Three Cases of Occult Pneumococcal Bacteremia

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Introduction

Streptococcus pneumoniae (*S. pneumoniae*) is the most frequent bacterial cause of otitis media and pneumonia and the third most common cause of meningitis in childhood¹⁾. It has been recently reported that this organism is also the cause of occult bacteremia in febrile children especially those under 2 years of age²⁾⁻⁶⁾. "Occult" bacteremia means bacteremia occurring in the febrile children without any apparent foci of infection or with trivial infections such as upper respiratory tract infection (URTI). Bacteremia is distinguished from sepsis by the absence of evidence of organ failures such as cardiovascular failure. Few cases of occult bacteremia have been reported in Japan. We present here three cases of occult bacteremia and discuss how to detect the children with occult bacteremia among febrile outpatients and how to prevent the subsequent complications.

Case 1

A 9-month-old previously healthy boy was brought to our hospital because of fever and ill temper at 1 o'clock. The temperature was 40°C, the respiration rate was 60/min, and the pulse was 180/min. Physical examination revealed a slightly injected throat. No moist rales were detected in the lung fields. Tympanic membrane was not injected. A chest roentgenogram showed no infiltration. Peripheral blood was obtained for a complete blood count and for blood cultures. The white blood cell (WBC) count was 14,800/mm³. We diagnosed him as having URTI. We administered a ceftizoxime suppository and reexamined him in the outpatient clinic before noon on that day. At the second visit, the temperature was 38°C and tachypnea had disappeared. Physical examination again revealed no apparent focus of infection. We prescribed oral cefaclor. Two days after the initial visit, the blood culture was shown to be positive for *S. pneumoniae*, and the patient was reviewed again the next day. He had neither fever, tachypnea, nor irritability and his appetite was good, so we didn't perform any further treatment or studies.

Case 2

A 1-year-old girl was admitted to our hospital because of a generalized tonic-clonic convulsion with fever. She had had no previous episodes of convulsion and no family members had epilepsy. The convulsion continued for 2 minutes without lateralization. She had suffered from cough and rhinorrhea for the previous 2 days. On admission, the temperature was 39.2°C and her consciousness was clear. Physical examination revealed only a slightly injected throat. No abnormal neurological findings were shown. The WBC was 20,300/mm³ with 51% neutrophils and the C-reactive protein (CRP) was 0.4 mg/dl. Cerebrospinal fluid showed no pleocytosis and normal levels of glucose and protein. Her electroencephalogram was also normal. We diagnosed her as having a simple febrile convulsion associated with URTI. She was treated with antipyretics and erythromycin. On the 2nd hospital day, the cultures of blood and throat swab

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Table Characteristics of the patients with pneumococcal bacteremia

Case number	Patient		Peak fever (°C)	White blood cell count ($\times 10^3/\text{mm}^3$)	Initial diagnosis	Antibiotic treatment	Day on which blood culture was positive
	Age (month)	Sex					
1	9	M	40.0	14.8	URTI	suppository, day 1 oral, day 2	3
2	12	F	39.2	20.3	febrile convulsion with URTI	oral, day 1	3
3	9	F	39.0	13.4	FUO	oral, day 2 intravenous, day 9	11

URTI: Upper respiratory tract infection FUO: Fever of unknown origin

obtained on admission became positive for *S. pneumoniae*. However, she had already become afebrile, so we performed no additional treatment.

Case 3

A 9-month-old girl was admitted to our hospital because of fever of unknown origin persisting for 8 days. She had suffered mild rhinorrhea and had been treated with oral antibiotics and antiepileptics. On admission, the temperature was 39°C but she appeared well. Physical examination revealed only a slightly injected throat. The WBC was 13,400/mm³ with 36% segmented neutrophils and 21% band neutrophils, and the CRP was 7.7 mg/dl. To determine the focus of the infection, the antibiotic treatment was discontinued for 24 hours and, thereafter, cultures of blood, throat swab, urine, and stool were obtained. Then cefzoname was administered intravenously. *S. pneumoniae* was isolated from blood on 2 days later, when she was afebrile. On the fifth hospital day, the otomicroscopic examination showed a trivially injected tympanic membrane. It was questionable whether this had been the focus of infection. Antibiotic treatment was continued until the CRP became negative. She was discharged on the 7th hospital day without any sequelae.

