Renal fungal balls in a newborn with neonatal candidiasis

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**Abstract**

Renal candidiasis is the result of hematogenous implantation of the fungus on the kidneys during an episode of candidemia or a consequence of an ascending urinary infection. Renal candidiasis may present as pyelonephritis, papillary necrosis, perinephritic abscess, fungus balls, urinary obstruction, calculi, nephrocalcinosis, ureterocele and hydronephrosis. We report the case of a newborn with renal candidiasis whose urine culture showed a count of colonies of Candida per milliliter that might have been taken as simple colonizations; however, the presence of Manan serum antigen by monoclonal Candida sp. antibodies in serum antigen studies, direct urine examination, creatinine clearance and renal ultrasound, established the diagnosis.

**Key words:** Fungus balls, candidiasis, pseudomycelium, renal failure.

Clinical features depend on the degree of urinary tract obstruction. Events that are more serious may result from urine retention with oliguria or anuria in cases with bilateral mycotic obstruction. Renal involvement is relatively common in systemic candidiasis, but may cause fungal obstruction and acute renal failure. Fortunately, in most cases, the clinical course is not so severe.4-6

The diagnosis of urinary tract Candida infection is based on the presence of more than 1,000 colonies per milliliter (UFC/mL) in urine obtained under sterile conditions through a suprapubic vesical puncture; or more than 10,000 UFC/mL in urine obtained by urethral catheterization. However, the most reliable diagnostic method is ultrasound (US) that should be performed in any patient suspected of coursing with candidiasis. Fungus balls are visible with US as echogenic foci within the duct system without an acoustic shadow.7-8

Traditional treatment for this condition has been surgical; however, recent reports indicate the successful use of systemic antifungal agents such as fluconazole and amphotericin B.9

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**Case report**

A six-hour newborn male, with irrelevant past history was admitted on January 1\textsuperscript{st}, 2000 to the Intensive Care Unit with the diagnosis of gastroschisis. On admission, he ventilated normally; soon after, he developed acute cardiogenic pulmonary edema and a cholestatic syndrome.

A complete blood cell count was normal for his age. On January 11\textsuperscript{th} he was given prophylactic dicloxacillin and cefotaxime, and operated for closure of the abdominal wall defect. On January 17\textsuperscript{th}, a blood culture revealed *Klebsiella pneumoniae* resistant to antibiotics whereupon he was started on meropenem. A transfontanellar ultrasound revealed findings compatible with ischemic-hypoxic encephalopathy. Renal and hepatic ultrasounds were normal. The patient developed severe jaundice with a total bilirubin of 29, indirect bilirubin of 10 and direct bilirubin of 19. He was given 3 mg/kg a day of phenobarbital as a choleretic.

On January 18\textsuperscript{th} the patient became febrile with a temperature of 38.5°C. Renal failure was diagnosed based on a serum creatinine of 0.58, blood urea of 31.4 and a 24 h creatinine clearance of 16.4 mL/min/m\(^2\). A renal ultrasound done on January 20\textsuperscript{th} showed normal size and shape of both kidneys, with a normal relation between cortex and sinus; there were no pyelocaliceal dilatations.

The patient remained febrile; on January 26\textsuperscript{th}, *Candida* sp pseudomycelia were found in the urine, and a urine culture showed *Candida albicans* with 1,200 and 2,000 UFC/mL (figure 1). A blood culture was negative but serum Manan antigen for *Candida* species was detected by means of monoclonal antibodies. He was started on amphotericin B 1 mg/kg/day. To rule out a renal infection caused by *Candida* sepsis another ultrasound was performed which showed increased echogenicity of the right renal parenchyma, prominence of the pyramids and the presence of round hyperechogenic images located in the caliceal areas, compatible with “fungus balls”. These findings were also present but less evident in the left kidney which also showed increased parenchymal echogenicity, increased prominence of the pyramids and greater echogenicity of some areas, especially in the upper collecting tubules (figure 2).

Direct examination of the urine was positive for blastoconidia and pseudomycelia as late as the 8\textsuperscript{th} day of antifungal treatment. However, a control ultrasound at the end of two weeks showed a decrease in the size of the lesions.

