Korean Journal of Pediatrics Vol. 52, No. 4, 2009
DOI : 10.3345/kjp.2009.52.4.508
■ Case report ■

A case of fatal pneumococcal 19A meningoencephalitis despite administration of seven-valent pneumococcal conjugate vaccines

Ah Rum Heo, M.D., Jun Hwa Lee, M.D.

Department of Pediatrics, Masan Samsung Hospital, Sungkyunkwan University School of Medicine, Masan, Korea

= Abstract =

Streptococcus pneumoniae is a major cause of serious invasive diseases in children, especially in young infants, valent pneumococcal conjugate vaccine (PCV7) is believed to prevent invasive pneumococcal pneumonia and mening young children. However, recently, the incidence of non-PCV7 serotype has increased after PCV7 vaccination. A old female patient presented at our emergency room with mental change and lethargy. Three days previously, she veloped fever and vomiting. After being admitted, she rapidly progressed to coma and brain death despite prompt a sive supportive treatment. She expired 20 days after admission with a final diagnosis of pneumococcal 19A (non-P type) meningoencephalitis despite having received PCV7 (Prevenar®) vaccinations on three occasions. The author r first fatality due to pneumococcal 19A meningoencephalitis in Korea and provides a brief review of the literatu
J Pediatr 2009;52:508-511)

Key Words : *Streptococcus Pneumonia* Infections, Meningoencephalitis, Serotype 19A

Introduction

Streptococcus pneumoniae is a major cause of serious invasive disease in both adults and children, but especially in young infants. The PCV7 is believed to prevent invasive pneumococcal pneumonia and meningitis in young children[1], and mass vaccination was adopted in Korea during 2003. However, the prevalence of non-PCV7 serotypes has since increased. In the present case, a 14 month-old female patient succumbed to a pneumococcal 19A meningoencephalitis after 3 previous PCV7 (Prevenar®) vaccinations. This report describes the first fatal case of pneumococcal 19A meningoencephalitis despite PCV7 vaccination in Korea and provides a brief review of the literature.

Case report

A 14-month-old female was admitted due to complaints of mental change and lethargy via our Emergency department. Three days previously, she had developed fever and vomiting. She had been taken to a private pediatric clinic two days previously and prescribed conservative medication. However, on the day of admission, she developed a high fever (39℃), vomiting and lethargy.

Her medical history included a normal spontaneous vaginal delivery at 40 weeks with a weight of 3,100 g. She had normal developmental milestones, her medical history was unremarkable, and her family history non-specific. She was the only child. Her vaccination history was complete for age and included three PCV7 injections.

At admittance, she had a stupored mental condition with a dilated left pupil. A laboratory investigation and brain CT were initiated promptly. The brain CT revealed slight brain edema (Fig. 1), and an immediately following CSF study revealed a turbid color, and a CSF pressure of 38 cmH_2O, a cell count 46/μL with neutrophil predominance (70%), CSF protein 317 mg/dL, CSF/serum glucose 10/120 mg/dL, and gram positive cocci by CSF gram staining. Other laboratory evaluations revealed; hemoglobin 13.1 g/dL, hematocrit 36.3%, WBC 5,100/μL, platelets 77,000/μL, sodium 139.9 mmol/L, potassium 3.92 mmol/L, GOT/GPT 124/26 IU/L, BUN/Cr 9.4/0.4 and CRP 428.5 mg/L.

Intravenous vancomycin 60 mg/kg/24hr, ceftriaxone 100

Received : 9 September 2008, Revised : 6 November 2008,
Accepted : 9 November 2008
Address for correspondence : Jun Hwa Lee, M.D
Department of Pediatrics, College of Medicine, Sungkyunkwan Univers
Masan Samsung Hospital, 50, Hapsung 2-Dong, Masan-si, 630-723,
Gyeongsangnam-do, Korea
Tel : +82.55-290-6140, Fax : +82.55-290-6044
E-mail : ljh3643@skku.edu, ljh3643@hanmail.net

mg/kg/24hr, acyclovir 11 mg/kg/24hr and initial mannitol 0.85 g/kg were promptly administered under the impression of bacterial meningoencephalitis. The next day, she developed a cyanotic skin color, full fixation of both pupils, a comatose mentality, and stopped breathing. Intubation, mechanical ventilation, and massive supportive treatment were instituted. A repeat brain CT evaluation, revealed whole ventricle collapsed and severe brain edema (Fig. 2). Brain MRI could not performed because of the severity of her condition.

