Neonatal liver abscesses due to *Candida* infection in a preterm infant, secondary to malpositioned umbilical lines – a rare entity

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Neonatal liver abscess is an uncommon seen condition in neonatology and it holds a very high neonatal mortality because of difficulty in diagnosis and treatment. Till today, only few instances are reported that too are mainly in preterm. Its diagnosis requires a high index of suspicion. Fungal hepatic abscess is very rare and in medical literature very few case reports are there in the medical literature. Here, we report a case of *Candida albicans* liver abscess in a preterm neonate, secondary to malpositioned umbilical lines that presented with respiratory difficulty and other clinical features of sepsis that was managed medically and discharged successfully.

Keywords: *Candida*, Candidemia, Liver abscess, Preterm infant

Introduction

Neonatal liver abscess is a rare clinical entity. The use of an umbilical venous catheter is a common practice in neonatal units and is subjected to strict rules of insertion and monitoring to detect potential complications. Hepatic abscess is one of these rare complications and fungal hepatic abscess is a very uncommon complication. The aetiology of it could be idiopathic or secondary to haematogenous spread of infection, umbilical venous catheterisation, systemic sepsis and abdominal surgery. Untreated, it leads to serious clinical sequelae and high mortality.¹

Case Report

A 25-day-old male preterm 30 weeks neonate, born to primigravida mother and product of non-consanguineous marriage with birth weight of 1.4 kg was referred to our nursery from a private hospital in view of clinical deterioration and impending respiratory failure. On examination by casualty department the infant was observed to have respiratory distress with a respiratory rate of 80/min, subcostal and intercostal retractions and audible grunting with a Silverman Anderson score of 5/10, delayed capillary refill time, tachycardia (172 bpm), low blood pressure (mean of

24 mmHg), off colour, poor perfusion and mild hypothermia. There was abdominal distension with visible veins present over the abdominal wall. The antenatal history of the mother was non-significant. The cause of prematurity was severe pre-eclampsia. The management history from the referring hospital showed that the infant had received inotropes, total parenteral nutrition, antibiotics amikacin, piperacillin–tazobactam and meropenam for sepsis. Umbilical venous lines were inserted after birth and were removed after 10 days. The infant was shifted to the nursery after stabilisation and was started on invasive ventilation for respiratory support and inotropes for cardiac support. The infant was started on antibiotic imipenem and vancomycin after sending blood culture. The treatment was started on the line of neonatal sepsis. On detailed systemic examination showed later, his chest was clear, cardiovascular system was normal with no murmur, hepatomegaly was noted (a liver span of 6 cm with liver around 3 cm under the costal margin) and nosplenomegaly. The blood investigations revealed blood sugar of 86 mg/dl, haemoglobin of 12.4 mg/dl, leucocyte count of 42 500 with neutrophilia of 90% and shift to the left and also showed the presence of toxic granules, platelet count of 39 000, C-reactive protein of 23 mg/dl. The infant was given a blood product transfusion with platelet concentrate and packed red blood cell. The blood culture showed growth of *Candida*

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albicans, hence fluconazole was added. The status of the infant did not improve over next 5 days with persistence of abdominal distention. Hence the infant was evaluated with ultrasound abdomen that showed hyper echoic, thick-walled, $60 \times 25 \times 40$ mm collection with air-fluid level in the liver (segment VI) and a massive amount of intra-abdominal free-fluid with internal echo patterns. The radiogram of the neonate done at the time of umbilical catheterisation was suggestive of malpositioned line inside liver, which directed us to conclude that umbilical line as the reason of this fungal hepatic abscess (Fig. 1). The umbilical line was used to infuse high osmolarity solution including total parenteral nutrition and very high concentration of inotropes. The abscess was drained using a pigtail drainage catheter and peritoneal drain was also inserted. The hepatic pus sent for culture showed growth of *C. albicans* and was started on amphotericin B. Liver function showed gross derangement with alanine aminotransferase (ALT) level being 920 IU/ml and aspartate aminotransferase (AST) level was 1400 IU/cc. The infant started improving after the drainage and we were able to successfully extubate after 2 weeks of airing. The entire course of amphotericin was for 4 weeks. Repeated ultrasound abdomen showed resolution of the abscess, with normal liver function test. The cause of hepatic abscess we thought could be because of umbilical venous catheter, which was inserted in initial days of life.

Figure 1 Radiograph of abdomen showing malpositioned umbilical line in liver that was inserted after birth.

