Occasional Review

Occult pneumococcal bacteraemia and febrile convulsions

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Abstract

Over two years 29 children had bacteraemia due to Streptococcus pneumoniae at this hospital. In 15 previously healthy children the site of infection could not be identified, and in most of them, bacteraemia was not suspected clinically. All 15 had high total white cell ($\geq 17 \times 10^9$/l) and neutrophil ($\geq 11 \times 10^9$/l) counts. Twelve children were under 4 years of age, and of these, 10 had been admitted because of a simple febrile convulsion and one had a prolonged febrile convulsion.

Occult pneumococcal bacteraemia has been reported in the USA for more than 10 years, but no series has been reported from the United Kingdom. Occult pneumococcal bacteraemia may be an important cause of febrile convulsions. Persisting bacteraemia and the development of focal infections, including pneumococcal meningitis, have been reported. Meningitis did not occur after occult bacteraemia in our patients. Studies to date have been retrospective, and thus the true incidence of the complications and the best treatment are not clear. A prospective study of children with febrile convulsions could provide answers.

Introduction

Pneumococcal bacteraemia occurring with focal disease, such as pneumonia or meningitis, is well recognised. Since Belsey first described it in 1967[1] there have been many reports in the United States of pneumococcal bacteraemia occurring without an apparent site of infection. It has been referred to as occult pneumococcal bacteraemia.[2-15] The results of studies in the US, done mostly on outpatients, showed that occult pneumococcal bacteraemia occurred frequently in young febrile children whose illnesses seemed trivial, and thus blood samples were not taken for culture. The only reference to occult pneumococcal bacteraemia in Britain suggested that it was not common.[16]

In the last half of 1981 in our unit blood cultures were frequently positive for *Streptococcus pneumoniae*. We decided to review all cases of bacteraemia in the hospital for 1980-2. We wished to define further the incidence and features of pneumococcal bacteraemia in a group of inpatients in Britain.

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Patients and methods

The results of cultures of all blood samples taken at this hospital during the two years 1980-2 were obtained from the records in the bacteriology department. The case notes of all children whose blood cultures were positive for *Strep pneumoniae* were examined to identify common features in presentation, course, and results of investigations.

Samples of venous blood were taken for all cultures, and these were inoculated into one bottle only. Bloodgrow (Medical Wire and Equipment Ltd, Bath, UK), a beef extract-glucose broth with para-aminobenzoic acid and agar suitable for aerobic and anaerobic culture, was used in all cases. Subcultures were made if turbidity was noted or at seven days on blood agar broth aerobically and anaerobically and also on chocolate agar with CO_2. *Strep pneumoniae* was identified first by morphological appearance and then confirmed by optochin-disc sensitivity and bile-salt solubility.

Results

During the two years 2919 blood samples were cultured. Of these, 205 (7%) grew an organism, and 110 (4%) were considered to be pathogenic to the patient. Enterobacteriaceae (28%) were the largest group of organisms, and two-thirds of these were *Escherichia coli*. *Strep pneumoniae* was the organism found most often (26%). The 29 patients with pneumococcal bacteraemia were divided into groups. Only four patients had underlying diseases. Three were neutropenic (one with lymphosarcoma, one with an uncharacterised reticulosis, and one with an undiagnosed illness), and one patient had hypogammaglobulinaemia. Two of these four patients had pneumonia and in two the site of infection could not be identified.

Of the remaining 25 previously healthy children, the site of infection was known in 10: six had pneumonia, two meningitis, one peritonitis, and one pericarditis. The other 15 had no identified site of infection, and these 15 children with occult pneumococcal bacteraemia have been divided into two groups according to age. Table I summarises the clinical features of the children under 4 years of age. All were feverish, and nine had temperatures above 38·5°C on admission. In all except two (patients 3 and 11) the reason for admission was a simple febrile convulsion. All except three (patients 2, 3, and 11) had prodromal upper respiratory tract or gastrointestinal symptoms. In nearly all an initial diagnosis of viral upper respiratory tract infection was made from the history and physical signs, such as pharyngeal injection and nasal discharge. One child (patient 12) developed unilateral otitis media two days after admission. In none of the others was the site of infection detected. In this latter group only two patients (6 and 11) were ill enough to require intravenous antibiotics. Both recovered uneventfully. All patients had lumbar punctures performed, and in all the cell counts were normal and the cultures negative.

