Streptococcus gallolyticus subspecies pasteurianus causing early onset neonatal sepsis complicated by solitary liver abscess in a preterm infant

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INTRODUCTION

Streptococcus gallolyticus subspecies pasteurianus (SGp) belongs to the Streptococcus bovis (S. bovis) group and was formerly known as S. bovis biotype II/2. S. bovis is a Gram-positive coccus that belongs to the Lancefield group D streptococcus. Streptococcus bovis is found in the human gastrointestinal microbiota, more often in neonates (23%) than in adults (5%) [1]. Recently SGp has been increasingly recognized as a cause of neonatal sepsis and meningitis [2–4] though biliary tract infections due to S. bovis group caused by SGp has been reported in adults over many decades [5, 6]. Liver abscesses are generally uncommon in neonates. Here we describe a case of SGp septicemia in a newborn infant that was complicated by liver abscess.

CASE REPORT

A female infant was born at 36+6 weeks gestation via normal vaginal delivery with a birth weight of 3776 g to a 37-year-old mother, who conceived via in-vitro fertilization. Apgar scores were 8 and 9 at 1 and 5 min of life respectively. Her high vaginal swab tested negative for group B streptococcal colonization and there was no history of prolonged rupture of membranes or maternal pyrexia. Apart from being a hepatitis B carrier, there was no other significant maternal past medical history. Maternal blood counts and urine analysis were unremarkable. The infant received Hepatitis B immunoglobulin and vaccine soon after birth.

The infant was noted to be grunting with nasal flaring and subcostal retractions, with borderline saturations in room
air at 5 min of life. Initially she required continuous positive airway pressure (CPAP) support but the respiratory distress worsened with increasing oxygen requirement, and was transferred to the Neonatal Intensive Care Unit (NICU) for further care. She was intubated at 13 h of life and the respiratory support was graded up to High Frequency Oscillatory Ventilation and nitric oxide. Chest X-ray suggested hyaline membrane disease. She required two doses of surfactant due to persistent hypoxia while on high ventilator support. Umbilical venous (UVC) and arterial catheters were inserted for glucose infusion and blood pressure monitoring. Imaging showed malpositioning of the UVC in to the right portal vein (Fig. 1) and was readjusted promptly.

On day 1 of life, septic work up was performed and she was treated for presumed sepsis with intravenous Penicillin and Gentamicin. Due to renal impairment (oliguria <1 ml hour⁻¹), Gentamicin was discontinued after the first dose and intravenous Cefotaxime was added. At birth, full blood count (FBC) and C-reactive protein (CRP, 0.2 mg l⁻¹) were unremarkable. Infective markers showed an upward trend by 12 h (CRP, 24 mg l⁻¹) and by day 2 of life (CRP, 170 mg l⁻¹). The blood culture at birth grew SGP, sensitive to Penicillin and Clindamycin. The organism was identified by using the matrix assisted laser desorption ionization time-of-flight technology (MALDI-TOF) using the VITEK MS instrument by bioMérieux (Marcy-l’Étoile, France). The *Streptococcus gallolytycus* subsp. *pasteurianus* isolate was identified with a probability score of 99%. The 16S RNA gene sequencing is usually only performed if necessary. The antibiotic sensitivity test was performed by disc diffusion using the Calibrated Dichotomous Sensitivity (Australian criteria). Her ear swab cultures showed light mixed growth of *SGp* as well as *Escherichia coli* sensitive to Ceftriaxone, Co-trimoxazole and Cefotaxime but resistant to Ampicillin and Gentamicin. Lumbar puncture was deferred due to increasing lability.

On day 4 of life, lumbar puncture was performed and the cerebrospinal fluid (CSF) studies returned negative for meningitis and the CRP showed a downward trend (48 mg l⁻¹). She developed fever (38.6 °C) on day 5 of life. The Infectious Disease (ID) team was involved in the care because of persistent fever and increasing lability. Her liver function test revealed conjugated hyperbilirubinemia and renal function normalized. CRP showed a second spike again to 165 mg l⁻¹. Blood culture was repeated and amikacin was added to optimize the antimicrobial coverage in view of the clinical deterioration. The blood culture was sterile. Umbilical lines were removed. Urine analysis was unremarkable. Echocardiogram was negative for structural heart disease and infective endocarditis. Imaging of the abdomen using ultrasound (US) scan showed the presence of a multi-loculated cystic structure, measuring 3.8×3.6×3.2 cm, in the right lobe of the liver, suggestive of liver abscess (Fig. 2a). The abscess cavity was reported to be in the proximity of a branch from the right portal vein (Fig. 2b). She became afebrile and was successfully extubated on day 6 of life. Penicillin and Amikacin were stopped on day 10 of life after 1 week course and she was continued on Cefotaxime.

