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Streptococcus Bovis Bacteraemia in Infants in a Regional Hospital in Hong Kong

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Abstract ***Objectives:*** To identify the features of infants infected by *Streptococcus bovis* in a regional hospital in Hong Kong. ***Design and setting:*** Case series. ***Main measurements:*** Clinical features of all patients infected by *Streptococcus bovis* were retrieved from the database of the Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital, from 1999 to 2009. A literature review was also performed concerning this infection in infants. ***Results:*** Eight infants were identified from the medical record. All of the patients had *Streptococcus bovis* bacteraemia. Only 2 of our patients had the bacteria isolated from cerebrospinal fluid. Four of the patients presented with fever. Six of the patients were born at full term while the other 2 were premature babies. Six of the patients presented within the first 7 days of life, while the other 2 presented on Day 23 and Day 46 of life. At least 7 days of intravenous antibiotics were given. All of the patients recovered and none of our patients died. To date, all of our patients had normal growth and development. ***Conclusions:*** In our case series, fever was the most common manifestation. Respiratory distress was common but gastrointestinal disturbance was uncommon, which is different from previous reports. Further research has to be performed for better understanding of this bacterial infection in the paediatric population.

Key words Bacteraemia; Meningitis; Newborn/Infants; *Streptococcus bovis*

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Introduction

Streptococcus bovis (*S. bovis*) infection can be associated with malignancies and other serious consequences in adults. In the Western World, the association between *S. bovis* bacteraemia and colorectal cancer has been established.[1] In Hong Kong, a local study has confirmed the association between *S. bovis* bacteraemia and biliary tract infection.[1] However, these studies were mainly targeted at adults. We do occasionally encounter infants who suffer from *S. bovis* bacteraemia in our medical practice in Hong Kong, and whether there was any disease association between S. *bovis* bacteraemia in infants and even their mother was a concern to paediatricians and obstetricians. It is therefore worthwhile to review cases of *S. bovis* infection in infants to improve our understanding about the problem.

Similar to the practice overseas,[2,3] our laboratory also uses the term *S. bovis* to designate viridans group Streptococci that now form the *Streptococcus bovis/ Streptococcus equines complex.*

Methods

The retrospective case series was conducted at Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital. Eligible subjects were all patients admitted to our neonatal ward from 1999 to 2009. The age limit was less than 1 month old at time of admission. Stillbirths were not included as these babies were not admitted to our ward. Infants who had positive growth of *S. bovis* from blood culture will be registered in a database in our department. Birth record, clinical information and microbiological information of these patients were retrieved from the medical record. Supplementary information was obtained from the hospital electronic clinical management system. The baby's gestational age, birth weight, sex, age at presentation, clinical presentation, progress and treatment given were obtained. Maternal age, antenatal problems and problems noted during labour were identified from the baby's birth record. As *S. bovis* bacteraemia was associated with infective endocarditis in adults, echocardiogram record of the babies were retrieved. In addition, the authors also paid special attention to any intra-partum antibiotics given to mother to see if this had any relationship with the infection. For babies being followed up or had been followed up in our out-patient clinic, their latest medical record had been retrieved to see if they had any growth and developmental problems. We have excluded babies with S. *bovis* only identified on culture of surface swabs because these may represent colonization instead of genuine infection. In this article, we defined bacteraemia as positive growth of the bacteria from blood culture, meningitis as positive growth of the bacteria from cerebrospinal fluid, urinary tract infection as positive growth of the bacteria from urine obtained by bladder catheterization or suprapubic tap, early onset disease as onset of symptoms within 14 days of life and late onset disease as onset of symptoms after 14 days of life.

Results

Eight patients were found to meet our criteria in our search (Table 1). There were 6 male and 2 female babies with birth weight ranging from 1.175 kg to 3.81 kg. Two babies were preterm infants, and 6 of these infants had the diagnosis of *S. bovis* infection made before day 7 of life. The ages of mothers of these babies ranged from 25 to 36 years old. In all cases there were some complications or medical problems in the antenatal period or during labour (Table 2).