The three patients aged over 4 years (table II) had an illness of sudden onset with no prodromal symptoms. The symptoms at presentation were fever, headache, vomiting, and drowsiness without meningism. The results of lumbar punctures were normal in all three. The first two patients were well and without fever within 48 hours and were discharged without treatment before the results of blood cultures were known. The third patient, a 10-year-old girl, deteriorated within 12 hours of admission with coagulopathy, haematemesis, and hyponatraemia. Encephalitis was the initial diagnosis. On admission the chest radiograph was normal, but a further film taken six days later showed consolidation of the left upper lobe. The initial blood culture

TABLE I—*Occult pneumococcal bacteraemia in children aged under 4 years*

Patients			Temperature on admission (°C)	Total white cell count (× 10⁹/l)	Neutrophil count (× 10⁹/l)	Initial diagnosis	Antibiotic treatment	Day on which blood culture was positive
Sex		Age (months)						
1	M	8	38·9	23·0	15·8	Viral URTI; simple convulsion	Oral, day 1	3
2	M	13	40·2	34·0	23·8	Viral URTI; simple convulsion	None	5
3	M	14	38·9	17·0	11·0	Viral illness	None	3
4	F	15	38·4	33·0	26·4	Viral URTI; simple convulsion	Oral, day 3	3
5	F	16	40·0	24·0	16·8	Viral URTI; simple convulsion	Intramuscular, day 1	2
6	M	22	38·6	51·0	39·8	Viral illness; multiple convulsions	Intravenous, day 2	3
7	M	24	39·9	30·0	24·0	Viral URTI; simple convulsion	Oral, day 1	2
8	F	24	39·0	32·0	22·4	Viral URTI; simple convulsion	Oral, day 3	3
9	F	24	38·3	34·0	27·2	Viral URTI; simple convulsion	Oral, day 2	5
10	M	38	39·0	18·0	14·4	Viral URTI; simple convulsion	None	2
11	M	40	39·5	24·0	21·8	?Meningitis; prolonged convulsion	Intravenous, day 1	3
12	M	42	37·7	26·0	21·0	Viral URTI; simple convulsion	Oral, day 2	3

URTI = Upper respiratory tract infection.

TABLE II—*Occult pneumococcal bacteraemia in children aged over 4 years*

Patient		Temperature on admission (°C)	Total white cell count (× 10⁹/l)	Neutrophil count (× 10⁹/l)	Presentation	Initial diagnosis and course	Day on which blood culture was positive
Sex	Age (years)						
M	4·5	38·0	34·0	30·0	Ill 8 hours, no fever, no headache, no vomiting, no drowsiness	Viral meningitis or a viral illness, discharged day 4, no treatment	5
M	6·5	38·8	28·0	24·6	Ill 12 hours, no fever, no headache, no vomiting, no drowsiness	Viral meningitis or a viral illness, discharged day 2, no treatment	4
F	10·5	39·9	29·0	20·0	Ill 8 hours, no fever, no headache, no vomiting, no drowsiness	Encephalitis, very ill by 12 hours, intravenous antibiotics day 2, pneumonia day 6	3

was sterile but one taken 12 hours after admission grew *Strep pneumoniae*.

This group of 15 patients with occult pneumococcaemia had total white cell counts $\geqslant 17 \times 10^9$/l and neutrophil counts of $\geqslant 11 \times 10^9$/l. All except two of the immunocompetent patients with focal infections also had similar cell counts. Cultures of nose, throat, and sputum were positive in 10 of 11 patients with occult bacteraemia but were positive in only two of eight patients with pneumonia.

Discussion

The incidence of bacteraemia in focal pneumococcal infections varies, and when bacteraemia occurs with pneumonia the incidence appears to be greater in adults (25-33%)[17] than in children (2-5%).[18] In contrast, occult pneumococcal bacteraemia is commoner in children than adults and is commoner in younger than older children. Furthermore, in almost all adults who have occult pneumococcal bacteraemia there is an underlying disease or diseases,[19] whereas this was true of only a few children in our study and in others.[4 8] We discuss the important features of the diagnosis and the course that occult pneumococcal bacteraemia took in our patients and refer to published reports.

PRESENTATION

We found that the subjective impression of toxicity is not an accurate indicator of occult pneumococcal bacteraemia.[1-3 5 6 8 13] Completing a questionnaire on the child's activity and combining this with a clinical assessment was more successful in identifying the children who were unlikely to be bacteraemic.[20] Clinical assessment alone poorly detected those who had occult bacteraemia. In our study most of the children aged under 4 years had prodromal upper respiratory or gastrointestinal symptoms and all but two had a simple febrile convulsion, features noted in earlier studies.[1-4]

In contrast, in the three children aged over 4 years the onset of illness was sudden, without a prodrome and with strikingly similar presenting symptoms. There have been few reports of occult pneumococcal bacteraemia in older children.[2 12] We report on only a few patients but their symptoms were similar and they had a normal lumbar puncture and neutrophil leucocytosis, which should lead to a suspicion of pneumococcal bacteraemia.

