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Candida tropicalis infection in a term neonate with gall bladder masses and infective endocarditis

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ABSTRACT

Candida endocarditis is extremely rare in term neonates, and gall bladder involvement due to candidemia has never been reported amongst neonates and infants. A term, appropriate for gestational age neonate developed *Candida tropicalis* blood stream infection in second week of life. He was started on conventional amphotericin B. However, he failed to show any clinical improvement, and candidemia keep on persisting. Repeat sanctuary sites screening revealed multiple echogenic masses in heart (vegetations) and gall bladder. On changing the treatment to liposomal amphotericin B and fluconazole, he recovered clinically, echogenic masses in gall bladder disappeared, and intracardiac vegetations decreased in size.

1. Introduction

Candida blood stream infections in the neonatal period have been increasing steadily during the past decade. The incidence of invasive candidiasis in neonatal care units ranges between 1.6% and 4.5%[1]. Endocarditis has been observed in up to 5% (range 0%-16%) cases of neonatal candidemia, and almost all of them were preterm low birth weight babies[2-4]. Amongst term neonates with normal birth weight, only a single case of *Candida* endocarditis has been reported[3]. *Candida* species reported to cause endocarditis are mainly *Candida albicans* and *Candida* parapsilosis. Gall bladder involvement due to candidemia has never been reported in infancy. Through this report, we wish to present the first case of *Candida tropicalis* infection associated with gall bladder masses and infective endocarditis in a term, appropriate for gestational age neonate.

2. Case report

A term male baby, weighing 3.05 kg, was born to 25 year old second gravida mother through caesarean section (indication: foetal distress with thick meconium stained liquor). He was non-vigorous at birth and required endotracheal suctioning followed by bag and mask ventilation for 1 min. His APGAR scores were 5, 8 and 9 at 1 min, 5 min and 20 min respectively. He was started on intravenous fluids and kept under observation in nursery. At 8 hrs of life, he developed respiratory distress. Sepsis screen was negative, chest X-ray was normal, and blood culture was sterile. However, he was started on injections cefotaxime and amikacin along with free flow oxygen. Respiratory distress gradually resolved over next 48 hrs and on day 3 of life, he was put on breast feeding. On seventh day of life, he developed rash over lower limbs and trunk. His activity was normal; vitals were stable; general physical examination showed icterus and petechial rashes over lower limbs and trunk; and systemic examination showed no abnormal findings. Investigations revealed haemoglobin 14.9 g/dL; total leukocyte count 14.5×10^9/L with 41% neutrophils (2% band cells and 39% mature neutrophils), 53% lymphocytes, 5% monocytes and 1% eosinophils; platelet count 47×10^9/L, C reactive protein (CRP) 4 mg/L; and micro erythrocyte sedimentation rate (μ ESR) 2 mm first hr. Serum bilirubin, aminotransferases and alkaline phosphatase were elevated (total bilirubin 117 mmol/L with direct bilirubin of 49 mmol/L, alanine aminotransferase