Fever was the most common manifestation of the disease. Some babies presented with signs of respiratory illness, which included cyanosis, tachypnoea and apnoea attack. Only one of the babies presented with signs of gastrointestinal illness i.e. regurgitated once after feed. Intra-partum antibiotics had been given to the mother in 2 of these cases, while only the 2 babies with later onset of disease (on Day 23 and Day 46 of life) had received antibiotics before disease presentation.

In our case series, *S. bovis* was isolated from blood culture in all of our patients. In two patients the bacteria were grown from the cerebrospinal fluid (CSF) obtained. All of these babies were treated with intravenous antibiotics for at least 7 days. All of the babies recovered from the disease. Repeat blood culture in all of the patients and CSF culture in the 2 patients with meningitis revealed no positive bacterial growth. Six of the babies had been followed up in our out-patient clinic. To date, all of them enjoyed good health with normal development. In our unit, liver enzyme levels and ultrasonography of the hepatobiliary system were not routinely done in babies with *S. bovis* bacteraemia. Serum bilirubin levels in neonates were usually affected by neonatal jaundice and did not reflect liver function. Our laboratory did not proceed to check the biotype of the bacteria.

Discussion

Although in this case series there were only 8 patients involved and strong scientific conclusions could not be made, we can use our data to compare with those cases previously reported from other parts of the world. In the year 2006, Gerber et al had reported a case series in *S. bovis* infection in 2 hospitals in the United States and had identified 7 patients managed at their institutions and 23 from the literature. *S. bovis* infection is more commonly found in young infants, particularly in the neonatal period.[2] In our case series, most of the babies presented early within the first 7 days of life, and the most common presentation was fever. It is possible that these babies acquire the infection in perinatal period.

Our findings contrast with cases described by Gerber et al[2] that, in their case series, most infants with *S. bovis* infection developed the disease after Day 14 of life, and presented with signs of gastrointestinal illness. In that case series 5 out of 7 babies presented with abdominal distension and diarrhoea. It remained uncertain how these babies acquired the infection. Fortunately in both of the case series,

Table 1 Clinical features of babies with *Streptococcus bovis* bacteraemia

Case number	Age at diagnosis	Sex	Maturity	Birth weight	Mode of delivery	Presentation	Child received antibiotics before presentation	Positive site of culture	Treatment	Echocardiogram	Outcome
1	Day 23	M	32 week and 5 days	2.25 kg	C/S (twin, pre-eclampsia in mother)	Fever and apnoea attack	Yes	Blood and CSF; Klebsiella from CSU	Ampicillin, cefotaxime, meropenem for 14 days	No echocardiogram	Normal development, defaulted BAEP, last seen in September 2008
2	Day 7	F	38 week and 4 days	2.6 kg	C/S (breech presentation)	Cyanosis, respiratory distress, septic shock	No	Blood	Amikacin and cefotaxime for 14 days	Coarctation of aorta, decreased left ventricle contractility, no signs of infective endocarditis	Normal development, last seen in March 2010
3	Day 7	M	38 week and 3 days	3.1 kg	Spontaneous vaginal delivery	Fever and irritable	No	Blood and CSF	Penicillin, ampicillin, cefotaxime, vancomycin for 21 days	Normal echocardiogram	Normal growth and development, last seen in 2004
4	Day 0	M	40 week	3.81 kg	C/S (failed VE)	Meconium aspiration	No	Blood	Penicillin and netilmicin for 14 days	Normal echocardiogram	Normal growth and development, last seen in 2006
5	Day 46	M	28 week and 2 days	1.175 kg	C/S (severe pre-eclampsia and breech presentation)	Tachycardia and desaturation	Yes	Blood	Vancomycin for 14 days	PDA on echocardiogram, no signs of infective endocarditis	Normal growth and development, last seen in 2006
6	Day 0	M	39 week and 4 days	3.3 kg	VE (prolonged 2nd stage)	Fever	No	Blood	Penicillin for 7 days, netilmicin for 5 days	No echocardiogram	No follow up
7	Day 1	F	37 week and 5 days	3.12 kg	Spontaneous vaginal deliver	Fever	No	Blood	Penicllin and netilmicin for 10 days	Normal echocardiogram	Normal development, last seen in 2009
8	Day 2	M	40 week	2.9 kg	Vacuum extraction	Regurgitate once after feed	No	Blood	Penicillin for 10 days, netilmicin for 5 days	No echocardiogram	No follow up