Discussion

Candida infections are responsible for present considerable mortality and morbidity among neonates admitted in nursery, and their incidence and severity appear inversely related to gestational age at the time of birth.² Extremely low birth weight (ELBW) neonates are most susceptible for fungal infection, leading to increased mortality rate and poor long-term outcomes in them.³ Several risk factors for neonatal candidiasis are central venous catheters, lack of enteral feeding, prolonged parenteral nutrition, particularly lipid infusion, H₂-blockers therapy, endotracheal intubation, broad spectrum antibiotics treatment and surgery.⁴

Neonatal liver abscess is particularly very rare in neonates, with one study reporting only 3 cases out of 11 403 neonatal admissions (0.03%). Causative agents in most cases are Gram positive cocci (like *Staphylococcus aureus*, *Gonococcus*, *Enterobacter*, coagulase negative *Staphylococcus*, *Staphylococcus epidermidis*) and Gram negative bacilli (especially *Escherichia coli*, *Klebsiella*, *Haemophilus parainfluenza*, *Serratia*).⁵ Neonatal LA due to *Candida* spp. and/or associated with candidemia is rarely described in the literature and there are <10 cases as best of our knowledge reported till now.^{6,7} The source of infection for liver abscesses could be from an ascending infection via the umbilical and portal veins as a result of central line catheterisation, haematogenous spread from another part of the body like renal fungaemia, or via the biliary tree, or via direct contiguous spread from neighbouring structures or necrotising enterocolitis (NEC).⁵

Immunodeficiency in the form of chronic granulomatous disease may also be implicated as risk factor.⁸ They usually present in atypical manner with features similar to neonatal sepsis, resulting in diagnostic difficulties and also delayed diagnosis.⁹ The non-specific signs includes off colour, delayed capillary refill time, shock, metabolic acidosis, septic appearance, fever, feed intolerance, vomiting, abdominal distention, abdominal tenderness and hepatomegaly are non-specific signs and these are frequently seen in NEC. The laboratory investigations are also non-specific with findings such as leukocytosis, leukopenia, neutropaenia or neutrophilia, thrombocytopaenia, high ESR and elevated liver enzymes.¹⁰⁻¹² The neonatal mortality has been reported to the tune of 50% in cases of neonatal hepatic abscess.^{13,14}

In our patient, there was a history of umbilical vein catheterisation and sepsis screen and blood culture was positive for *Candida*, which proved that umbilical lines were responsible for liver abscess. This has been described in many cases of hepatic abscess, which are caused by umbilical lines.^{11,14-16} Posterior portion of the right lobe has been found to be

more affected as also seen in the present patient, which may be due to the portal venous flow.¹⁷

Diagnosis of hepatic abscess requires a high index of suspicion as it has varied presentation and makes neonatologist to think horizontally. It is usually based on clinical awareness of health care personals in a neonate with ongoing sepsis of unknown origin and not responding to routine treatment of neonatal sepsis (especially if an umbilical line has been *in situ*). Early diagnosis is key to success as morbidity and a high mortality are known to happen. The radiographic signs of liver abscesses may not be conclusive, especially in the former stages of abscess formation. In advance condition, one can see gas in the abscess cavity that could be visible on abdominal X-ray.¹⁸ Availability of ultrasound, especially the portable machine has been a major breakthrough to diagnose this condition and with improved awareness of this condition, there is an expected rise in the number of cases of neonatal liver abscess. Performing routine bedside US to look for a liver abscess in all septic preterm or term newborns without an identifiable septic focus may ensure early diagnosis. Ultrasound usually shows hepatic abscess as areas of increased echogenicity and breakdown. In the recent days, CT scan has also come out as a very diagnostic tool for diagnosis of hepatic abscess. The diagnostic tap needs to be done under ultrasound guided technique to find out the real microbial organism for precise treatment.¹⁹

Complications of hepatic abscess include rupture in surrounding structures, including peritonitis, empyema if it ruptures in the pleural space, acute glomerulonephritis and portal vein thrombosis and also rarely metastatic septic emboli to the brain.^{20,21}

Treatment of hepatic abscess would include diagnostic or therapeutic drainage of the abscess by needle aspiration, surgical drainage and intravenous antibiotic therapy for 4–6 weeks. The fungal hepatic abscess needs to be treated with adequate anti-fungal. Presently, amphotericin B and fluconazole are the first choice drugs for the treatment of neonatal candidiasis and have almost similar efficacy and safety. There have been few case reports of use of caspofungin for treatment of hepatic abscess with positive results.⁷

Cascio *et al.* reported recently three neonates with *C. albicans* hepatic abscess and in their review showed total 10 cases reported till now and eleventh case being ours.⁶ Filippi *et al.* reported three cases of neonatal fungal abscess and showed efficacy of caspofungin in treatment of abscess.⁷

Conclusion

The diagnosis of hepatic abscess should be considered in any neonate whose condition is not

explained by clinical examination as the signs and symptoms are non-specific and related to those of sepsis. Liver ultrasonography should be performed in all the neonates with severe signs of neonatal sepsis, especially in cases of proven blood culture positive *Candida* infection and/or hepatomegaly and/or gross derangement of liver enzymes. Umbilical lines should be taken out as soon as possible. Abscess culture should be performed for microbiological diagnosis to know the sensitivity pattern of the organism and start appropriate antibiotics. The duration of therapy should be at least 4 weeks.

Disclaimer Statement

Contributors DS, MC: Substantial contributions to the conception or design of the work and the acquisition, analysis, or interpretation of data for the work. SS, PS, DS: Drafting the work or revising it critically for important intellectual content. DS, MC, SS, PS: Final approval of the version to be published. DS, MC, SS, PS: Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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