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The significance of group B streptococci in neonatal pneumonia*

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Abstract. Thirty-eight infants admitted to a neonatal intensive care unit because of pneumonia (14 patients) and pulmonary maladaption syndrome (PMA) (24 patients) were included in the study. Samples of potentially pathogenic, facultatively anaerobic bacteria were taken from the external ear, blood, throat, nasopharynx, umbilicus and gastric aspirates of the children, and from urethra and cervix of the mothers. Group B streptococci (GBS) and *Escherichia coli* were the only potentially pathogenic bacteria isolated from the infants. Out of 14 infants with pneumonia 11 (79%) harboured one of these bacteria, in contrast to 3 out of 24 (13%) with PMA ($P<0.001$). GBS was found in 8/14 infants with pneumonia and in 1/24 infants with PMA ($P<0.001$). The respective frequencies for *Escherichia coli* were 3/14 and 2/24 (not significant). The infant and/or the mother in 10/14 pneumonia cases harboured GBS, in contrast to 4/24 pairs in the PMA group ($P<0.001$). The levels of antibodies against GBS in sera of mothers to infants with pneumonia did not differ from the antibody levels in control sera (parturient GBS-carriers giving birth to healthy infants). The results gave evidence for an important manifestation of neonatal GBS-infection: pneumonia without septicemia. The incidence of the disease is estimated to be 1:25 parturient GBS-carriers. Finally, maternal fever, gestational age above 42 weeks, more severe respiratory difficulties and the occurrence of severe changes in fetal heart rate during the first stage of labour were found to be typical characteristics of pneumonia, as compared to PMA.

Key words: Streptococci group B - *Escherichia coli* - Neonatal pneumonia - Pulmonary disease

Introduction

Escherichia coli and group B streptococci (GBS) are important aetiological agents of neonatal septicaemia and meningitis, constituting together 80% of the bacteria isolated in these cases [12]. The infections are associated with a high mortality and usually present with respiratory difficulties within hours of birth [3]. In this context, it is of interest that a high incidence of pneumonia has been demonstrated in infants with GBS septicaemia, in retrospective investigations of X-rays and at autopsies in fatal cases [13, 17]. Frequently, the radiographic findings are initially indistinguishable from idiopathic respiratory distress syndrome (IRDS) [4, 19] and pulmonary maladaption syndrome (PMA) [14].

Many infants treated in neonatal intensive care units for pneumonia do not have bacteria in the blood, at least initially. The aetiology in these cases is often obscure, although GBS might be suspected for several reasons. Infants born to mothers harbouring GBS in the urine have a high incidence of pneumonia [18]. A relation between abnormal fetal heart rate [FHR] recordings as well as fetal blood pH values below 7.20, frequently early signs of pneumonia, and maternal carriage of GBS has been demonstrated [9]. Finally, infants of mothers who are urogenital tract carriers of GBS were reported to be more frequently transferred to neonatal intensive care units because of pneumonia, than infants born to non-carriers [11].

The present paper concerns a prospective study of the bacterial colonisation of infants with pneumonia, compared to infants with PMA. The results indicate an important manifestation of neonatal group B streptococcal infection; pneumonia without septicaemia.

Materials and methods

Infants. During the period June to November 1981, 38 infants admitted to the neonatal intensive care unit, University Hospital, Lund were included in a prospective study of pneumonia (14 patients) and PMA (24 patients). The criteria for recruitment were: (a) within 12 h of age signs of respiratory difficulties, i.e. tachypnea, cyanosis, nasal flare, intercostal retractions and/or grunting; and (b) a chest X-ray compatible with pneumonia or PMA. In typical cases, infants with pneumonia showed lobar or patchy infiltrates in both lungs and occasionally reticulogranularity or haziness, whereas the typical PMA or 'wet lung' picture showed streaked infiltrates or interstitial perivascular oedema and fluid in the fissures and occasionally haziness [14]. PMA was differentiated from IRDS by repeated evaluation of venous admixture or right-to-left shunt measurements, which increased during 0-24 h of age in IRDS, but decreased or were unchanged in PMA and pneumonia.

In many cases, it was difficult to differentiate between pneumonia and PMA on a roentgenological basis. A diagnosis of pneumonia was therefore given to children fullfilling the clinical and roentgenological criteria above, and concomitantly showing elevated blood values for C-reactive protein (CRP) ($\geqq 5$ mg/ml) and/or high percentage of non-segmented leukocytes and/or low number of platelets ($\leqq 10^5$/mm blood). On the other hand, infants with normal values in all three tests were considered to suffer from PMA.

