# Case Report

# Cerebrospinal Fluid Lymphocytosis in an Infant with Acute *Streptococcus pnuemoniae* Meningitis: A Case Report

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*A 10 month-old female infant presented with one day of high fever with drowsiness and seizures. Physical examination showed meningeal irritation and mild cyanosis. The cerebrospinal fluid (CSF) profile revealed opening pressure of 27 cm$H_2O$, closing pressure of 17 cm$H_2O$, red blood cells 310 cells/μL, white blood cells 100 cells/μL of which 90 percents were lymphocytes, protein 391 mg/dl, sugar 0 mg/dL and blood sugar 74 mg/dl. Numerous gram positive diplococci were found on CSF Gram-stained smear. Bacterial meningitis was diagnosed and cefotaxime 300 mg/kg/day plus vancomycin 60 mg/kg/day were given empirically. The patient developed hypotension, poor tissue perfusion, dyspnea and disseminated intravascular coagulopathy (DIC). She expired 10 hours after hospitalization. The CSF and blood culture grew out Streptococcus pneumoniae serotype 6B with the minimal inhibitory concentration (MIC) of 0.5 and 1.5 μg/mL for penicillin and cefotaxime respectively. Atypical characteristics of CSF in bacterial meningitis may cause delay in empirical antimicrobial therapy. Gram-stained smear of CSF is helpful for rapid diagnosis and proper management.*

***Keywords:*** *Streptococcus pneumoniae meningitis, CSF, Lymphocytosis*

***J Med Assoc Thai 2010; 93 (Suppl. 5): S49-S52***
***Full text. e-Journal:*** *http://www.mat.or.th/journal*

*Streptococcus pneumoniae* is an important cause of bacterial meningitis in children with high morbidity and mortality. The estimated incidence of pneumococcal meningitis was 1-2.2/100,000 in Thai children[1]. The cerebrospinal fluid (CSF) examination is crucial in making diagnosis of bacterial meningitis. Typical findings of low glucose, elevated protein, and pleocytosis with polymorphonuclear cell predominate permit provisional diagnosis and help differentiate bacterial from viral, fungal, and tuberculous meningitis[2].

We report a case of severe pneumococcal meningitis in previously healthy child who had CSF lymphocytosis, an unusual CSF finding of bacterial meningitis.

## Case Report

A previously healthy 10-month-old girl presented with high grade fever of 39°C, purulent nasal discharge, poor feeding, vomiting, watery diarrhea and drowsiness for one day before hospitalization, and developed two episodes of generalized tonic clonic seizure on the day of admission. Neurological examination revealed neck rigidity. The diagnostic lumbar puncture was performed and revealed clear CSF with 127 white blood cells (WBC)/μL of which 91 percent were lymphocytes. There were 151 red blood cells (RBC) /μL. The CSF glucose was 53 mg/dL and protein was 209 mg/dL. Her concomitant blood glucose was 139 mg/dL. The complete blood count revealed hemoglobin of 10 g/dL, total WBC count of 5.14 x $10^3$/μL with 11% neutrophils and 89% lymphcytes, and platelet count of 200 x $10^3$/μL. She was diagnosed as acute viral meningoencephalitis and recieved intravenous phenobarbital and oral diazepam every 8 hours to control convulsion. Six hours after admission, she developed high grade fever, dyspnea, repetitive vomiting and stuporous Endotracheal intubation and mechanical ventilation was placed. She was transferred to Phramongkutklao Hospital.

Her vital signs on arrival were: temperature of 38.5°C, blood pressure, pulse, and respiratory rate were 90/69 mmHg, 150/minute, and 80/minute, respectively.

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The respiratory symptoms revealed poor air entry, subcostal retraction, mild cyanosis, and no adventitious sound on both lungs. Her liver was palpable at 4 cm below right costal margin. She exhibited withdrawal response to pain stimuli. The pupils were equal and reacted to light both eyes. The Babinski's sign was dorsiflexion both sides. Stiffness of neck and Kernig's sign were positve. The laboratory investigations revealed hemoglobin of 11.3 g/dL, peripheral WBC count of 0.7 x $10^3$ µL with 40% neutrophils, 53% lymphocyte, 4% monocyte, 1% eosinophils, 1% basophils, and platelet count of 102 x $10^3$ µL. The ESR was 30 mm/hr. The serum electrolytes were: Na 131.5 mmol/L, K 3.94 mmol/L, Cl 99.1 mmol/L, $CO_2$ 17.8 mmol/L. The liver profile showed albumin 24 g/L, globulin 29 g/L, AST 219 U/L, ALT 45 U/L, total billirubin 29 µmol/L, direct billirubin 10 µmol/L, alkaline phosphatase 195 U/L, and coagulogram were prolonged which included APTT, PT and TT.

