF on day 2 of admission revealed 324 WBC (288 PMN, 36 L)/mm^3, sugar 32 mg/dl (blood sugar 100 mg/dl), protein 96 mg/dl and no bacteria. He was observed for 7 days without any antibiotic, during which he was doing well except for intermittent fever up to 39°C and mild hepatomegaly. The CSF on day 8 (March 16) showed 3,300 WBC/mm^3 with 70% PMN, and protein 150 mg/dl. Several Gram-positive coccobacilii were found in centrifuged CSF. The peripheral blood examination revealed progressive increase in WBC to 29,000/mm^3 with 80% PMN on day 8. Computerized tomographic examination of his head did not show any abnormality. Penicillin G 0.6 million units/kg/day was given for 14 days with some

improvement of peripheral leukocytosis and CSF findings without any change in his clinical findings. Routine bacterial culture of his CSF specimens did not grow any organism. But the specimen having Gram-positive coccobacilli on the smear which was cultured by cold-enrichment grew *Listeria monocytogenes.* After a week of "cold enrichment" at 4°C a few tiny colonies of 1-2 mm in diameter with beta-hemolysis on sheep blood agar were detected from the culture plate after 24 hour incubation. The organism had tumbling motility, consisted of Gram-positive coccobacilli, and had biochemical characteristics of *L. monocytogenes.* Unfortunately, the organism did not grow on subculture for antibacterial susceptibility test and several cutures were repeated without success.

Intravenous ampicillin 400 mg/kg/day and TMP/SMX of 10 mg TMP/kg/day were started on April 1, which was 2.5 months after the onset of his illness. His temperature gradually decreased and CSF findings improved. He was afebrile on day 4 of this regimen. Both drugs were given for 6 weeks. He completely recovered without any neurological deficit or relapse of meningitis.

He had been healthy before this illness. His immunologic function was evaluated. It was found that he had normal serum immunoglobulin levels, slightly elevated anti-streptolysin 0 titer, normal reaction to tuberculin and dinitro-chlorobenzene skin test, and normal nitroblue tetrazolium test.

This patient is unique in several aspects. He did not have any predisposing factors for listeriosis, belonged to the age group in which listeriosis is extremely rare, he remains the first and the only case of human listeriosis in Thailand until now, and his meningitis was chronic and subtle. His presentation in Thailand where listeriosis had never been diagnosed together with negative bacterial culture caused difficulty in management.

Almost all of reported patients with central nervous system listeriosis were in extreme age groups or had an underlying immuno-compromising conditions (Bortolussi *et al,* 1987). The first 3 weeks of life and the years beyond 40 comprise almost 90% of all cases. Primary listeria meningitis in children, adolescents, and young adults is comparatively rare and is often superimposed on other disorders (Medoff *et al,* 1971; Visintine *et al,* 1977). Rarely, listeriosis was seen in children who had been otherwise well.

Listeria meningitis is usually acute which is indistinguishable from meningitis caused by other bacteria. The disease is also reported as being extremely variable in presentation (Armstrong, 1990). This patient presented with chronic meningitis and was almost asymptomatic except for fever. He had stiffness of the neck only during the early course of his illness; besides that he did not have any abnormal neurological findings or meningeal signs even when his CSF contained 1,000-3,000 WBC/ml. He had 2-3 months of meningitis but finally recovered completely.

Although listeriosis has been known as a worldwide disease, this patient remains the only case of human listeriosis in Thailand. A study by the Study Group on Bacterial Meningitis in Thai Infants and Children (Sirinavin, unpublished data) revealed that he was the only case of listeria meningitis among 420 cases of culture- or serology-proven bacterial meninigitis in non-immunocompromised Thai infants and children, of which 70 were neonates. The reason for almost non-existence of this disease in Thailand is unknown. It is possible that the disease could be missed because routine culture failed to detect the organism, but some cases would have been expected to be detected at least by Gram stain of CSF.

The patient partially responded to high-dose penicillin G therapy and was successfully treated with ampicillin 400 mg/kg/day plus TMP/SMX for 6 weeks. It is possible that the organism was intermediately susceptible to penicillin G and susceptible to ampicillin and/or TMP/SMX. Unfortunately antibiotic susceptibility testing was unsuccessful. Penicillin G resistant *L. monocytogenes* is not unusual, therefore ampicillin is preferred in treatment of listeria infection.

We report a case of unusual presentation of listeria meningitis which occurred as the first and only case of human listeriosis in Thailand. Awareness of this uncommon disease together with careful examination of CSF and using cold-enrichment technique in bacterial culture would be helpful in making the diagnosis of human listeriosis in Thailand.

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