Serial follow-up US scan of the liver showed slow regression of the abscess and on day 28 of life the abscess measured 2.4×1.8×1.5 cm. On day 35 of life, ID team reviewed, and a needle aspiration and biopsy of the lesion was performed under US guidance (Fig. 3a). The aspirate yield was scanty and a biopsy was obtained from the solid hypo-to-isoechoc component of the solid-cystic nodule. Haematoxylin and
eosin stained sections showed cores of liver tissue featuring ghost cells and necrotic debris with acute inflammatory infiltrate associated with a fibrous wall at the interface. These histopathological findings are compatible with an abscess cavity (Fig. 3b, c). Gram-stain, acid-fast stain and special stains for fungi were negative. The bacterial and fungal cultures were sterile.

Follow-up US on day 37 of life showed further resolution of the abscess cavity measuring 1.9×1.6×1.2 cm. Parenteral antibiotics were discontinued after 5 weeks and continued with oral Co-amoxiclav for 3 weeks. Imaging at 3 months of age revealed significant resolution of the liver abscess. Sequential liver US scans were done and at 16 months of age showed abscess cavity to be 0.9×0.3×0.4 cm with dystrophic calcification (Fig. 4). She is being followed-up for growth and developmental assessment while continuing to monitor liver function test. Her growth and neurodevelopmental assessments were appropriate for age. Her Hepatitis B surface antibody was 947 mIU l⁻¹ at 9 months of age.

The course of illness of this infant is depicted in the timeline (Fig. 5).

**DISCUSSION**

*Streptococcus bovis* is a Gram-positive and catalase-negative coccus belonging to *Streptococcaceae family*. *Streptococcus bovis* is also known as *Streptococcus gallolyticus* and used interchangeably. In the adult population, *S. bovis* has been shown to be associated with infective endocarditis, meningitis, non-malignant diseases of the gastrointestinal and hepatobiliary-pancreatic systems, as well as colorectal carcinoma [7].

*Streptococcus bovis* and its subspecies have not been thoroughly studied in paediatric population. It is important to have proper identification of the *S. bovis* subspecies as it has its own clinical implications. The *Streptococcus bovis* conglomerate could be differentiated by means of 16S rRNA gene sequencing into the four following major genomospecies. *Streptococcus gallolyticus ssp. gallolyticus* (former biotype I), and *S. gallogettssus ssp pasteurianus* (SGp) (former biotype II/2) being genetically closely related while, *Streptococcus infantarius ssp. coli* (former biotype II/1) and *S lutetiensis* being distantly related [8, 9]. Still no uniform microbiological classification exists. While *S. gallogettssus ssp. gallogettlicus* is linked to colonic carcinoma and endocarditis [9], *Streptococcus infantarius* is associated with non-colonic cancers [10] whereas SGp is a pathogen causing meningitis and bacteremia in infants and adults [11, 12].

There are case reports that highlight the need for paediatric fraternity to be familiar with childhood infections due to strains of *S. bovis*. Sporadic case reports by Gavin et al. and Onoyama et al. showed SGp as a cause of neonatal meningitis before the emergence of the strains worldwide [12, 13]. Klatte et al. evaluated meningitis in four epidemiologically different infants less than 2 weeks of age due to SGp between 2008 and 2010 [2]. A total of 51 neonatal cases of SGp sepsis have been described till 2018. A recent report of two newborn infants with sepsis and endocarditis highlights the importance of recognizing SGp as a virulent pathogen manifesting in newborn infants [4]. There are case reports where SGp has also been found to be a coloniser of the female genital tracts, thus causing maternal infections and neonatal colonization [14]. *Streptococcus bovis* has been isolated from vaginal secretions in 3.4% of women aged 18–45 years, but no sub-classification was done [15]. Fikar and Levy had reported a case of *S. bovis* meningitis in a neonate whose maternal vaginal and rectal swabs grew *S. bovis* [16].