On day 3 post-admission, a follow up CSF study failed, which we attribute to an obstructed CSF circulation due to severe brain edema. The comatose mentality persisted. Initial CSF latex agglutinin testing was wholly negative (this test includes *streptococcus B*, *hemophilus influenzae type b*, *Streptococcus pneumoniae*, *Neisseria meningitides* ACY W135, and *Neisseria meningitides B/Escherichia coli K*[1]).

Five days post-admission, streptococcus pneumoniae were isolated from blood and CSF specimen in blood agar media, and susceptible to cephalothin, teicoplanin and vancomycin. Portable electroencephalography (EEG) revealed excessively suppressed background activity, indicating brain death (Fig. 3).

The initial CSF sample was sent to National Institute of Health, Korea Centers for Disease Control and Prevention for confirmation and serotyping of *Streptococcus pneumoniae*. The initial CSF sample was sent to National Institute of Health, Korea Centers for Disease Control and Prevention for confirmation and serotyping of *Streptococcus pneumoniae*. The isolate was confirmed as *Streptococcus pneumoniae* by conventional methods including colony morphology on blood agar plate, gram staining, bile solubility, optochin susceptibility and positive slide agglutination (Slidex Pneumokit II, bioMérieux, France). Serotyping was performed by the Quellung reactions with pool and serotype/group-specific antisera provided by the Staten Serum Institute, Denmark. *Streptococcus pneumoniae* isolate represented serotype 19A.

She expired despite massive supporting care 20 days after admission.

Discussion

Streptococcus pneumoniae is a major bacterial pathogen in children and adults. The World Health Organization estimated that 1 million children aged below 5 years of age die of pneumococcal pneumoniae, meningitis, and/or sepsis annually[2]. There are 91 known pneumococcal serotypes, the last of which was only discovered recently. However, 23 serotypes are known to produce the majority of cases of

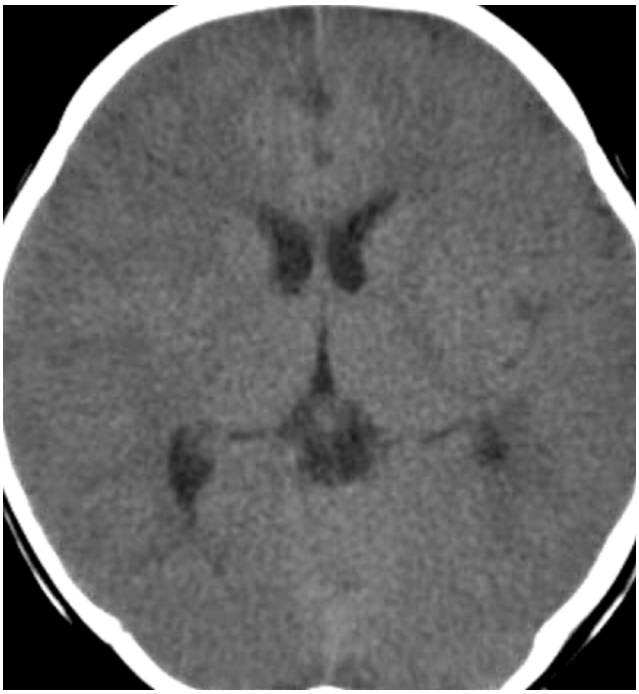

Fig. 1. Initial brain CT images show ill-defined low-density lesions in the cerebral cortex and subcortical regions and effacement of brain sulci.

