A pneumococcal meningoencephalitis with a small spleen

Short running title: Splenic size analysis of 8 cases

Keiichiro Tsunoda, Kota Sato, Yoshiaki Takahashi, Koh Tadokoro, Ryo Sasaki,

Emi Nomura, Mami Takemoto, Nozomi Hishikawa, Yasuyuki Ohta, Toru Yamashita,

and Koji Abe*

Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikatacho, Okayama 700-8558, Japan.

Corresponding author: Koji Abe
Address: Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikatacho, Okayama 700-8558, Japan.
Phone: +81-86-235-7365, Fax: +81-86-235-7368
E-mail: me18046@s.okayama-u.ac.jp

Abbreviations: ABPC, ampicillin; CRP, C-reactive protein; CSF, cerebrospinal fluid; CT, computed tomography; CTRX, ceftriaxone; DEX, dexamethasone; GCS, Glasgow coma scale; HJB, Howell-Jolly body; OPSI, overwhelming post splenectomy infection; MRI, magnetic resonance imaging; SBT/ABPC, sulbactam/ampicillin; VCM, vancomycin.

Abstract

Streptococcus pneumoniae is a major cause of bacterial meningitis usually in children or elder adults. We report a case of a 38-year old man having pneumococcal meningoencephalitis with a small spleen (35 cm^3), compared to seven previous patients with pneumococcal meningitis in our department. Among the eight patients, four cases were due to sinusitis, but the origin could not be identified in the other four cases, including the present case who was the youngest patient with the smallest splenic size. Of interest in the present analysis was the negative or positive correlation between splenic size and age, with or without sinusitis. This is the first report on pneumococcal meningoencephalitis that takes into consideration age, splenic size, and the origin of infection.

Key words: age, meningoencephalitis, sinusitis, small spleen, *Streptococcus pneumoniae*

Introduction

Streptococcus pneumoniae (*S. pneumoniae*) usually causes meningitis in children less than two years of age or in adults over 50 years old, but not in young adults. Exceptions to the latter group are young adults in which pneumococcal meningitis is due to immunosuppressive therapy, diabetes mellitus, HIV infection, alcoholism, or a history of splenectomy. The spleen is an important blood-filtering organ that eliminates bacteria. Splenectomy sometimes causes severe sepsis of *S. pneumoniae* referred to as overwhelming post splenectomy infection (OPSI). There are several reports of cases of meningitis accompanied by functional hyposplenism due to asplenia or OPSI [1-2], but only few due to a small spleen [3]. Here we report a case of pneumococcal meningoencephalitis with a small spleen, compared to seven previous pneumococcal meningitis patients in our department.

Case Report

A 38-year-old healthy man felt severe headaches and fever (38.4-40.0 °C), so he was admitted to a local hospital on the next day. He was diagnosed with a fever of unknown origin with a high leukocyte count (13,730/μl, neutrophils 96.5 %) and C-reactive protein (CRP, 19.7 mg/dl), so intravenous sulbactam/ampicillin (SBT/ABPC 3 g) was administered. However, he developed disturbed consciousness disturbance and nuchal rigidity, and cerebrospinal fluid (CSF) was cloudy and showed increased initial pressure (340 mmH_2O), cell count (1,879/μl, neutrophils 94.6 %) and protein content (384 mg/dl) with the loss of CSF sugar (0 mg/dl). Since CSF analysis showed Gram-positive cocci and a positive *S. pneumoniae*

antigen, he was diagnosed with bacterial meningitis and was transferred to our hospital.