AGE

As in previous studies[2 4 5 7 11] most of our patients were under 4 years and nine of the 15 were under 2. Those at greatest risk are aged from 6 to 24 months. Cole *et al*[21] found a 10% incidence of recurrent episodes of pneumococcal bacteraemia in children who were first diagnosed when under 2 years, but no gross deficiency in concentrations of immunoglobulins or complement. Polyvalent pneumococcal vaccine is not very effective in this age group,[22] and it is tempting to suggest that there is a subtle immune deficiency related to age.

FEVER

All but one of our patients had a temperature $\geqslant 38$°C at presentation, with two-thirds being $\geqslant 39{\cdot}9$°C. All remained feverish for at least 24 hours after admission. The results of many studies[5 7 10 11 14] show that the incidence of bacteraemia increases linearly with a rise in temperature, and positive cultures may occur in over 20% of young children with temperatures $\geqslant 41$°C.[10 14] When the site of infection cannot be identified most will have pneumococcal bacteraemia.[5 7 8 10 11 13 14]

FEBRILE CONVULSION

Of all the children admitted in 1980-2 to the hospital with a febrile convulsion, 2·3% had occult bacteraemia. The true incidence is undoubtedly higher because four of the 11 children were from our unit, which is one of four units, and they presented in the last six months of 1981, during which we cultured blood in children with fevers more frequently than before. The only reported estimate of the incidence of bacteraemia in children with febrile convulsions is 6%,[23] which is similar to the incidence of bacteraemia with fever in the age group prone to febrile convulsions.[5 8 10 11] To use the figures from Nottingham,[24]

occult bacteraemia ranks fourth as a cause of febrile convulsions after upper respiratory tract infection, tonsillitis, and otitis media. Our figure of 2% indicates that it is a commoner cause of febrile convulsions than meningitis or urinary tract infection.

Our patients with febrile convulsions may probably be compared to those in the North American series, though they do not send patients with simple febrile convulsions to hospital. Furthermore, blood is not often cultured for these children.[25] Indeed, of four recent reviews[24 26-28] three,[26-28] including the consensus statement of the National Institutes of Health, did not mention blood cultures.

WHITE CELL COUNTS

The results of a retrospective study of over 900 children[29] showed that a segmented neutrophil count $\geqslant 10 \times 10^9$/l or a band neutrophil count $\geqslant 5 \times 10^9$/l increased the risk of a severe bacterial infection to 80%. Others have reported that a white cell count of $\geqslant 15 \times 10^9$/l can predict severe infection.[7 10] All of our patients with occult bacteraemia had high white cell and neutrophil counts though none had raised band counts. Ten of our patients with focal infection, who had been well before, also exceeded these limits.

Some dispute whether white cell counts indicate bacteraemia.[14 20 30] Others have found both a total white cell count $\geqslant 15 \times 10^9$/l and a neutrophil count $\geqslant 10 \times 10^9$/l in most bacteraemic children.[2-4 13 15] In at least 75%[2-4 15] of children with pneumococcal bacteraemia cell counts exceeded these levels.

By combining age, temperature, and white cell count it is possible to delineate a group of children with a very high incidence of bacteraemia. McGowan *et al*[5] found a 28% incidence of bacteraemia in children aged 7 to 14 months with temperatures $\geqslant 39{\cdot}5$°C and white cell counts $\geqslant 20 \times 10^9$/l. Baron and Fink[13] found a 40% incidence in a similar group of children by using more exacting criteria for white cell count. In the only prospective study in which blood was cultured for all patients[7] there was an incidence of 8·7% by using criteria similar to those of McGowan.[5]

OTHER INVESTIGATIONS

Cultures of superficial swabs from nose or throat were positive in only half our patients with positive blood cultures. As about 40% of healthy children have pneumococci in their upper respiratory tract,[31] the cultures from this site are neither specific nor sensitive for bacteraemia.

Teele *et al*[32] reviewed other diagnostic tests in pneumococcal bacteraemia.

OUTCOME

Occult pneumococcal bacteraemia may resolve spontaneously in a short time or persist, thus remaining unlocalised or leading to infections in soft tissue, the most important and serious of which is meningitis. Of our 15 patients, two had focal infections (otitis media and pneumonia) and none had meningitis, though in all lumbar punctures were done when blood samples were taken for culture. All recovered uneventfully. Five patients did not require antibiotic treatment and three were ill enough to require intravenous antibiotics before the results of blood culture were known.