Discussion

S. pneumoniae is the most frequent bacterial cause of otitis media and pneumonia in childhood¹⁾. It has been recently reported that this organism is also the cause of occult bacteremia in febrile children especially those under 2 years of age^{2)~6)}. Because a small number of the affected children develop the serious complications such as meningitis, how to detect occult bacteremia have been also earnestly discussed^{2)~6)}. Among children with occult bacteremia, about 85% of positive blood cultures yield encapsulated bacteria, including *S. pneumoniae* and *Hemophilus influenzae* (*H. influenzae*)⁶⁾. Teele *et al.*²⁾ reported that the majority of such bacteremia is caused by *S. pneumoniae* (approximately 65%) with *H. influenzae* accounting in about 25%, and other bacteria for the rest. In Japan, few cases of occult bacteremia have been reported⁷⁾⁸⁾. We suppose that this is firstly because blood cultures are seldom obtained at the first visit, secondly because antibiotics are widely prescribed for febrile outpatients, and thirdly because this clinical entity is not enough known by physicians. Since Besly⁹⁾ first described it in 1967, there have been many reports in the United States^{2)4)~6)}. Nevertheless in other countries including Britain³⁾ and Japan⁷⁾⁸⁾, this disease is not so common as in the US. The frequency of the occult bacteremia may thus have regional differences.

To diagnose the occult bacteremia is difficult because of the lack of the specific physical findings. A number of physical and laboratory findings have been reported to increase the risk of bacteremia. Teele *et al.*²⁾ listed the risk factors for occult bacteremia, including an age between 6 to 24 months, a fever of over 38.9°C, and a WBC of over 15,000/mm³. In children in these features, they reported the frequency of occult

bacteremia to be about 4%. Many reports have noted the significance of these three factors^{4)~6)}. In our cases, these three factors were also positive except for the WBC of case 1 and case 3. Other additional risk factors, including a raised CRP and erythrocyte sedimentation rate were reported²⁾⁵⁾¹⁰⁾. Nelson¹¹⁾ used clinical observation scores while McCarthy *et al.*¹²⁾ investigated the physician's assesment of activity level, feeding, and sleeping patterns, etc. McIntyre *et al.*³⁾ reported that 10 out of 29 occult bacteremia cases had been admitted because of a simple febrile convulsion initially. They suggested that occult bacteremia might be an important cause of febrile convulsions, especially under 4 years of age. In fact, a febrile convulsion was associated with bacteremia in our case 2. The association of febrile convulsions and occult bacteremia should be further evaluated in a larger study. To detect the children with occult bacteremia, we believe that it is important to use the combination of these physical and laboratory risk factors and to obtain blood culture if occult bacteremia is suspected.

There remains a controversy regarding whether all children with occult bacteremia should be treated or not. In many cases occult bacteremia resolved self-limitedly, and in only a small number of patients develop subsequent meningitis or other serious infections²⁾⁶⁾. The risk of these complications remains uncertain. *S. pneumoniae* isolated from our three cases were very sensitive to used antibiotics by disc method (minimum inhibitory concentrations were not examined). However, case 1 and case 2 may have improved spontaneously. Teele *et al.*²⁾ recommended that the febrile children at risk should be treated with antibiotics. But in their report, 2 of the 51 children not treated at the first visit developed subsequent meningitis, while 2 of the 47 given treatment also developed meningitis. Recent data also suggest that oral antibiotic therapy may be ineffective in preventing infectious sequelae of bacteremia¹³⁾. We believe that regardless of whether antibiotics are given or not, such children should be carefully observed either at home or in the hospital, and should be reexamined until they become afebrile.

There is a general agreement that children with asplenia or immunodeficiency must be treated with antibiotics soon after they develop fever. Pneumococcal bacteremia in these high-risk children may progress to serious complications. Vaccine against pneumococcal polysaccharides, now available, should be indicated for such children. Oguri¹⁴⁾ examined the drug-susceptibilities of *S. pneumoniae* obtained from clinical specimens and reported that approximately 40 to 70% of the strains were resistant against tetracycline and chloramphenicol, and that 0.01% were resistant against β -lactam antibiotics. Because β -lactam-resistant strains were usually isolated from the patients under treatment with β -lactam antibiotics¹⁴⁾, we think that even now penicillins and cepheems are effective to *S. pneumoniae* isolated from the children at the first visit to outpatient clinic.

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潜在性肺炎双球菌菌血症の3例

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潜在性肺炎双球菌菌血症 (occult pneumococcal bacteremia) の3症例を報告した。3例とも臨床症状だけでは菌血症の存在は推測できず、初診時の診断は、それぞれ急性上気道炎、急性上気道炎に合併した熱性痙攣、不明熱であった、3例とも年齢は2歳以下、体温は39℃以上、白血球増多が認められ白血球数はそれぞれ14,800/mm³、

20,300/mm³、13,400/mm³であった。3症例とも抗生物質の投与により合併症なく治癒した。本症の報告はわが国では稀である。発熱を主訴とする外来患者に対して、年齢、発熱の程度、白血球数などの危険因子を組合わせ、本症が疑われる場合には血液培養を施行することが肝要と考えられた。