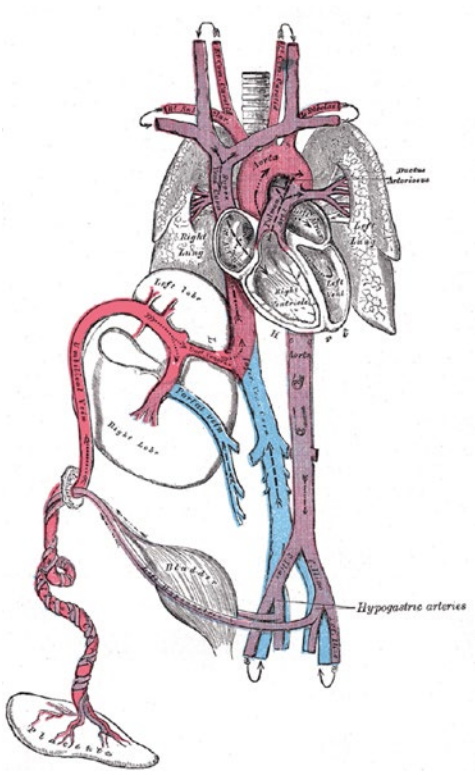
SWISS SOCIETY OF NEONATOLOGY

A perfect culture medium



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Title figure:
Anatomy of the umbilical vein (source: www.wikipedia.org)

INTRODUCTION

Neonatal liver abscess is uncommon, carries a high mortality and is difficult to diagnose. Since first reports in the 1930s, fewer than 100 cases have been reported in the literature (1). Major risk factors are culture-proven sepsis, umbilical catheterization, central parenteral nutrition catheters, necrotizing enterocolitis, surgery and prematurity.

In this report, we present the case of a premature neonate with catheter-associated late-onset sepsis and multiple hepatic abscesses (HAs) due to methicillin-sensitive Staphylococcus aureus (MSSA).

This premature female baby was born at 28 5/7 weeks of gestation by normal vaginal delivery as the first twin of a monochorionic-diamniotic spontaneous pregnancy. At 28 2/7 weeks' gestation, the mother had been admitted for tocolysis due to premature contractions. She had received a complete course of antenatal corticosteroids. There was no evidence of chorioamnionitis, and vaginal smears remained negative.

The girl adapted well with Apgar scores of 7, 7 and 8 at 1, 5 and 10 minutes, respectively. The arterial umbilical cord pH value was 7.15. The infant's birth weight was 1070 g (P25 – 50). Initially, she required bag and mask ventilation for some minutes due to poor respiratory effort; she was then transitioned to nasal CPAP for respiratory distress, without supplemental oxygen. An umbilical venous catheter (UVC) was inserted for parenteral nutrition. Standard X-ray control after the procedure revealed placement of the catheter tip within the liver, and the UVC was drawn back into a pre-hepatic position (4.5 cm) (Fig. 1). On day of life (DOL) 3, the UVC was replaced by a peripherally inserted central catheter (PICC). No antibiotics were given at birth, and a first septic work-up remained negative.