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Mothers. All mothers had been checked during pregnancy at antenatal clinics and data relating to the pregnancy concerned were collected from these clinics. The obstetrical care at our clinic has been described previously [10].

Procedures for measuring and interpretations of FHR changes have also been described previously [15]. The following FHR-patterns were recorded as severe in the present study: tachycardia (>160 heart beats/min), bradycardia (<120 beats/min) and late decelerations appearing alone or in combination.

Bacteriological examinations. From all infants, specimens were collected with sterile cotton swabs from the external ear, throat, nasopharynx and umbilicus, and gastric aspirates were obtained. From each mother, two pairs of specimens were taken with sterile cotton swabs from urethra and cervix and one pair of specimens was placed in selective broth medium for culture of GBS [2]. With the exception of the latter specimens and the gastric aspirates, all specimens were transported to the laboratory in haematin agar tubes (within 24 h). Furthermore, at least one blood culture was taken from each infant.

The specimens were investigated for potentially pathogenic, facultatively anaerobic bacteria (e.g. GBS, Enterobacteriaceae, *Pseudomonas*-species, *Staphylococcus aureus* and upper respiratory tract pathogens) as described previously [7], whereas *S. epidermidis* and α-streptococci were considered to be normal flora and not registered.

Identification and serological grouping and typing of GBS were performed as previously described [5]. Serological typing of *Escherichia coli* for somatic, capsular and flagella antigens by agglutination and immunoelectrophoresis was kindly performed by the International *Escherichia* and *Klebsiella* Centre (WHO) with the use of previously published methods [23].

Quantitation of antibodies to GBS. Antibodies to GBS types Ia, Ib, II and III were measured in sera from all mothers using radioactively-labelled protein A; this method is useful for quantitation of IgG antibodies [6]. The results were compared to those obtained with sera from mothers harbouring types Ia, Ib, II and III GBS urogenitally (ten in each group) and giving birth to healthy infants. Each of these control sera were tested against the type of GBS found in the woman. The antibody levels in the control sera were against type Ia: 597–2863 cpm; against type Ib: 1001–2064 cpm; against type II: 627–1673 cpm; and against type III: 433–1692 cpm.

Statistical methods. Student's *t*-test was used to compare antibody levels in controls and mothers of infants with pneumonia. The other results were evaluated using Fisher's exact test (n.s. = not significant, $P<0.05$).

Results

Bacteriological findings. GBS and *Escherichia coli* were the only potentially pathogenic bacteria isolated from the infants with pneumonia and PMA. Out of 14 infants with pneumonia (79%) harboured one of these bacteria, in contrast to 3 out of 24 (13%) with PMA ($P<0.001$) (Table 1). GBS alone was found in 8 out of 14 (57%) infants with pneumonia and in 1 out of 24 (4%) of infants with PMA ($P<0.001$). The respective frequencies for *Escherichia coli* were 3/14 (21%) and 2/24 (8%) (n.s.). All blood cultures were negative.

Bacteriological findings in the infants with pneumonia and their mothers are compared in Table 2. Five out of eight mothers of infants harbouring GBS carried the same type of GBS as that isolated from their respective infant. Two out of three mothers of infants with *Escherichia coli* were urogenital carriers of *Escherichia coli*, the same type as isolated from their respective infants. Taken together, the infant and/or the mother in 13 out of 14 (93%) infant/mother pairs in the pneumonia cases harboured GBS or *Escherichia coli*, to be compared to 6 out of 24 (25%) in PMA-cases ($P<0.001$) (Table 1). For GBS alone, the respective frequencies were 10/14 (71%) and 4/24 (17%) and 4/24 (17%) ($P=0.001$) (Table 1).

Table 1. Neonatal pneumonia and pulmonary maladaption syndrome (PMA): recovery of group B streptococci (GBS) and *E. coli* from infants and their respective mothers

Infant/mother pairs	No. of infants with		*P*-value
	pneumonia	PMA	
Carrying GBS			
Both infant and mother	5	0	<0.01
Infant only	3	1	n.s.
Mother only	2	3	n.s.
Total No.	10	4	0.001
Carrying E. coli			
Both infant and mother	2	1	n.s.
Infant only	1	1	n.s.
Mother only	0	0	n.s.
Total No.	3	2	n.s.
Culture negative			
Total No.	1	18	<0.001
No. of infants investigated	14	24	–

