Obstructive renal candidiasis in a premature infant
Harkensee C and Gibbs J, Department of Neonatology (HC), Royal Victoria Infirmary, Newcastle upon Tyne, Department of Paediatrics and Neonatology (GJ), Countess of Chester Hospital, Chester, UK
A male neonate of 24 weeks gestation was born vaginally to a healthy 29-year-old P1/G1 following premature rupture of membranes associated with a urinary tract infection. Two doses of steroids were given antenatally.

The neonate’s initial condition was reasonable (Apgars 4 at 1 minute and 8 by five minutes), and birth weight was 860 g. Intubation, surfactant and assisted ventilation were required for the respiratory distress syndrome. Weaning from mechanical ventilation was achieved rapidly and he was extubated onto nasal CPAP on day 5 with an FiO₂ of 0.24.

Penicillin was given for 7 days, and netilmicin for 5 days, in view of prolonged rupture of membranes and a maternal vaginal swab culture of Group B streptococcus, although the neonate was not clinically septic and blood cultures were negative. Enteral feeding with expressed breast milk was introduced from day 6 and full enteral feeds were tolerated by day 28.

Despite the initial good respiratory progress, the neonate subsequently experienced a stormy course. On day 9, he was re-intubated and ventilated for 6 days, then again for 11 days from day 31. Both these episodes were associated with coagulase-negative septicemia. On the second occasion, signs of early necrotising enterocolitis developed but did not progress. Between episodes of ventilation, supplemental oxygen (up to an FiO₂ of 0.5) was given via nasal CPAP.
On the first day of life, cerebral ultrasound had revealed a right-sided subependymal hemorrhage that progressed to a grade III intraventricular hemorrhage over the first week of life but without abnormal neurological signs. A significant PDA was closed with indomethacin.

The neonate’s skin cracked extensively during the first week. From day 6, candida albicans was cultured from skin swabs and so oral and topical nystatin were administered. On day 15, candida albicans was cultured from a long line tip and from endotracheal secretions. Fluconazole was given intravenously, although the neonate did not appear clinically septic and there were no blood indices of infection. Fluconazole was stopped after 18 days once no further candida was grown from repeated blood and endotracheal or pharyngeal samples. However, candida was persistently detected from skin swabs, so oral and topical nystatin were continued. Candida albicans was also found, on several occasions, in urine collected externally and was thought to have originated from skin colonisation but no suprapubic sample was obtained.

From day 58, the patient deteriorated, no longer tolerated enteral feeds and again required intubation and ventilation. Antibiotics were given but no bacteria were isolated from blood cultures. Two days later, he became anuric, mildly oedematous and large, firm flank masses were felt bilaterally. An urgent ultrasound of
US left kidney: echogenic material (arrow) obstructing renal pelvis and proximal ureter.
US left kidney: echogenic material (arrow) obstructing the renal pelvis.
US right kidney: echogenic material (arrow) obstructing renal pelvis and proximal ureter.
the abdomen revealed echogenic material distending both renal pelvices, consistent with renal fungal balls (Fig. 1-3).

Liposomal amphotericin was commenced and the infant transferred to the regional neonatal intensive care unit. His weight was 975 g. A left nephrostomy tube was inserted under ultrasound guidance but no urine drained and so hourly dialysis cycles were started through a peritoneal catheter. Two days later, bilateral nephrostomies were created surgically and thick gelatinous material was extracted from the renal pelvices that were then irrigated but subsequently no urine was passed. The gelatinous material proved to be candida albicans on culture, sensitive to amphotericin and flucytosine. Over the next few days candida was grown from the peritoneal dialysis fluid and so flucytosine was added to the liposomal amphotericin treatment.

The parents were counselled that, in such a small infant, there was a high chance of the peritoneal dialysis failing within a few days. Fortunately, dialysis continued uneventfully for the following 3½ weeks by which time good volumes of urine were being produced and dialysis was withdrawn. The maximum serum creatinine during dialysis was 222 mcmol/l. Assisted ventilation was required throughout the period of peritoneal dialysis, with low inspiratory pressures and an FiO2 of 0.3-0.4. It was possible to withdraw ventilation once the dialysis stopped.
Serial renal ultrasound scans showed progressive, complete atrophy of the right kidney and a slowly growing left kidney with poor cortico-medullary differentiation. A small residual mass was noted in the left renal pelvis. The flucytosine was stopped after 4 weeks but the amphotericin was continued for a total of 8 weeks, until repeated urine cultures were clear of candida and there was no longer any mass visible in the left renal pelvis on ultrasound.