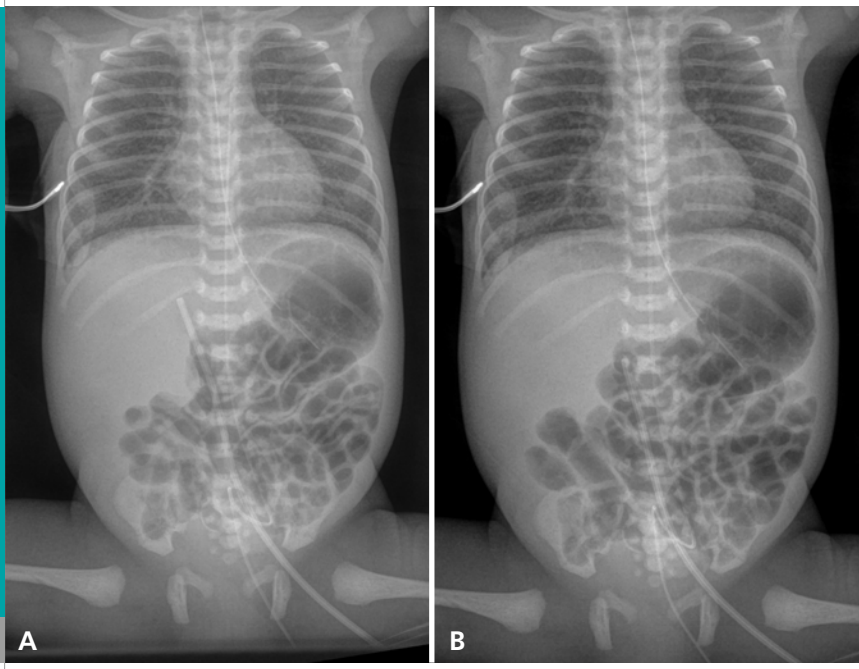

Fig. 1

Babygrams after placement of umbilical catheters: the intrahepatic position of the UVC (A) was corrected to a prehepatic position (B).

On DOL 4, her clinical condition deteriorated, with diminished peripheral perfusion, hyperglycemia and a C-reactive protein (CRP) elevation to 37 mg/l. Late-onset sepsis was suspected, and empirical intravenous antibiotic therapy with vancomycin and gentamicin was initiated. Analysis of a CSF specimen was normal. Blood cultures were positive for a methicillin-sensitive Staphylococcus aureus (MSSA), and antibiotic therapy was switched to flucloxacillin and gentamicin. Cultures of the UVC tip also were positive for MSSA; a placental smear, on the other hand, remained negative.

On DOL 5, an abdominal ultrasound (US) was performed within a clinical study on catheter-associated complications and, unexpectedly, revealed multiple hepatic non-vascularized hypoechogenic lesions (Fig. 2). The differential diagnosis included traumatic hematomas or infectious lesions.

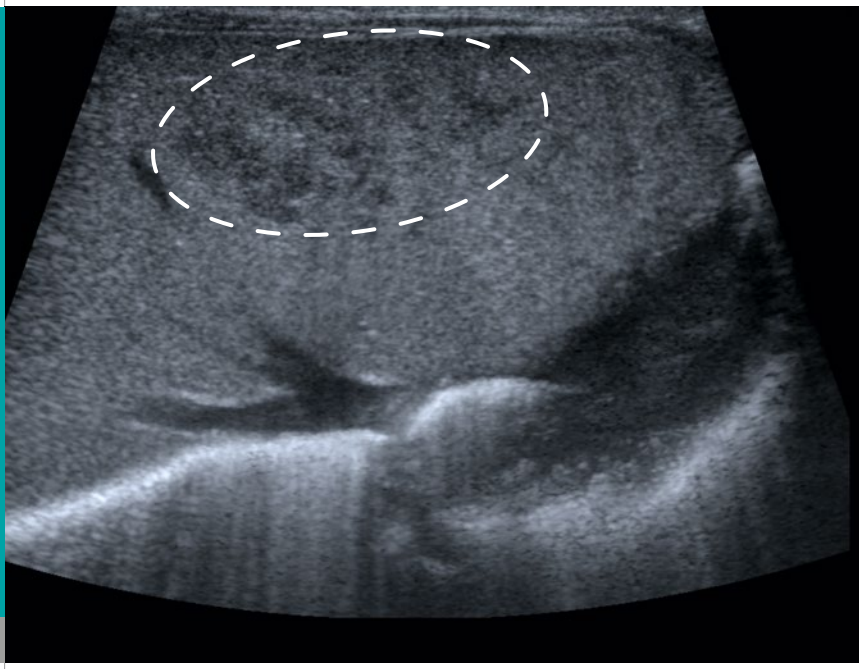

Fig. 2

Axial ultrasound examination of the liver on DOL 5: multiple poorly delineated and non-vascularized hypoechoic lesions in the hepatic parenchyma.

Two days later, the sonographic image of the lesions changed with the appearance of an echogenic center. Moreover, a thrombus of the Arantius duct was found with an unusual heterogeneous appearance (Fig. 3). These findings supported the hypothesis of an infected thrombus with several embolic hepatic abscesses (HA). Liver function remained un-altered.