Table 2. Bacteriological findings in the infants with pneumonia

Case No.	Birth-weight (g)	Gestational age (weeks)	Bacteriological findings in	
			infant	mother
1	3410	41	GBS type Ia	–[a]
2	3510	40	GBS type Ib	GBS type Ib
3	2630	37	GBS type Ib	GBS type Ib
4	1920	32	GBS type Ia	–
5	3450	41	GBS n.t.[b]	–
6	4390	43	GBS type II	GBS type II
7	4090	42	GBS type III	GBS type III
8	3220	44	GBS type Ib	GBS type Ib
9	4140	43	*E. coli* type 017 : K53 : H18 and 09 : K+ : H–	*E. coli* type 017 : K53 : H18
10	2925	41	*E. coli* type 06 : K–:H–	–
11	3510	39	*E. coli* type 06 K15 : H31	*E. coli* type 06 : K15 : H31
12	4310	41	–	GBS type II
13	3720	37	–	GBS type III
14	3520	42	–	–

[a] –= no potentially pathogenic bacteria recovered
[b] n.t. = not typable

Table 3. Isolation of group B streptococci (GBS) and *E. coli* from different sites of infants with neonatal pneumonia and maladaption syndrom (PMA)

Case No.	Diagnosis	Bacteria isolated	Culture from				
			ear	throat	umbilicus	gastric aspirate	nasopharynx
1	pneumonia	GBS type Ia	+[a]	+	+	−	+
2	pneumonia	GBS type Ib	−	−	+	−	−
3	pneumonia	GBS type Ib	+	+	−	−	+
4	pneumonia	GBS type Ia	+	+	+	+	+
5	pneumonia	GBS not typable	+	−	+	+	−
6	pneumonia	GBS type II	+	−	+	+	−
7	pneumonia	GBS type III	+	+	−	−	+
8	pneumonia	GBS type Ib	+	−	+	−	−
9	pneumonia	*E. coli* type 017;K53 : H18 and 09 : K+ : H−	+	+	−	+	−
10	pneumonia	*E. coli* type 06 : K− : H−	+	+	+	+	+
11	pneumonia	*E. coli* type 06 : K15 : H31	−	+	−	−	−
15	PMA	GBS type III	−	−	+	−	−
16	PMA	*E. coli* type 09 : K34 : H−	−	−	−	+	−
17	PMA	*E. coli* type /.33 : K− : H4	−	+	−	−	−
No. of cases positive			9	8	8	6	5

[a] + = positive; − = negative

Out of 11 culture-positive infants with pneumonia 9 were colonised at two or more sites with GBS or *Escherichia coli* whereas all three culture positive infants with PMA were colonised at one site only ($P<0.05$) (Table 3).

The type distribution among the GBS strains isolated from the infants with pneumonia and their mothers is shown in Table 2. This distribution did not differ significantly from the type-frequencies among healthy infants at our obstetrical department [8].

Serological findings. Sera from mothers of infants with pneumonia were tested for antibodies against the type of GBS isolated from the infant and/or the mother itself. The values of type-specific antibodies were in all cases within the range found in the control sera from mothers harbouring the respective type of GBS in the urogenital tract but giving birth to healthy infants. The values were for mothers of infants exposed to type Ia: 771–1192 cpm (control sera range: 597–2863); type Ib: 1233–2848 (control sera range: 1001–2064); type II: 630–789 (control sera range: 627–1673); and type III: 739–946 (control sera range: 433–1692). No statistically significant difference was found between the mothers of infants with pneumonia and the controls.

Clinical findings. Clinical data on the infants with neonatal pneumonia and PMA are shown in Table 4. No difference between the two groups were observed with respect to breech presentation, toxemia, fetal growth retardation, or diabetes mellitus; no cases of multiple pregnancies occurred among the mothers included. Furthermore, prematurity and caesarean sections were not associated more with one group than the other. However, three infants of mothers with intrapartum fever contracted pneumonia, whereas no fever was registered among the mothers of infants with PMA ($P<0.05$). Furthermore, three additional infants with a gestational age more than 42 weeks contracted pneumonia, in contrast to the absence of infants with gestational age above 42 weeks in the PMA-group ($P<0.05$).

Table 4. Comparison of some selected clinical data in infants with pneumonia and pulmonary maladaption syndrome (PMA)

Parameter	No. of infants with		*P*-value
	pneumonia	PMA	
High-risk pregnancy[a]	4	6	n.s.
Maternal fever (≧38.5° C) during labour	3	0	<0.05
Cesarean section	5	4	n.s.
Gestational age: <37 weeks	1	4	n.s.
>42 weeks	3	0	>0.05
Apgar score < 7: at one min	5	4	n.s.
at five min	2	0	n.s.
Tachypnea as single symptom	1	9	<0.05
No. of infants investigated	14	24	

[a] Breech presentation, toxemia, foetal growth retardation, multiple pregnancy and diabetes mellitus.