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286 IU/L, aspartate aminotransferase 292 IU/L, and alkaline phosphatase 820 IU/L). Urine examination, renal function tests, prothrombin time (PT), activated partial thromboplastin time (aPTT), blood glucose and serum electrolytes were normal. Antibiotics were changed to meropenem after taking fresh sample for bacterial blood culture. His second blood culture was also sterile. No fresh petechiae occurred further, however icterus kept on worsening and he was transferred to our hospital on day 11 of life. At admission in our hospital, baby was active and alert; his vitals were stable; general physical examination showed deep icterus; and systemic examination showed firm hepatomegaly (3 cm below costal margin). Fundus examination was normal. Haemogram showed haemoglobin 12.8 g/dL; total leukocyte count 10.3×10^9/L with 49% neutrophils, 46% lymphocytes, 4% monocytes and 1% eosinophils; and platelet count 34×10^9/L. P was 16 mg/L (< 8 mg/L). Liver function test showed total bilirubin 234 mmol/L with direct bilirubin of 113 mmol/L, SGPT 320 IU/L, SGOT 420 IU/L, alkaline phosphatase 860 IU/L, prothrombin time 17 sec (control 14 sec), and protein 62 g/L with albumin of 33 g/L. Abdominal ultrasonography showed hepatomegaly with altered echotexture. Blood culture (fungal BACTEC) showed *Candida tropicalis* (*C. tropicalis*), sensitive to amphotericin B and fluconazole. Risk factors like use of anti-histaminics, corticosteroids, parentral nutrition and central catheterization were absent. Cerebrospinal fluid (CSF) examination, urine examination, chest X-ray, echocardiography, and cranial ultrasonography were normal. Urine, CSF and bacterial blood (bacterial BACTEC) cultures were sterile. Repeat detailed ocular examination was also normal. Serological tests for toxoplasma, syphilis, rubella, cytomegalovirus, and herpes were negative in the baby as well as in the mother. Human immunodeficiency virus (HIV) serology and hepatitis B surface (HBs) antigen were negative in the mother, and HBs antigen and hepatitis C immunoglobulin M were negative in the baby. He was started on injection amphotericin B, however icterus didn't improve and no weight gain occurred over next two weeks. Repeat blood cultures done on day 7 and 14 of amphotericin B therapy showed same (*C. tropicalis*) growth. Repeated bacterial blood cultures done were sterile. Baby was again screened for focus of persistent *Candida* infection (ocular examination, urine microscopy and culture, echocardiography, and cranial and abdominal ulrasonography) and this time echocardiography showed three echogenic masses (vegetations) present over tricuspid valve, its papillary muscle and right ventricle apex measuring 3.5 mm × 4.1 mm, 4 mm × 5 mm and 3.4 mm × 4 mm respectively; and abdominal ultrasonography revealed two rounded echogenic masses in gall bladder lumen along with thickened walls (Figure 1 & 2). The presence of intracardiac and gall bladder masses in association with persistent *C. tropicalis* blood stream infection, and negative bacterial blood cultures suggested the diagnosis of disseminated *C. tropicalis* infection associated with infective endocarditis and gall bladder involvement. Conventional amphotericin B was replaced with injections liposomal amphotericin B and fluconazole. After 7 days of this combination therapy, baby started gaining weight normally on exclusive breast feeding, and blood culture became sterile. By the end of the third week end, there was complete clinical and biochemical resolution of hepatitis, and platelet counts became normal; and after 5 weeks gall bladder masses also disappeared. However, intracardiac vegetations size remained same on serial echocardiography done after one, three and six weeks of combination therapy. Baby received total six weeks of liposomal amphotericin B and fluconazole. Cardiothoracic surgical opinion was sought, and was advised to continue with conservative therapy. Since the appearance of vegetations in echocardiography remained stable, gall bladder masses disappeared, hepatitis recovered completely and baby started gaining weight adequately; he was discharged on long term prophylaxis with oral fluconazole. On serial follow ups over next 1.5 years (still under follow up), he remained asymptomatic and achieved appropriate growth parameters and developmental milestones for his age, and intracardiac vegetations almost completely disappeared with minimal residual leaflets thickening.

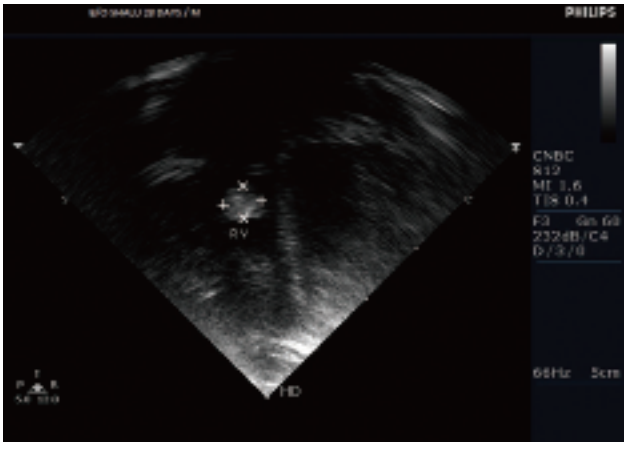

Figure 1. Rounded echogenic mass (vegetation) seen in right ventricle.