Infection with this organism may have similar presentation as Group B Streptococcal infection [17]. In early onset sepsis, respiratory distress is the most common clinical manifestation presenting within the first 5 days of life [16] as noted in our reported case. Alvarez et al. reported seven infants diagnosed with *S. bovis* bacteremia, and all of them had early onset sepsis.
and presented with respiratory distress. Five of them had meconium stained liquor and two had aspiration pneumonia [18]. In our reported case there was no meconium stained liquor. In late onset sepsis, meningitis and urinary tract infections are more common [11]. Neurological symptoms such as irritability and seizures were more commonly reported in cases of late onset sepsis or with relapse, due to higher incidence of meningitis. In late onset sepsis, the pathogen is believed to be acquired postnatally either from handling of the child by caregivers, ingestion of infected breast milk or from nosocomial sources [3, 19]. Floret et al. described five cases of SGp sepsis in France. All infants presented as late onset sepsis with acute abdominal symptoms and, there was suspicion of health care worker transmission from one child to another [3].

SGp is sensitive to beta-lactams and Vancomycin and there are clinical reports of adequate response to Penicillin and Cefotaxime [11–13], although resistant strains are emerging [20]. In our case the infant responded well to beta-lactams and did not need escalation of antibiotics.

Polymicrobial infection accounts for nearly 50% of liver abscess [21]. Staphylococcus aureus, Streptococcus pyogenes, Escherichia coli, Klebsiella spp., and Pseudomonas spp. are among the common pathogens causing liver abscesses in children. Rarely organisms like Corynebacterium acnes, anaerobic bacteria, Candida spp. and Mycobacterium tuberculosis have been reported to cause liver abscesses in neonates and infants [22–24]. We also tested the aspirate from the liver abscess for acid-fast stain, fungal smear and culture and all were negative.

An earlier publication by Tan et al. reported a case series of neonatal liver abscesses but none were due to SGp [23].

Liver abscesses are generally considered an uncommon entity in neonates. Risk factors that have been associated with development of liver abscess during neonatal period include maternal chorioamnionitis, abruptio placentae, prematurity, malposition of umbilical catheters, sepsis, abdominal surgery and necrotizing enterocolitis [23–26]. The possible access of microorganism causing liver abscess in a newborn infant can be ascending infection through the umbilical vein and portal veins or via biliary tract, hematogenous spread, and by direct contiguous spread from neighbouring organs [23, 26]. Powers & Tooley had described the incidence of contamination and its association with technique of using umbilical lines in causing sepsis in newborn infants [27]. Balagtas et al. reported 52% colonization in umbilical catheters with 8% of bacteraemia in newborn infants [28]. Thus, umbilical catheterisation becomes a risk factor for infectious or noninfectious hepatic abscess with an added inherent risk of infection due to misplaced UVC [27–29]. The UVC can be malpositioned at the first insertion attempt in nearly 51% of cases [30]. In any case of sepsis there should be a high index of suspicion of liver abscess if there is no identifiable focus of infection or no response to appropriate intravenous antibiotics. Abdominal ultrasound is usually the first investigation that can detect, locate, and define a liver abscess [23, 31]. In a large study by Chen et al. the lobulated a wedge shape lesions with hyper echogenicity and heterogeneity were features of UVC-related hepatic lesions [32]. Hepatic lesions were located in 72.7% of
cases in the left lobe, 21% in the right lobe and 6% in both lobes. But in the study by Tan et al. [23] the hepatic abscess was mostly in the right lobe. It was thought that the portal venous flow contributes to right-sided lesions.

There is no uniformity about the shape of the hepatic abscess and site of abscess to estimate whether the umbilical catheter has a role in the formation of the abscess. It can be postulated that the liver abscess developed as a result of hematogenous seeding of the microorganism, secondary to the bacteremia. It is arguable that the initial malposition of umbilical venous catheter could have resulted in bacterial seeding within the liver in our case as the abscess is seen closely associated with a branch from the right portal vein in the first ultrasound (Fig. 2b). As the infant’s ear swab also grew the same organism, the chances of contaminating the central lines could not be ignored. However, it can be argued that the finding of a multiseptated, well-organized abscess early on at day 6 of life in our case could also be likely to be an antenatal event, given that it would have taken time to organize. Objectively, both postulations are possible but the actual sequence of events cannot be confirmed.