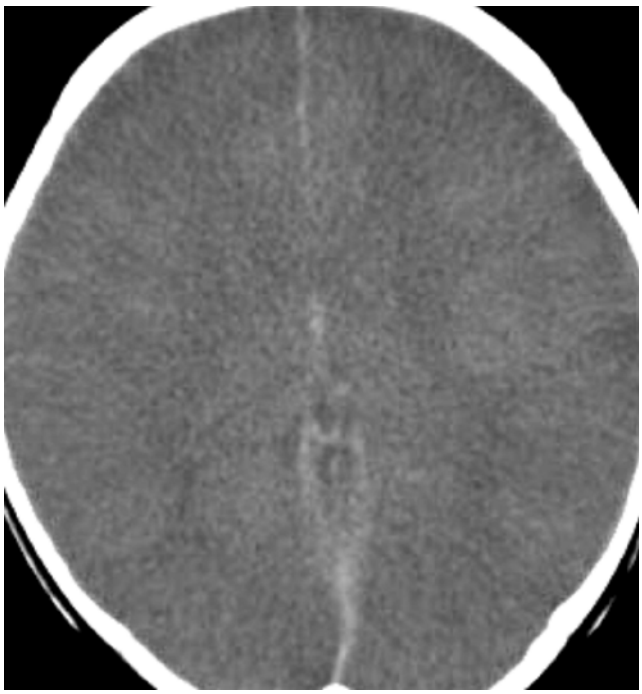

Fig. 2. Follow-up brain CT images on the second day of admission show diffuse brain swelling with ventricle collapse.

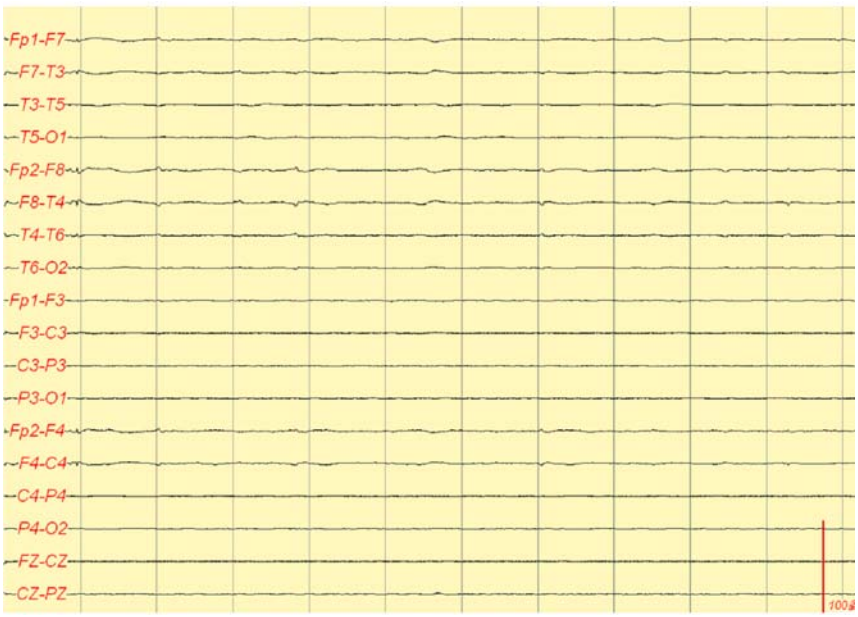

Fig. 3. Electroencephalogram at 5 days post-admission shows excessively suppressed background activity, indicating brain death.

invasive pneumococcal disease (IPD)[3].

Studies conducted in the United States on PCV7 and serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, showed that the vaccine is safe and effective at preventing IPD in children. In addition, a trial of the 9-valent conjugate pneumococcal vaccine, which includes also serotypes 1 and 5, concluded that the vaccine is effective at reducing mortality in Gambian children[2].

