CASE REPORT

Streptokinase therapy in the treatment of neonatal obstructive renal candidiasis

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SUMMARY

A 6-week-old ex-25-week gestation male infant developed candidal sepsis with subsequent bilateral acute obstructive nephropathy that was not responsive to intravenous antifungal therapy. Bilateral percutaneous nephrostomies were performed and irrigation with fluconazole started. Owing to the persistence of the candidaemia and left renal obstruction, streptokinase was administered through the nephrostomy with eventual resolution of obstruction and improvement in his kidney function. This case report discusses the use of the streptokinase therapy as an adjunct therapy in the clearance of fungal bezoars.

BACKGROUND

Candidal infection is one of the causes of late onset sepsis in very low birth weight neonates.¹ Several risk factors have been recognised for candidaemia, including prematurity, low birth weight, prolonged central line access, broad-spectrum antibiotics, post-natal steroids and intravenous nutrition.^{2–3} The kidney is a frequent site of involvement in these infants. The prevalence of renal candidiasis has been reported to be between 5% and 33% in infants with candidaemia.⁴ Fungal bezoars are a rare complication of renal candidiasis that can often lead to obstructive nephropathy. Several cohort studies have shown that about 11–35% of neonates with fungal urinary tract infection had evidence of renal fungal bezoars.^{5–6} The use of fibrinolytic therapy has been described in two case reports of obstructive renal candidiasis.^{7–8} Our case adds to the evidence for the potential use of this therapy in the treatment of obstructive renal candidiasis that is refractory to antifungals and drainage.

CASE PRESENTATION

Our patient is a male infant who was born at 25 weeks gestation (birth weight 910 g) via caesarean section following spontaneous onset of labour. Apgar scores were 4 and 7 at 1 and 5 min, respectively. He was intubated and ventilated at birth and received two doses of surfactant. His initial clinical course was complicated by severe respiratory distress and persistent pulmonary hypertension, requiring high-frequency oscillatory ventilation and inhaled nitric oxide. He also received dopamine infusion due to persistent hypotension. He remained ventilated for 6 weeks and was successfully extubated to continuous positive airway pressure while receiving a prolonged, tapering course of dexamethasone. He was treated with a 2-week

course of vancomycin and gentamicin for presumed coagulase-negative *Staphylococcus* sepsis at 3 weeks of age. He received total parenteral nutrition after birth and had insertion of umbilical catheters and subsequent peripherally inserted central catheter on day 10 of his life.

On day 44 of his life, he developed clinical signs of sepsis with increased frequency of apnoeas. A workup revealed a leucocyte count of $22 \times 10^9/L$, platelet count of $525 \times 10^9/L$ and C reactive protein (CRP) of 17 mg/L. Empiric antibiotics were started due to his clinical deterioration. His blood culture and urine culture subsequently grew *Candida albicans*. A lumbar puncture was negative for growth. Antibiotics were stopped and he was treated with intravenous fluconazole (12 mg/kg/day) and flucytosine (50 mg/kg/day). Echocardiogram and eye examination were normal. Two days later, he developed anuria and had evidence of acute kidney injury with elevated creatinine of $160 \mu\text{mol/L}$. A renal ultrasound revealed the presence of bilateral fungal bezoars filling both renal pelvises causing acute urinary obstruction (figure 1). Emergent bilateral percutaneous nephrostomies were performed and both renal pelvises were irrigated with fluconazole (0.04 mg/mL), with some improvement of the mechanical obstruction.

Repeat blood cultures taken 4 days later revealed the persistence of candidaemia. CRP remained elevated at 68 mg/L and platelets had decreased to $64 \times 10^9/L$. Caspofungin (1 mg/kg/day) was added to the regimen. A nephrostogram showed passage of contrast to the urinary bladder from the right drain but not through the left.

TREATMENT

A decision was made in consultation with the urology team to use streptokinase through the left nephrostomy to relieve the obstruction. A total of 15 000 IU streptokinase in 5 mL of the saline (3000 IU/mL) was used to irrigate the left nephrostomy and clamped for 10 min. This was performed twice a day for a total of 3 days. A subsequent renal ultrasound showed significant clearance of echogenic material in the left kidney. Both drains were removed 2 weeks after insertion. Urine output and renal function tests eventually normalised.

OUTCOME AND FOLLOW-UP

The patient completed a 6-week course of intravenous fluconazole, with clearance of *Candida* from blood and urine. A follow-up renal ultrasound (figure 1) and a radionuclide scan postdischarge showed a complete resolution of debris in both

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Figure 1 Ultrasound findings of bilateral non-shadowing echogenic fungal masses and dilated renal tracts (A and B) with resolution of findings on follow-up (C and D).

pelvicalyceal systems with no evidence of renal cortical scarring. An 8-month follow-up at the clinic revealed a normotensive infant with no evidence of renal dysfunction.