Reliable FHR-recordings were obtained from all infants with pneumonia and 14 with PMA. Severe FHR-changes were more frequent among the infants contracting pneumonia than among the infants with PMA (7/14 and 1/14, respectively; $P<0.05$).

The proportion of infants with low Apgar score did not differ between the pneumonia and the PMA-group (Table 4). The signs of respiratory difficulties registered were tachypnoe, cya-

nosis, intercostal retractions, alae nasi flutter and grunting 28 infants showed two or more of these symptoms, whereas 10 infants showed tachypnea as the only symptom. Nine of the latter patients contracted PMA (<0.05; Table 4).

Discussion

Our data demonstrated a strong association between neonatal pneumonia without septicaemia, and GBS. Thus, 8 (57%) out of 14 infants with pneumonia were colonised with GBS, compared with 1 (4%) out of 24 infants with PMA (Table 1); the overall colonisation rate of infants immediately after birth at our obstetrical department was 10% in 1978–79 [8]. Furthermore, 7 (50%) out of 14 mothers of infants with pneumonia were urogenital carriers of GBS (Table 2), whereas the 'normal' colonization rate of parturients in our district 16% in 1978–79 [8].

As concerns *Escherichia coli,* the material did not demonstrate a significant association with pneumonia, possibly because the number of patients studied was too small. The *Escherichia* genus is antigenically complex, up to date comprising some 170 somatic (O), 90 capsular (K) and 60 flagella (H) antigens. *Escherichia coli* capsular polysaccharide K1 has been strongly associated with neonatal meningitis [20]. This antigen is found with a lower frequency in strains from blood cultures of neonates without meningitis, and in strains from blood, urine and stool cultures from adults and rectal cultures from infants [22]. In accordance with these findings none of the *Escherichia coli* strains isolated in the present investigation carried the K1-antigen. Future examination of *Escherichia coli* strains from neonatal pneumonia will show whether special phenotypic traits are characteristically associated with this disease.

Radiological findings consistent with neonatal pneumonia are frequently seen in newborns with GBS septicemia [1, 21]. Ingram et al. [16] in a report of GBS antigen detection included 19 neonates with early onset GBS pneumonia. However, no clinical data on the infants were given. Several investigations have demonstrated that mothers of infants with GBS septicemia have low levels of serum antibodies against the type infecting the respective infant [3]. This has been valid also with the method for antibody quantitation used in the present study [6, 10]. The sera from mothers of infants with pneumonia were within the normal range of anti-GBS antibodies. It is possible that the presence of IgG-antibodies in the maternal sera might partially protect the infants with pneumonia, explaining why the infants developed pneumonia but not septicaemia. The presence of septicaemia cannot be excluded on the background of one negative blood culture specimen. The results of antibody quantitation supported the idea that neonatal GBS pneumonia can occur without concomitant septicaemia.

From a practical point of view, neonatal pneumonia and PMA are frequently indistinguishable in the initial phase. In the present study some notable differences were found; maternal fever, gestational age above 42 weeks, more than one symptom of respiratory difficulties and the occurrence of severe FHR-changes during the first stage of labour were typical characteristics of pneumonia. We have previously noted an association between high gestational age and maternal carriage of GBS [9]; the reason for this association is not yet clear. Finally, we have also previously shown a connection between maternal carriage of GBS and severe FHR-changes and low fetal blood pH values [9]. In addition to haematological and serological tests [4] and thorough bacteriological examinations the clinical observations mentioned above should be useful to differentiate pneumonia from other respiratory disorders such as PMA and IRDS during the first days of life.

During the study period, approximately 1500 infants were born in our department. Supposing that 10 of the pneumonia cases here described were caused by GBS, and that 16% of the parturients at our clinic were GBS-carriers, the incidence of GBS-pneumonia without septicemia per GBS-carrier would be about 1:25; this frequency is about 10 times higher than the expected incidence of GBS-septicemia [3]. From a cost-benefit point of view, these new findings enhance the value of screening for GBS-carriage during pregnancy. The recognition of the manifestation of neonatal GBS-infection as pneumonia without septicaemia suggests a revision of the present view on GBS-carriage during pregnancy.

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