Before PCV7 was introduced in the United States in 2000, the seven covered pneumococcal serotypes caused 80% of IPD cases among young children. but after this introduction, overall IPD coverage rates among children aged below 5 years were 77% lower in 2005, and an estimated 13,000 fewer cases of IPD occurred, compared with the years preceding vaccine introduction in 1998 to 1999 according to the CDC in the United States[4], and several other reports have also concluded that percentage coverage rates fell to 40-96%[5-9].

In addition, some have reported that PCV7 might cross-protect against serotype 19F. Lee et al. reported that the structures of the pneumococcal capsular polysaccharides in types 19F and 19A are identical[10]. Furthermore, Jakobsen et al. reported that PCV7 induced cross-protective immunity versus serotype 19A in a murine pneumococcal pneumoniae model[11].

Recently, Singleton et al. reported that serotype 19A was responsible for 28.3% of IPD cases in rural native Alaskan children below 2 years of age from 2004 to 2006[12]. In addition, recent studies conducted in Massachusetts and Texas concluded that a multidrug-resistant serotype 19A is becoming an important cause of IPD[13, 14].

Farrell et al. studied 0 to 14 year old children in the USA from 2000 to 2004, and found that the proportion of isolates covered by PCV7 serotypes decreased from 65.8% over the 1st year, to 34.7% and 27.0% during the 3rd and 4th study years. Furthermore, similar changes were observed at regional and state levels. The most common serotypes in the 4th year were nonvaccine serotypes, i.e., 19A (19.0% of all isolated), 6A (7.8%), 3 (7.6%), 15 (6.3%) and 35B (5.8%) and the vaccine serotype 19F (12.7%)[15].

Choi et al. studied Korean children younger than 5 years of age and reported that the proportion of serotype 19A isolated in IPD is increasing, that is, from 0% in 1991-1994, 8-10% in 1995-2000, 26% in 2001-2003, and 20% in 2004-2006[16]. Moreover, during 2004-2006 vaccine coverage was less than 25%.

The present report describes the case of a patient who developed fever, vomiting, and mental change caused by a non-PCV7 serotype 19A pneumococcal meningoencephalitis despite having received three PCV7 vaccinations. She was treated promptly with massive antibiotic administrations and supportive care, but nevertheless rapidly progressed to coma and death.

한 글 요 약

7가 폐구균백신 접종에도 치명적인 폐구균 19A 수막염 1예

성균관대학교 마산삼성병원 소아청소년과

허아름 · 이준화

폐구균(*Streptococcus pneumoniae*)은 소아, 특히 어린 영아에서 심한 침습성 질병을 일으키는 중요한 원인균이다. 2003년부터 우리나라에서 접종하기 시작한 7가 폐구균백신(PCV7)은 소아에서 침습성 폐구균성 폐렴과 수막염을 예방하는 것으로 알려져 왔다. 그러나 최근 7가 폐구균백신을 접종한 이후부터 비7가 폐구균 혈청형(non-PCV7 serotype) 감염 발생률이 증가하고 있다.

14개월 된 여아가 내원 3일 전부터 열과 구토가 있었으나 증상 치료만 하고 있던 중 갑작스런 의식불명과 기면(lethargy)으로 응급실로 내원하였다. 입원 후 즉각적인 진단과 치료를 시행했음에도 불구하고 환자는 빠르게 혼수와 뇌사 상태로 진행하였다. 환자는 이전에 3회의 7가 폐구균백신을 접종하였으나 최종 진단은 비7가 폐구균 혈청형인 폐구균 19A 수막염이었고, 입원 20일째 사망하였다. 이는 한국에서 문헌상 보고된 적이 없는, 폐구균 19A 혈청형 수막염으로 사망한 첫번째 증례이므로 이에 보고하는 바이다.