Fourteen cases of meningitis are known to have occurred after occult pneumococcal bacteraemia. In the largest single series[9] were two cases of meningitis out of 51 patients, giving an incidence of 4%. In nine of the 14 reported cases the patient was already receiving antibiotic treatment when meningitis was diagnosed. In two patients this was oral treatment only, in four intramuscular plus oral, and in three intravenous. In no case was the dose as high as that normally used to treat meningitis. The failure of suboptimal antibiotic treatment to eradicate pneumococci from the cerebrospinal fluid has been noted.[16]

The pathogenesis of meningitis in occult bacteraemia is not clear. Bacteria may have seeded the cerebrospinal fluid but failed to produce an immune response at the time of initial lumbar puncture.[7 33] Santoshan and Moxon[34] found that all children with bacteraemia and meningitis had $> 10^4$ organisms per millilitre in the blood culture. A more recent study[35] used quantitative blood cultures routinely. Twenty of the 26 patients with pneumococcal bacteraemia and either upper respiratory infection or otitis media had fewer than 10 organisms per millilitre of blood, and five patients had 10-100 organisms per millilitre. All recovered uneventfully with or without antibiotics. One patient with otitis media had 640 organisms per millilitre and developed meningitis within 24 hours. Quantitative blood culture may be valuable for identifying children with occult pneumococcaemia at risk of complications.

Performing a lumbar puncture in a person who has bacteraemia may cause meningitis. Teele *et al*[36] found an important association between lumbar puncture during bacteraemic infection and meningitis that was most pronounced in children under the age of 1 year. Twenty years ago cisternal punctures done in dogs that had pneumococcal bacteraemia resulted in meningitis[37] if there were $\geqslant 10^2$ organisms per millilitre of blood. It would not be surprising if this was true in man because the degree of bacteraemia and lumbar puncture both have a part in the pathogenesis of meningitis. Few children with occult pneumococcaemia would be at risk of developing meningitis from lumbar puncture because most would have low bacterial counts in the blood.[35]

The best treatment for occult bacteraemia has not yet been established. Some suggest that because meningitis occurs high doses of intravenous penicillin should be given for at least two days.[2 6 8 38 39] Others say that no treatment should be given or that oral antibiotics may be sufficient for those who are well and without fever at follow-up.[9 12 32] The value of expectant treatment on the basis of the known risk factors for occult bacteraemia is also not clear. How serious the bacteraemic infection is may be the most important factor in finding the right treatment, and how to treat will undoubtedly become clearer as quantitative cultures of blood are more commonly analysed.

A large prospective study is needed to give an accurate incidence of the complications and to assess the value of early treatment in suspected occult bacteraemia. In the United Kingdom children with febrile convulsions are generally admitted to hospital and often receive a lumbar puncture. Some remain at home and are treated by their general practitioners. About 5% of all cases are bacteraemic. Febrile convulsions and pneumococcal infections commonly occur in young children seen in hospital and in general practice. We have shown that cultured blood has a higher positive yield than culture of cerebrospinal fluid or urine. Nevertheless, the danger of missing a case of meningitis justifies doing a lumbar puncture in a febrile child who has a convulsion. Moreover, we believe that blood should be cultured for children with a white cell count $\geqslant 15 \times 10^9$/l and a neutrophil count $\geqslant 10 \times 10^9$/l. We can make no recommendation about early treatment with penicillin. A multicentre prospective study of this large inpatient population could provide the answer to many of these unresolved problems.

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Letters to a Young Doctor

Careers outside hospital and general practice

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A great advantage of qualifying in medicine is that so many different careers are then open to you. There are between 50 and 60 specialties, so that a satisfying career is available for virtually every taste. There is no need for blinkered vision, believing that there are only the two mainstreams of general practice and hospital medicine. It is perhaps unfortunate that most graduates think only of these, though there is tremendous variety in each of them. Yet not everyone is happy in hospital medicine or general practice, nor is everyone successful in them. The reason may be a lack of motivation caused by inadequate understanding of oneself and one's vocation. You should not feel like a failure in recognising that the classic traditions of medical practice are not for you. You must recognise the immense complexity of medicine today in both its internal and its external relations. Doctors are needed at many points in the machinery to keep the whole of it functioning.

It is a curse of medicine that an informal snobbish hierarchy has developed, so that some occupations in medicine may appear intrinsically more important and worth while than others. Medicine is probably no worse in this than other vocations, but it may result in a scramble for places at the top of the hierarchy while other parts lack the manpower for their proper purposes, which have their place and importance. Indeed, the mainstream of medicine may very well depend on medical education, administration, journalism and communication, the pharmaceutical industry, military service, and many other activities.

In 1982 there were relative shortages of manpower in general

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