Upon admission to our hospital, he was in a stupor with Glasgow Coma Scale (GCS) of 14 (E3V5M6), complained of headaches, and had a body temperature of 39.0 °C. Neurological examination showed strong nuchal rigidity and Kernig sign, but without other focal neurological deficits. A blood test revealed elevated leukocytes (16,230/μl, neutrophils 94.7 %) and CRP (18.4 mg/dl), but no Howell-Jolly body (HJB). Brain magnetic resonance imaging (MRI) showed septic embolus in the brain parenchymal right corona radiata and bilateral ventriculitis (Fig. 1a, middle, arrows). He was diagnosed as having septic meningoencephalitis and was treated with meropenem (MPEM, 8 g/d) and vancomycin (VCM, 2 g/d) (Fig. 1a, bottom). Dexamethasone (DEX, 26.4 mg/d) and glycerol (40 g/d) were administered for four days. On Day 2, his headache and consciousness improved, but whole body computed tomography (CT) revealed a small spleen (35 cm^3, Fig. 1a, middle, arrowhead) on Day 6. Based on drug sensitivity of blood culture, MPEM was replaced by ceftriaxone (CTRX, 4 g/d) from Day 6, and VCM by ampicillin (ABPC, 4 g/d) from Day 11. His body temperature and inflammatory markers gradually improved (Fig. 1a, top). Cell count in CSF normalized (7/μl, lymphocytes 100 %) on Day 13, and he was discharged on Day 42 without any residual symptoms.

Discussion

The present 38-year-old male presented septic meningoencephalitis due to *S. pneumoniae* infection alongside a small spleen without HJB. A total of eight patients with pneumococcal meningitis were

admitted to our department over the past few decades (Table 1), four of which were due to sinusitis. However, the origin could not be identified in the other four cases, including the present case. We calculated the splenic size of 8 patients by CT scan imaging performed when they were admitted. The spleen becomes smaller in normal aging (Fig. 1b, open circles, [4]), but that of our seven cases of meningitis were smaller than their generational means except for case 4 (Table 1), while three cases (cases 1, 2, and 7) were smaller, even after their body weight was calculated (1.1 cm^3/kg, [5]).

Hyposplenism or splenic atrophy is sometimes observed in sickle cell disease, gastrointestinal, hepatic, and autoimmune disorders, as well as in infectious disorders such as pneumococcal meningitis [6]. Only one report exists for pneumococcal meningitis with splenic atrophy [3], but the present case is the first report of pneumococcal meningoencephalitis with a small spleen. Of interest was that splenic size was negatively or positively correlated to age, with or without sinusitis, when considering our previous cases of pneumococcal meningitis (Fig. 1b, filled triangles and squares). Cases of meningitis with sinusitis showed that younger patients had smaller spleens (Fig. 1b, filled squares), and the present case was an extreme example. This is the first report on pneumococcal meningitis that takes into account age, splenic size, and the origin of infection. Further studies are required to elucidate the exact relationship between these factors.

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References

[1] Iijima S. Sporadic isolated congenital asplenia with fulminant pneumococcal meningitis: a case report and updated literature review. BMC Infect Dis. 2017; 17: 6.

[2] Gilbert B, Menetrey C, Belin V, Brosset P, de Lumley L, Fisher A. Familial isolated congenital asplenia: a rare, frequently hereditary dominant condition, often detected too late as a cause of overwhelming pneumococcal sepsis. Report of a new case and review of 31 others. Eur J Pediatr. 2002; 161: 368-372.

[3] Shimatani Y, Naka Y, Sato K. Pneumococcalmeningitis in hyposplenism. Neurology and Clinical Neuroscience. 2017; 5: 1.

[4] Harris A, Kamishima T, Hao HY, et al. Splenic volume measurements on computed tomography utilizing automatically contouring software and its relationship with age, gender, and anthropometric parameters. Eur J Radiol. 2010; 75: e97-101.

[5] Koga Y, Fujita M, Nakahara T, et al. Splenic volume in severe sepsis is associated with disease severity and pneumococcal infection. Acute Med Surg. 2016; 3: 339-344.

[6] Di Sabatino A, Carsetti R, Corazza GR. Post-splenectomy and hyposplenic states. Lancet. 2011; 378: 86-97.

Figure Legends

Fig. 1 (a) Clinical course and treatment of the present case. Brain MRI (DWI) showing cerebral septic embolus and ventriculitis (arrows), and the small spleen (arrowhead). (b) Relationship between splenic size and age. Open circles show average splenic size of healthy subjects, while filled triangles and squares indicate pneumococcal meningitis patients with or without sinusitis, respectively.