References

1) Albrich WC, Baughman W, Schmotzer B, Farley MM. Changing characteristics of invasive pneumococcal disease in Metropolitan Atlanta, Georgia, after introduction of a 7-valent pneumococcal conjugate vaccine. Clin Infect Dis 2007;44:1569-76.
2) Munoz-Almagro C, Jordan I, Gene A, Latorre C, Garcia-Garcia JJ, Pallares R. Emergence of invasive pneumococcal disease caused by nonvaccine serotypes in the era of 7-valent conjugate vaccine. Clin Infect Dis 2008;46:174-82.
3) Brueggemann AB, Pai R, Crook DW, Beall B. Vaccine escape recombinants emerge after pneumococcal vaccination in the United States. PLoS Pathog 2007;3:e168.
4) Centers for Disease Control and Prevention(CDC). Invasive pneumococcal disease in children 5 years after conjugate vaccine introduction--eight states, 1998-2005. MMWR Morb Mortal Wkly Rep 2008;57:144-8.
5) Kaplan SL, Mason EO Jr, Wald ER, Schulze GE, Bradley JS, Tan TQ et al. Decrease of invasive pneumococcal infections in children among 8 children's hospitals in the United States after the introduction of the 7-valent pneumococcal conjugate vaccine. Pediatrics 2004;113:443-9.
6) Whitney CG, Pilishvili T, Farley MM, Schaffner W, Craig AS, Lynfield R, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study. Lancet 2006;368:1495-502.
7) Poehling KA, Talbot TR, Griffin MR, Craig AS, Whitney CG, Zell E, et al. Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. JAMA 2006;295:1668-74.
8) Von Kries R, Hermann M, Al-Lahham A, Siedler A, Reinert RR. Will the 7-valent pneumococcal vaccine have a similar impact on all invasive pneumococcal infections in children in Germany as in the Kaiser Permanente Trial? Eur J Pediatr 2002;161(Suppl 2:)S140-3.
9) Bricks LF, Berezin E. Impact of pneumococcal conjugate vaccine on the prevention of invasive pneumococcal diseases. J Pediatr (Rio J) 2006;82(Suppl 3):67-74.
10) Lee CJ, Fraser BA. The structures of the cross-reactive types 19 (19F) and 57 (19A) pneumococcal capsular polysaccharides. J Biol Chem 1980;255:6847-53.
11) Jakobsen H, Sigurdsson VD, Sigurdardottir S, Schulz D, Jonsdttir I. Pneumococcal serotype 19F conjugate vaccine induces cross-protective immunity to serotype 19A in a murine pneumococcal pneumonia model. Infect Immun 2003;71:2956-9.
12) Singleton RJ, Hennessy TW, Bulkow LR, Hammitt LL, Zulz T, Hurlburt DA, et al. Invasive pneumococcal disease caused by nonvaccine serotypes among Alaska native children with high levels of 7-valent pneumococcal conjugate vaccine coverage. JAMA 2007;297:1784-92.
13) Pelton SI, Huot H, Finkelstein JA, Bishop CJ, Hsu KK, Kellenberg J, et al. Emergence of 19A as virulent and multidrug resistant pneumococcus in Massachusetts following universal immunization of infants with pneumococcal conjugate vaccine. Pediatr Infect Dis J 2007;26:468-72.
14) Messina AF, Katz-Gaynor K, Barton T, Ahmad N, Ghaffar F, Rasko D, et al. Impact of the pneumococcal conjugate vaccine on serotype distribution and antimicrobial resistance of invasive streptococcus pneumoniae isolates in Dallas, TX, children from 1999 through 2005. Pediatr Infect Dis J 2007;26:461-7.
15) Farrell DJ, Klugman KP, Pichichero M. Increased antimicrobial resistance among nonvaccine serotypes of Streptococcus pneumoniae in the pediatric population after the introduction of 7-valent pneumococcal vaccine in the United States. Pediatr Infect Dis J 2007;26:123-8.
16) Choi EH, Kim SH, Eun BW, Kim SJ, Kim NH, Lee JH, et al. Streptococcus pneumoniae serotype 19A in children, South Korea. Emerg Infect Dis 2008;14:275-81.