The infant underwent laser treatment at 5 months of age for stage 3 retinopathy of prematurity and developed ataxic cerebral palsy, but without a hemiplegia. Currently, at 3 years of age, he is an active and inquisitive young boy who has a serum urea of 10 mmol/l, a creatinine of 60-70 mcmol/l, takes amlodipine for hypertension, has a moderate delay in motor and language skills, bilateral convergent strabismus and normal vision and hearing.

Fungal septicemia is rarely diagnosed promptly and usually presents either with low grade sepsis unresponsive to antibiotic treatment, or with complications related to fungal masses in the central nervous system, the heart, the urogenital tract or other organs and tissues. Therefore, it is very important to consider screening and prophylaxis as part of the management of neonatal fungal infection.
Epidemiological data from neonatal intensive care units suggest that colonisation with Candida albicans is common but not necessarily pathological (1). 10% of term infants develop cutaneous, gastrointestinal and respiratory tract colonisation within 5 days of birth. Preterm infants have a much higher colonization rate with 30% colonized by 5 days and 80% colonized by 14 days (2). This is probably due to an immature immune response and an increased likelihood of nosocomial transmission due to the large number of carers and procedures involved in supporting a very premature infant.

Various single risk factors for developing invasive candidiasis have been identified (3,4), but it seems that the highest risk results from a combination of being an ill, small, premature infant requiring intense monitoring and treatment (especially the use of central venous lines, intubation and broad spectrum antibiotics). Apart from septicemia, renal candidiasis following hematogenous spread or ascending infection is probably the most common manifestation of invasive candidiasis. Candiduria is thought to occur in 0.5% of patients admitted to a neonatal intensive care unit (5), and almost half of these have renal fungal masses. The mortality rate of patients with manifest obstructing renal fungal masses is high (35-50%).

Strict hygiene measures, such as careful hand washing, are probably more important than prophylactic drugs
in preventing neonatal invasive candidiasis. There is controversy over the efficacy, cost-effectiveness and adverse effects of oral (nystatin) and intravenous (fluconazole) prophylactic drugs. Targeting the use of prophylactic fluconazole to those at highest risk seems to reduce the incidence of invasive candidiasis (6). Screening for invasive fungal disease is important but not straightforward since blood cultures are relatively insensitive for candida so serial cultures are required and fungi usually take many days to grow sufficiently to be detected. Due to the filtering and concentrating action of the kidneys, there is a higher likelihood of identifying candida albicans in the urine when there is either fungemia or fungal renal infection. Fungi detected by surface swabs indicate colonisation, but this is poorly predictive of invasive fungal disease. Therefore, whenever fungi are detected in urine collected non-invasively this should be followed by a more invasive urine sample, for example a supra-pubic aspirate, in order to search for invasive candidiasis either by culture or the identification of hyphae on microscopy.

Treatment for invasive candidiasis consists of a prolonged course of an intravenous antifungal drug such as fluconazole or amphotericin (7). Liposomal amphotericin seems to be much less nephrotoxic than the standard preparation. Most authors recommend a course of six weeks, or until at least two fungal blood cultures are negative, although regular renal
ultrasound scan and urine cultures are required to monitor renal fungal infection (5,7). The management of obstructive renal fungal balls does not have a reliable evidence base and is derived largely from anecdotal experience. Nephrostomies should be created in obstructive renal failure and there are reports of instilling amphotericin, fluconazole, streptokinase or methylene blue through nephrostomies to relieve acute obstruction and decontaminate the urinary tract. If, as in this case, acute renal failure persists despite attempts to relieve the obstruction, then dialysis is required but may prove impossible to sustain due to the technical challenges presented by small, premature infants.

With the permission of the parents, we would like to publish an e-mail message that reached us from the patient’s mother shortly after this case was published:

I am the mother of the 24 week premature baby featured in your case of the month, regarding renal candida fungal balls. I wish to express my deep gratitude to all the medics who saved his life, and for Chris for taking the time to submit this case to you. I hope this learning will help other lives to be saved. Our son is now healthy, fun, active and intelligent. Thank you.

We appreciate the parent’s feed-back on an extraordinary story.