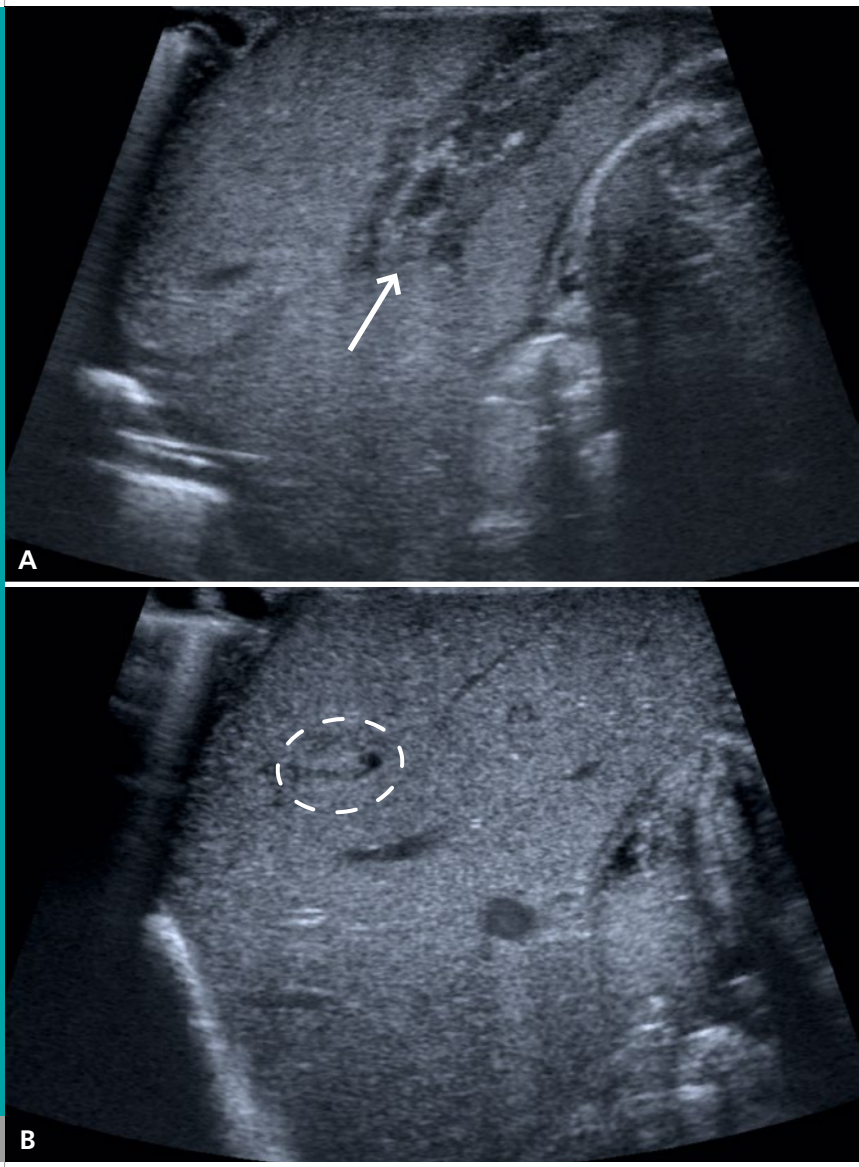

Fig. 3

Sagittal ultrasound of the liver on DOL 7: A) large inhomogeneous thrombus of the ductus venosus Arantii (arrow); B) liver abscess with hyperechoic center and hypoechoic halo.

On antibiotic treatment, clinical condition rapidly improved, but inflammatory parameters and repeat blood cultures remained positive until DOL 9. CRP started to fall from DOL 7 (maximum level 85 mg/l), and the first blood culture became negative on DOL 12. The PICC line was changed on DOL 7 and a broader septic work-up, including cardiac and brain US, as well as cutaneous fungal smears, all remained negative.

On DOL 13, rifampicin was added to improve organ penetrance, and gentamicin was stopped on DOL 19. Antibiotics were entirely discontinued 6 weeks after the first negative blood culture. Serial hepatic US examinations were performed and demonstrated regression of the hepatic lesions 6 weeks after the initial diagnosis.

DISCUSSION

Hepatic abscesses (HAs) are usually classified into two anatomical types, solitary or multiple. The latter is more common and clinically associated with generalized sepsis. A solitary HA, in contrast, is typical for localized infection usually associated with a more subacute course and relative lack of systemic symptoms (2). Our patient had multiple HAs with septic symptoms at onset.