DISCUSSION

Several mechanisms have been proposed to be involved in the development of fungal bezoars with subsequent obstruction. It has been postulated that renal bezoar formation is likely secondary to intravascular fungal dissemination.^{2–5} Chronic renal inflammation in the presence of fungal organisms leads to proliferation in the renal medulla and papillary necrosis. Pseudohyphae growth around the affected area leads to the formation of a mycelial ball. This can lead to obstruction of the

urinary tract.⁴ Neonates with urinary tract abnormalities were also found to be predisposed to the development of renal bezoars.² This tended to occur at an earlier time point in infants of older gestation.

Diagnosis can be made by ultrasound findings of non-shadowing echogenic fungal masses. Obstructive candidiasis can be accompanied by the presence of dilated renal tracts where only parenchymal changes may be noted in non-obstructed cases. Most cases of obstructive renal candidiasis with partial obstruction can be managed with the use of antifungals without the need for instrumentation.^{2–4} The use of amphotericin B and fluconazole is the mainstay of the treatment for candidal infections, with flucytosine as an adjunct. In situations where there is

Table 1 Cases of obstructive kidney injury caused by fungal bezoars treated with streptokinase reported in the literature^{7–8}

Patient information	Ultrasound findings	Medical therapy	Streptokinase protocol	Notes
2-month-old ex-26-week infant with <i>Candida albicans</i> sepsis, develops bilateral enlarged kidneys, acute kidney injury and candiduria	Bilateral renal enlargement, echogenic foci in dilated collecting systems, perirenal and peritoneal fluid	Amphotericin B, fluconazole intravenously, bilateral nephrostomy tube and local irrigation with an amphotericin (for 10 days)	Transvesicular ureteral catheter streptokinase 15 000 IU in 5 mL twice daily and clamped for 1 h×3 days	After 10 days, clinical and ultrasound finding were normal, blood urea nitrogen and creatinine levels were normal
1-month-old ex-27-week infant developed anuria with candida pyelonephritis	Marked bilateral hydronephrosis with echogenic material obstructing both pelvi-ureteric junctions	Amphotericin B and flucytosine intravenously, bilateral nephrostomy and irrigation with amphotericin B; L side continued to have obstruction	Streptokinase irrigation via left nephrostomy (15 000 IU in 5 mL twice daily) and clamped for 1 h×3 days	Systemic antifungal continued for 2 weeks after irrigation. Successful clearing of echogenic material, improving urine flow, no recurrent hydronephrosis
6-week-old ex-25-week infant with <i>C. albicans</i> sepsis and acute obstruction of the renal pelvis leading to anuria	Bilateral renal enlargement and pelvicalyceal obstruction with echogenic material	Fluconazole, flucytosine and caspofungin intravenously, bilateral nephrostomy and irrigation with fluconazole; L side continued to have obstruction	Streptokinase irrigation via left nephrostomy (15 000 IU in 5 mL twice daily) and clamped for 10 min×3 days	Clearance of the left renal echogenic material. Complete resolution with follow-up ultrasounds and radionuclide scan

dilation of the collecting system and evidence of renal dysfunction, drainage with percutaneous nephrostomy may be required. Irrigation of the nephrostomy with antifungals has also been used successfully to clear focal fungal infections in the kidney.

Fibrinolytic therapy has been used in cases of obstructive renal candidiasis that were refractory to antifungals and drainage. Two other cases utilising streptokinase have been reported in the literature.^{7 8} Clinical information from all three cases is summarised in table 1. Streptokinase was successful in clearing the fungal material in all cases. It is thought to be helpful in the dissolution of fibrin that may have accumulated and adhered to the fungal bezoar. The dose of streptokinase used in our patient is similar to that previously described, with the exception that the nephrostomy was clamped for 10 min instead of an hour. The shortened duration was chosen due to concerns about the bleeding complication associated with streptokinase.⁹

Studies of newborns with fungal bezoars indicate that prompt detection and treatment of this condition would typically lead to good recovery of renal function and no long-term renal dysfunction.² A review of newborns with fungal bezoars suggests

that ultrasound findings of fungal bezoars persist long after clearance of candida from the urine.² This is thought to represent a sterile accumulation of debris, dead hyphae and papillae. Antifungal therapy was typically stopped long before the resolution of ultrasound findings. As such, ultrasound findings should not be used to guide the length of therapy and the cessation of growth of viable fungal organisms in the urine should be used instead.

Contributors All the authors listed have participated in the concept, analysis of data, drafting of the manuscript and have approved the manuscript as submitted.

Competing interests None.

Patient consent Obtained.

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Learning points

- Renal candidiasis is a common complication of neonates with candidaemia.
- Prompt detection and treatment of fungal bezoars can lead to a good recovery of the renal function and decreased risk of long-term renal dysfunction.
- Antifungal therapy is the mainstay of the treatment for obstructive renal candidiasis and streptokinase irrigation though percutaneous nephrostomy may be useful in cases that are poorly responsive to antifungal therapy.

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