BAEP: brainstem auditory evoked potential; C/S: Caesarean Section; CSF: cerebrospinal fluid; CSU: catheterized urine; F: female; M: male; PDA: patent ductus arteriosus; VE: vacuum extraction

Table 2 Gestational complications and condition at birth of babies with *Streptococcus bovis* bacteraemia

Case number	Age at diagnosis	Sex	Maternal age	Gestational complications/ condition after delivery	Local/ Mainland mother	Intra-partum antibiotics given
1	Day 23	M	28	Severe pre-eclampsia Perinatal pneumonia treated with continuous positive airway pressure and antibiotics, no positive growth	Mainland	1 dose
2	Day 7	F	28	Fetal distress, thin meconium stained liquor	Local	No
3	Day 7	M	36	Fetal distress, delayed crying at birth	Local	No
4	Day 0	M	32	Fetal distress, thick meconium stained liquor	Local	No
5	Day 46	M	31	Severe pre-eclampsia	Local	No
6	Day 0	M	31	Vacuum extraction for prolonged second stage	Local	No
7	Day 1	F	36	Gestational impaired glucose tolerance	Local	No
8	Day 2	M	25	Fetal distress, thick meconium stained liquor Mother had chronic hepatitis B	Local	1 dose

Note: In case 1, there was no growth from placental swab and mother's high vaginal swab, another twin was normal and was not infected by *S. bovis*. In case 8, placental swab revealed moderate growth of Group D Streptococcus but no growth from mother's high vaginal swab. In other cases these swabs for bacterial cultures had not been obtained. None of these mothers had blood cultures taken before or after delivery of these babies.

including the babies who suffered from bacteraemia and meningitis, none of the babies died.

S. bovis has been reported to cause infective endocarditis, meningitis, bones and joints infections and biliary tract disease in humans.[1-4] In one local study done concerning *S. bovis* in both adults and children, it was found out that in *S. bovis* bacteraemia, 38% of the patients had underlying acute cholangitis or cholecystitis and 11% had infective endocarditis. There were 11% of patients with underlying carcinoma of colon. In 40% of these patients, no infective foci could be identified.[1] However, these associations were not well established in children.

In our case series, primary infective foci could not be identified in six of our patients. In addition, there was no associated biliary tract disease or infective endocarditis, though such conclusion was based mainly on clinical grounds. There was no tenderness on abdominal examination, no heart murmur and no signs of heart failure. Because of these negative physical signs, we performed ultrasonography of the liver in none of our patients. Trans-thoracic echocardiogram was performed in five of our patients and none of them had features suggestive of infective endocarditis. *S. bovis* bacteraemia had been found associated with diseases of the gastrointestinal and hepatobiliary systems, and Gerber et al demonstrated that gastrointestinal disturbance was common in young infants with *S. bovis* infection.[2] However such presentation was not common in our case series. Only one baby in our case series presented with gastrointestinal disturbance (regurgitated once after feeding).