After three weeks of antifungal treatment and a total dose of 21 mg/kg of amphotericin B, the patient was discharged from the Intensive Care Unit. A renal ultrasound on February 14\textsuperscript{th} showed normal size and shape kidneys, free of fungus balls. Serial fresh urine specimens were negative for pseudomycelia and blastoconidia. Urine and blood cultures at 14, 21 and 30 days were also negative.
blood cultures at 14, 21 and 30 days were also negative. Manan antigen for Candida species was negative. Creatinine clearance upon completion of the treatment was normal. The patient remains asymptomatic and is followed in the outpatient department.

**Discussion**

Several criteria have been proposed for the diagnosis of urinary tract Candida infections; most of them are based on urinary symptoms and urea and creatinine values. Ultrasound findings have also been depended upon for diagnosis.

The presence of candidiuria in a pediatric patient may be the result of different situations, among which are colonization of the urinary tract in the absence of symptoms, primary cystic candidiasis, mycotic pyelonephritis and the presence of fungus balls. However, it is difficult to differentiate these conditions without an oriented diagnostic approach.\[3,11\]

One of the most useful parameters to establish the diagnosis of Candida urinary tract infection is the UFC/mL. A UFC/mL above 10,000 is highly significant. On the other hand, a UFC/mL above 100,000 indicates a bacterial urinary infection. However, a UFC/mL ranging from \(10^4\) to \(10^5\), according to Kass, is not indicative of the presence nor absence of a urinary infection; in other words, within that range, the diagnosis of bacterial urinary infection can neither be established nor discarded.\[1,2\] The same situation may occur in some Candida urinary infections.

Yet, at the present time, there are no studies of UFC/mL substantiating the range of predictable renal candidiasis. It should be kept in mind that the criterion for a positive result of >10,000 UFC/mL for Candida is merely an extrapolation of the standard obtained for bacteria. This is based on a study of nine patients with histopathologically confirmed renal candidiasis in which 10,000 to 40,000 UFC/mL of Candida were obtained.\[3\] On the basis of this study done on a small number of cases a mycotic urinary infection cannot be discarded with a UFC <10,000, such as in the newborn herein presented whose urine cultures showed Candida UFC/mL, considerably below 10,000 (average of 1,600 UFC/mL).

The lack of studies on the predictability of Candida urinary infections based on UFC/mL is due to the infrequent diagnosis of this condition; this makes it difficult to undertake prospective studies. Most papers on Candida urinary infections indicate that the diagnostic approach is based on the presence of blastoconidia (yeasts) and on the number of UFC/mL of Candida in urine cultures; however, an oriented study to detect the presence or absence of pseudomycelia in urine has not been done. The presence of pseudomycelia has been specifically documented only in patients who eliminate “fungus balls” in the urine, which is very unusual.

The oriented search of pseudomycelia in the urine is very important since during the pseudomycelia stage (mycelial) originating from blastoconidia, fungi are immune to phagocytosis; furthermore, this is the stage allowing fungi to invade various tissues. Blastoconidia are the saprophytic form whereas pseudomycelia are the pathogen or parasitic form.\[13-15\]

Our patient eliminated large numbers of blastoconidia and pseudomycelia, which were visible by direct examination in centrifuged fresh urine specimens. In this case, the UFC/mL count might have been considered as “negative”, i.e. as the result of a simple colonization (average of 1,600 UFC/mL); however, the presence of Candida sepsis, renal insufficiency and numerous pseudomycelia in the urine, suggested an invasive renal process, which prompted the need for an oriented diagnostic approach with an ultrasound study to establish the diagnosis of a renal infection.

At present there is no established therapeutic pattern for this condition. Several authors have proposed parenteral therapy, bladder irrigation with amphotericin B and surgical removal of pelvicaliceal mycelia. There are reports on the successful treatment of this condition with fluconazol; other reports indicate recurrences or no response.\[16\] Our patient was treated with 1 mg/kg/day of amphotericin B because he had developed a septic condition.

While the length of antymycotic treatments has not been established, we propose that the medication should be continued until urine is negative for fungus; when urine and blood cultures are also negative and there is total absence of “fungus balls” with normal kidney images by ultrasound.

Our patient responded to the antymycotic treatment without surgery in 21 days. We suggest that the diagnostic approach for renal Candidiasis should include serial blood cultures, detection of serum Manan antigen for Candida sp by monoclonal antibodies, the search for blastoconidia and pseudomycelia in serial centrifuged urine, urine culture with colony counts and ultrasound renal screening.
REFERENCES