The CSF was re-examined and found to be turbid. CSF cell count showed WBC of 100 cells/µL with 90% lymphocyte and RBC of 310 cells/µL. CSF glucose was 0 mg/dL while serum glucose was 75 mg/dL, and CSF protein was 391 mg/dL. The opening and closing pressure were 27 and 17 cm$H_2O$. The CSF Gram stain showed numerous Gram-positive lancet shape diplococci (Fig. 1). Provisional diagnosis was acute bacterial meningitis. She was initially treated with cefotaxime 300 mg/kg/day plus vancomycin 60 mg/kg/day and antituberculosis drugs. She rapidly deteriorated and developed hypotention, poor tissue perfusion, dyspnea and disseminated intravascular coagulopathy (DIC). The antibiotic regimen was changed to meropenem 120 mg/kg/day in a few hours later, and vancomycin 60 mg/kg/day was continued. Blood components and inotropic drug were given. After eight hours of admission, she had status epilepticus which was controlled by intravenous phenytoin but her clinical condition deteriorated. She expired 10 hours after hospitalization at our center.

The CSF culture and blood culture taken before initiation of antimicrobial therapy grew out *Streptococcus pneumoniae* serotype 6B. The antimicrobial susceptibility by E-test showed minimal inhibitory concentration (MIC) of 0.5 and 1.5 µg/mL for penicillin and cefotaxime respectively. The organism was susceptible to vancomycin and meropenem. She never recieved pneumococcal vaccination.

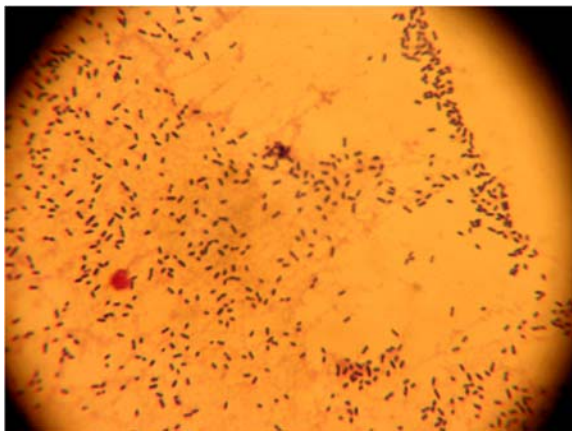

**Fig. 1** Gram-stained smear of CSF showed numerous Gram positive dipplococci with one lymphocyte cell.

## Discussion

*Streptococcus pneumoniae* meningitis remains a life threatening disease that may be rapidly fatal, and lead to severe neurological sequelae in survivors. The mortality and post infection sequelae remain high despite access to effective antimicrobial therapy. Timely administration of antibiotics therapy soon after symptoms emerge is essential for favorable outcome. We report a case of fatal *Streptococcus pneumoniae* meningitis with CSF lymphocytosis (more than 50 percent lymphocyte or mononuclear cells) in an infant. CSF lymphocytosis in acute bacterial meningitis is rare and made it difficult to diffentiate from viral, fungal, or tuberculous menigitis. Powers WJ reported in 1985 that CSF lymphocytosis occurred in 14 of 103 cases of bacteriologic proved acute bacterial meningitis in children and adults, and accounted for 32 percents of all patients with a CSF cell concentration of 1,000/mL or less. The CSF lymphocytosis was significantly more common in neonates and those without meningismus, but was found in all ages[3]. The most common organisms were *Streptococcus pneumoniae* followed by *Haemophillus influenzae* and *Neisseria meningitidis*. In 1988, Bonadio WA retrospectively analysed 112 cases of pediatric bacterial meningitis to determine the rate of CSF lymphocytosis at initial evaluation over 3- year period. The study found only one instance of CSF lymphocytosis occurred in which CSF exhibited pleocytosis, hypoglycorrhachia, abnormally elevated protein content, and the organism was visuallized on Gram-stained smear[4]. When CSF showed low glucose and high protein concentration, CSF Gram-stained smear and acid fast stained smear should be carefully examined.