Solitary liver abscess can be drained effectively by percutaneous aspiration or drainage [31]. Lee et al. treated 7 out of 8 newborn infants who had liver abscess with percutaneous aspiration and long-term antibiotics and had good outcome [33]. The early diagnosis and needle aspiration together with appropriate intravenous antibiotics helped in the fast recovery of the infant without any major morbidity.

Given the initial size of the liver abscess in our case, it might have been beneficial to consider early intervention to drain the abscess. This could potentially reduce the duration of intravenous antibiotic therapy for this baby and mitigated the need to keep the long line in situ for an extended duration. We have to be mindful that the risk of central line-associated bloodstream infections (CLABSI) increases proportionately with the duration of central line in situ. Another pitfall was that no placental histopathology was done as mother was well and she had no signs of chorioamnionitis. No organism could be grown from the aspirate of the liver abscess as the percutaneous drain was done 5 weeks after intravenous antibiotics were initiated and it would have been rendered sterile.

CONCLUSIONS

There is a role for evaluation of the hepatobiliary systems in the event of SGp infection, especially in the background of a malpositioned UVC and positive surface swab colonization. Being a perinatal pathogen causing fatal fulminant infections, neonatologists should be aware of the spectrum of illness that can be caused by this organism.

Family’s perspective

We were very worried about the diagnosis of liver abscess and the need for prolonged treatment. We had concerns of long-term morbidity due to persistence of abnormal liver imaging findings. Thankfully her liver abscess resolved over months and she is growing well.

**Contribution to the field statement**

*Streptococcus gallolyticus ssp pasteurianus* infections are rare in neonatal and paediatric population. Only recently clusters of cases of neonatal sepsis and meningitis were reported worldwide and the awareness has increased among the health care professionals. This bacteria colonises the female genital tract and can thus be a pathogen causing ascending neonatal infection like group B streptococcus in the presence of prolonged rupture of membranes. Till date only neonatal sepsis, meningitis and endocarditis were reported. No case of liver abscess due to *S. gallolyticus* has been reported in the literature. Liver abscess is uncommon in neonates. Being a major morbidity prevention should be the key responsibility. Malposition of umbilical lines in the liver can cause liver abscess as well as generalized sepsis if the infant is colonized. Early neonatal sepsis due to uncommon organisms warrant ultrasound of the liver in addition to the usual septic work up. Here we report a late-preterm infant who had early onset neonatal sepsis and liver abscess. She had skin colonization with malpositioned umbilical venous catheter in the liver. The response to treatment using beta lactam antibiotics was inadequate, leading to aspiration of the abscess and biopsy of the liver. Histopathology confirmed liver abscess. Further follow-up showed a slow resolution while on prolonged antibiotic therapy. This case highlights the pathogenicity of *Streptococcus gallolyticus* in new born infants and the need for imaging hepatobiliary tract while doing septic work up.

**Funding information**

The authors received no specific grant from any funding agency.

**Acknowledgement**

We would like to acknowledge the immense support from A/Prof Harvey Teo Eu Leong, Senior consultant in department of Diagnostic and Interventional Imaging, KK Women’s and Children’s Hospital, Singapore for his contributions to the reporting of X-ray and ultrasound images. We also like to acknowledge A/Prof Matthias Maivald, Senior consultant in the Department of Pathology and Laboratory Medicine, KK Women’s and Children’s Hospital, Singapore for his contributions in the methodology of the case.

**Author contributions**

C.C. and O.G., treated the infant, wrote the manuscript and performed the final edits. S.C. and C.M.C., reviewed and revised the manuscript critically for important intellectual content; T.W.H., was involved in treating the infant and contributed to the liver abscess section of the manuscript and reviewed the manuscript; K.M., edited and contributed to the histopathological aspects of the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

**Conflicts of interest**

The authors declare that there are no conflicts of interest.

**Ethical statement**

Written informed consent was obtained from the minor(s) legal guardian for the publication of any potentially identifiable data included in this report.
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