Bacteria may reach the liver by several pathways: 1) direct invasion from a contiguous infection; 2) through the hepatic artery during hematogenous dissemination; 3) through the biliary ducts; and 4) through the portal circulation draining the gastrointestinal system.

The umbilical vein is the most frequent source in the neonate (1–3, 7) and the most probable infection route in our case. Several reports have described the association between HAs in neonates with malpositioned UVCs in the hepatic parenchyma or in pre-hepatic positions (2, 11).

In addition, the infusion of hypertonic solutions, such as parenteral nutrition (PN) or high concentration dextrose solutions through malpositioned UVCs are known to contribute to a terrain that facilitates bacterial growth and abscess formation. In the presented case, the tip of the UVC initially projected over the liver on X-ray, but was rapidly repositioned to a

pre-hepatic position, before PN was started. The thrombus in the ductus venosus of Arantii, probably created by an endothelial lesion from the UVC, may have been the source of septic emboli through the portal system. In addition, prematurity and very low birthweight are classical risks factors for HAs due to decreased adherence and chemotaxis of neutrophils.

While common clinical findings include fever, lethargy and vomiting, abdominal distension and hepatomegaly (3 – 4) may be found. Diagnosis based on clinical features alone is difficult, as the signs and symptoms are non-specific (5). Radiographic signs of liver abscesses can be subtle, but abdominal ultrasound with high-frequency linear probes has been shown to be a very good screening and monitoring method, usually showing hypoechoic areas initially, evolving into a more clearly defined hyperechoic lesion that disappears during treatment after a few weeks. Sometimes, dystrophic calcifications can be seen (5). Additional imaging studies are usually not required. Laboratory investigations are not helpful since liver function tests may remain normal. In the presented patient, the hepatic lesions were discovered incidentally (in the context of a clinical study), but a high index of suspicion is justified when blood cultures remain positive despite appropriate antibiotic therapy.

The most common organisms implicated in HAs development included gram-positive cocci, namely

Staphylococcus spp. (Staphylococcus epidermidis, Staphylococcus aureus) or Streptococcus spp., and gram-negative bacilli, such as hemophilus parainfluenzae, Serratia spp., Enterobacter spp. and Klebsiella spp., as well as Candida spp. Finally, Pseudomonas aeruginosa has also been identified as causative agent in some preterm patients (3, 6).

Therapy of a neonatal hepatic abscesses relies on two major strategies: long-term antibiotic therapy and surgical drainage. Small and multiple HAs, as in the present case, are generally managed conservatively as they are not suitable for surgical drainage or image-guided percutaneous drainage. Because of the microbiological variety found in HAs cases, initial broad-spectrum therapy is necessary while awaiting identification of the causative agents.

Early ultrasound guided needle aspiration is recommended when the abscess fails to resolve on serial sonographies, or microbiological identification is urgently required. Indications for drainage of solitary HAs include failure to improve on conservative management within 24–48 hours after commencement of therapy or the development of signs of peritonitis (8).

In the past, HAs carried a high mortality rate of up to 42% (3), but more recent small case series report better outcomes with the combination of long-term

antibiotic therapy and needle aspiration or surgical drainage if needed (9). The lack of larger epidemiological studies in the pediatric population seems to reflect the rarity of this condition. Clinical underdiagnosis cannot be formally excluded but seems unlikely since it would probably result in death in most cases.

CONCLUSION

We report a rare case of multiple HAs developing shortly after the placement of a pre-hepatic UVC. In this case, the principle of «primum non nocere» may translate into ensuring rigorous sterile placement of UVCs even under resuscitation conditions and confirmation of the catheter tip position before its use for parental nutrition and/or substances with high osmolarity.

The clinical picture of a neonatal HAs is non-specific and mainly based on bedside ultrasound examination. Survival rates have distinctly improved in recent years, most likely because of early diagnosis and treatment. A high index of suspicion is essential and should lead to confirmation/exclusion by bedside abdominal ultrasound.

We recommend performing an abdominal US examination as part of the standard work-up in late-onset sepsis when there is persistence of positive blood cultures despite appropriate antibiotic therapy particularly in the presence of risk factors such as umbilical venous catheterization.

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