The low peripheral white blood cell count was another significant prognostic factors for sequelae

and mortality in several studies of bacterial meningitis[5-7]. The MIC of *S pneumoniae* in this report case showed resistant to penicillin and intermediate resistant to cefotaxime. The reccommended antimicrobial therapy are combination of vancomycin and high dose ceftriaxone or cefotaxime and may add rifampin[8]. The presented patient died despite the *in vitro* effective antimicrobial therapy. This suggested the high virulence of *S. pneumoniae* in infants. This case supported the use of vaccine in young infant. *Streptococcus pneumoniae* serotype 6B is a predominant serotype causing invasive infection in Thailand. This serotype is included in the 7-valent pneumococcal conjugate vaccine[9,10].

The CSF lymphocytosis is rare in bacterial meningitis and may mislead the diagnosis to be viral, fungal or tuberculous meningitis which may contribute to delay in initiating appropriate antimicrobial therapy causing increased morbidity and mortality. Although culture is considered to be the definitive diagnostic test of bacterial meningitis, it takes time and may not yield positive results if the samples was not carefully handled. The microscopic examination of a Gram-stained specimen of CSF may provided immediate information on the causative microorganism[11]. Rapid diagnosis of bacterial meningitis by CSF Gram-stained smear should be done regardless of pattern of CSF cell concentration and differential count. The bacterial antigen detection may also be useful. Bacterial meningitis with normal CSF or low CSF cell count with lymphocyte predominate has been reported to associated with high rates of sequelae and mortality[12]. In this situation, the value of careful examination of Gram-stained smear of CSF cannot be overemphasized. Other findings such as low glucose and high protein levels should alert for possible bacterial meningitis and be considered initiating empirical antimicrobial therapy despite CSF lymphocytosis.

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## *เยื่อหุ้มสมองอักเสบจากเชื้อสเตร็พโตค็อกคัส นิวโมเนียอีที่มีลิมโฟซัยท์สูงในน้ำไขสันหลังในทารก: รายงานผู้ป่วย 1 ราย*

***ฤดีวิไล สามโกเศศ, เดชวิจิตร์ สุวรรณภักดี, วีระชัย วัฒนวีรเดช, พิรังกูร เกิดพาณิช***

*รายงานผู้ป่วย 1 ราย เป็นทารกเพศหญิง อายุ 10 เดือน มีอาการไข้สูง ซึม และ ชักกระตุก 1 วัน ตรวจร่างกายพบมีไข้มีอาการแสดงของเยื่อหุ้มสมองอักเสบเจาะน้ำไขสันหลังพบความดันเปิด 26 เซนติเมตรน้ำ ความดันปิด 17 เซนติเมตรน้ำ เม็ดเลือดแดง 310 เซลล์ต่อเดซิลิตร เม็ดเลือดขาว 100 เซลล์ต่อเดซิลิตร เป็นลิมโฟซัยต์ร้อยละ 90 ความเข้มข้นของโปรตีนในน้ำไขสันหลัง 391 มิลลิกรัมต่อเดซิลิตรกลูโคสในน้ำไขสันหลัง 0 มิลลิกรัมต่อเดซิลิตร ในขณะน้ำตาลในเลือด 75 มิลลิกรัมต่อเดซิลิตรพบเชื้อกรัมบวกดิโพลค็อกคัสจำนวนมากในน้ำไขสันหลัง จากการย้อมสีกรัมได้ให้การวินิจฉัยว่าเป็นเยื่อหุ้มสมองอักเสบจากการติดเชื้อแบคทีเรีย ได้เริ่มการรักษาด้วย cefotaxime ขนาด 300 มก./กก./วัน ร่วมกับ vancomycin ขนาด 60 มก./กก./วัน แต่ผู้ป่วยมีอาการเลวลง และเสียชีวิต 10 ชั่วโมงหลังรับไว้ในโรงพยาบาล ผลเพาะเชื้อจากเลือดและน้ำไขสันหลังแยกได้เชื้อ Streptococcus pneumoniae, serotype 6B ซึ่งมี MIC ต่อ penicllin และ cefotaxime 0.5 และ 1.5 ไมโครกรัม/มล. ตามลำดับ การที่พบลิมโฟซัยต์ในน้ำไขสันหลังของผู้ป่วยเยื่อหุ้มสมองอักเสบทำให้ไม่สามารถแยกจากสาเหตุของเยื่อหุ้มสมองอักเสบจากเชื้ออื่นเช่น ไวรัส ราและวัณโรค และอาจทำให้เริ่มยาปฏิชีวนะช้าได้จึงควรย้อมสีกรัมเสมอ*