In this study we have reviewed the records of our patients concerning the use of intrapartum antibiotics to the mothers of these babies. In all our 8 cases, none of the mothers of the babies had received more than 1 dose of intrapartum ampicillin. Because of the small number of cases, it is difficult to conclude whether intrapartum antibiotics can prevent or decrease the number of babies suffering from *S. bovis* infection. However, this postulation can be valid. A 16-year prospective study performed in Spain had shown that the rate of penicillin resistance was 0% among *S. bovis* isolates.[5] Therefore intravenous ampicillin given to mothers may act against both Group B Streptoccoccus and also *S. bovis*, thus lowering the chance of babies being infected by both bacteria. This may also explain the low incidence of *S. bovis* infection in neonates in our locality. However, it has been documented that intrapartum antibiotics could not lower the incidence of late onset Group B Streptococcal disease in neonates. Whether the same can be applied to *S. bovis* infection cannot be proven yet. In the case series by Gerber et al, late onset *S. bovis* infection was in fact more common than early onset diseases. Gerber postulated that in their case series the babies presented late because of use of intrapartum antibiotics for prevention of Group B Streptococcus infection. In our case series, only 1 out of 6

mothers with babies who suffered from early onset disease had received intrapartum antibiotic before delivery of their baby (Table 2). This may account for the difference in timing of presentation in the 2 case series.

All except one of the babies in our case series were treated with beta-lactam group of antibiotics. The most common choice was intravenous Penicillin G. All of our *S. bovis* isolates were sensitive to penicillin. Although our laboratory did not report the actual figures concerning antibiotic sensitivities of *S. bovis* because of the small number of isolates,[6] the findings in our case series and the reports from Gerber et al[2] and Corredoira et al[5] suggested that β-lactam group of antibiotics are reasonable first line treatment of *S. bovis* infection. In a local study by Lee et al, all of the *S. bovis* isolates were sensitive to penicillin, cephalothin and vancomycin.[1] The only one baby that we treated with vancomycin was a 46-day-old premature infant with central venous catheter in-situ. Vancomycin was used in this case because the case doctor would like to include coverage of Methicillin resistant Staphylococcus aureus (MRSA) and coagulase negative Staphylococcus (CONS), which were common culprits of central venous line infection in our neonatal intensive care unit.[6] In case 2 cefotaxime and amikacin (an aminoglycoside) was given to obtain synergistic effect to treat the bacterial infection.

It was previously reported that the mortality rate of neonatal *S. bovis* bacteraemia was over 20%. However, none of the patients in our cases series and Gerber's case series died.[2] In addition, for the 6 out of 8 babies who were followed up in our out-patient clinic, all of them enjoyed good health with normal development. It seems that the mortality of neonatal *S. bovis* infection was lower than previously reported, and with suitable treatment, these patients may enjoy good health and normal development as other children. The difference in mortality rate might be related to improvement in neonatal care over these 20-30 years. In the article by Gerber et al, a number of neonates infected by *S. bovis* were born in 1978-1982. Over these 20-30 years there had been a lot of improvement in neonatal care, e.g. better ventilator support, better nursing care, better incubator, more easily accessible medications including antibiotics and better catheters for us to obtain venous access.

In this study we noticed that in all cases there were some complications or medical problems in the antenatal period or during labour (Table 2). No good postulations can be offered by the authors why there was such association. This may be explained by reporting bias but warrants further research before we can make any conclusion.

Conclusion

S. bovis infection, particularly bacteraemia, has been the research interest of different parties because of its association with colon cancer.[1] Today with better understanding of the disease and the bacteria, it was found out that the picture was much more complicated. In the paediatric age group our understanding of the disease is still limited. In our case series, most of the babies presented with fever and respiratory distress within first 7 days of life. This was different from the finding of Gerber et al[2] that most of the babies presented with gastrointestinal disturbance after Day 14 of life. Fortunately, all of the babies survived, and in our case series, the babies enjoyed good health and normal development. Mortality from the disease was lower than previously reported.[2] However, as the bacteria can cause potentially serious infection such as bacteraemia and meningitis, further research is warranted for better understanding of the disease.

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