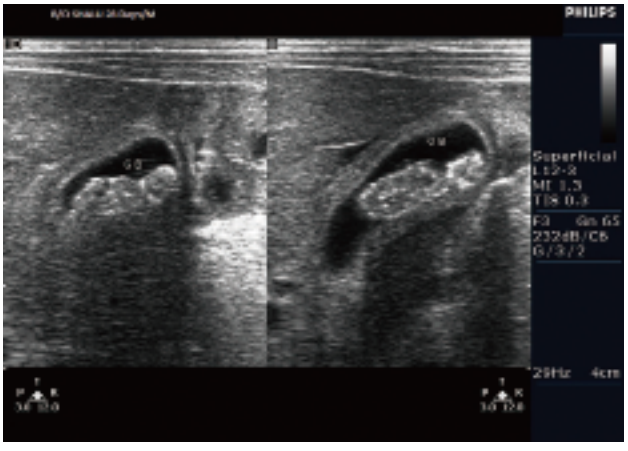

Figure 2. Rounded echogenic masses seen in gall bladder lumen along with thickened walls.

3. Discussion

Invasive fungal infection is an important cause of mortality and morbidity in very low birthweight (VLBW) infants [1]. Extremely preterm and low birth weight infants are at highest risk because of the intensive and invasive nature of the care that these infants receive. However, our patient was a term neonate with normal birth weight. Additional specific risk factors include indwelling vascular catheter, prolonged use of parenteral nutrition, exposure to broad-spectrum antibiotics and histamine type 2 receptor blockers[5]. Neonatal candidemia is a source of significant morbidity as a result of its complications such as meningitis, ventriculitis, brain abscess, uveitis, endophthalmitis, renal abscess, arthritis and endocarditis[2,3]. Endocarditis is an uncommon complication of neonatal candidemia and occurs most frequently as part of a disseminated fungal infection, in patients following cardiac surgery, or in those who develop an intracardiac thrombus or valvular injury due to a central venous catheter (CVC)[6]. In our patient, broad spectrum antibiotics were used for 11 days prior to positive fungal blood culture, however CVC was never put, which is quiet unusual especially in the setting of fungal endocarditis.

Candida species are the most frequently reported cause of fungal endocarditis in children, accounting for 63% of documented cases. Amongst its species, *Candida albicans* (*C. albicans*) still remains the most common (41%), however newer species like *C. parapsilosis*, *Candida glabrata* (*C. glabrata*) and *Candida krusei* (*C. krusei*) are also gradually becoming more prevalent[7]. *C. tropicalis* was the species isolated in our case, which has been rarely reported to cause endocarditis in neonates[7]. Neonatal fungal endocarditis usually affects right sided chambers of heart[3], also observed in present case. The clinical presentation of neonatal endocarditis is variable and non-specific, and may be indistinguishable from those of congenital heart disease or septicemia. In our patient too, the clinical presentation was non specific and there were no thromboembolic manifestations. An abnormal echocardiogram that demonstrates intracardiac vegetations, in association with candidemia and negative bacterial blood cultures is almost diagnostic of *Candida* endocarditis[8]. All these three parameters were present in our case. Another important finding observed in present case was presence of two echogenic masses in gall bladder, which too in the presence of candidemia, negative bacterial blood cultures and resolution after antifungal therapy, appears to be causally related to *C. tropicalis*. However, bile culture was not done. Gall bladder involvement due to candidemia has never been reported in infancy.

To conclude, present case is the first ever reported case of *C. tropicalis* infection associated with gall bladder masses and infective endocarditis in a neonate. Secondly, repeat sanctuary sites screening such as echocardiography, abdominal and cranial ultrasonography, and urine and CSF examination should be considered in patients with persistent fungemia.

Conflict of interest statement

We declare that we have no conflict of interest.

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