


Neonatal Urinary Tract Infection and Renal Nodular Lesion: A Rare Case of Xanthogranulomatous Pyelonephritis

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Abstract

Xanthogranulomatous pyelonephritis (XPN) is an uncommon variant of chronic pyelonephritis with a poorly understood pathogenesis and a challenging diagnosis. It is rare in pediatric patients, particularly in the neonatal period. We report the case of an 18-day-old female neonate admitted to the emergency room due to macroscopic hematuria and poor feeding. Urinalysis revealed leukocyturia and she was initially admitted under the clinical suspicion of acute pyelonephritis. Renal ultrasound and magnetic resonance imaging (MRI) revealed a progressive nodular lesion in the middle third of the left kidney. Given the suspicion of renal abscess or neoplasm, the patient was transferred to our tertiary hospital. Urinary catecholamines and tumor markers had normal values. Percutaneous kidney biopsy confirmed XPN. Posterior computed tomography scan excluded extension to neighboring structures. A conservative management with systemic antibiotic therapy was decided. She completed 7 weeks of systemic antibiotic therapy (ampicillin and cefotaxime) with progressive reduction of lesion size and posterior calcification. Follow-up at 3 years was uneventful. The lipid profile and study of neutrophil function were normal. Voiding cystourethrography excluded vesicoureteral reflux. The authors intend to highlight the importance of a high index of suspicion of XPN to allow preoperative diagnosis. Histopathological assessment is mandatory to confirm XPN and exclude other entities mimicked by focal and unilateral progressive disease. There are only a few published cases of optimal clinical evolution solely with broad-spectrum antibiotics; however, this may allow a beneficial nephron-sparing approach in selected patients.

Keywords

xanthogranulomatous pyelonephritis, biopsy, foam cells, conservative treatment

Introduction

Xanthogranulomatous pyelonephritis (XPN) is a rare form of chronic pyelonephritis due to chronic infiltration of renal tissues with lipid-laden macrophages, which may lead to impairment of renal function.¹

The pathogenesis is poorly understood and possibly multifactorial; however, it is generally associated with long-term renal obstruction or infection. Classically, XPN is seen in middle-aged female patients with staghorn calculi. In the pediatric setting, XPN is an unusual entity, and it can be encountered in approximately 16% of nephrectomy specimens. Most cases occur in children under 5 years of age (60%–75%) and it is extremely rare in neonates.^{2–5}

Two variants of XPN were described: diffuse XPN (75%–90% of cases) and focal XPN, which is uncommon and frequently observed in children.⁶ Xanthogranulomatous pyelonephritis is known as the “great imitator” of various

benign and malignant conditions, as clinical and radiographic characteristics can be nonspecific and misdiagnosis is quite common. This is particularly true in focal XPN, also termed

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“pseudo-tumoral” form as it can mimic renal tumors (eg, Wilms tumor, clear cell carcinoma). Therefore, definitive diagnosis relies on histopathological findings.^{1,7}

Due to the limited number of cases in pediatric literature, there are no consensual guidelines for management of XPN in this group of patients. A total nephrectomy is usually required in the diffuse type, as it leads to a non-functioning, infected kidney. On focal XPN, a partial nephrectomy is typically preferred. There are a few reports of focal XPN successfully treated with broad-spectrum antibiotics and/or percutaneous drainage; however, most practitioners still prefer surgical treatment due to uncertain prognosis.^{1,6}

The authors report a challenging diagnosis of focal unilateral XPN on a neonate, successfully treated using broad-spectrum antibiotics, with an uneventful follow-up at 3 years.

Case Report

An 18-day-old female neonate was admitted in the emergency room of another hospital due to macroscopic hematuria and poor feeding with 24 hours of evolution. Fever was not reported. Past medical history was unremarkable and prenatal ultrasounds were described as normal. There was a family history of urolithiasis (mother).

On arrival, she was clinically pale and there was no reference to dysmorphic features or congenital anomalies, palpable abdominal masses, or organomegaly. Initial laboratory tests showed leukocytosis ($26\,900\ \mu\text{L}^{-1}$), thrombocytosis ($784\,000\ \mu\text{L}^{-1}$), and elevated C-reactive protein (213.9 mg/L), with normal creatinine values. Urinalysis demonstrated leukocyturia ($500\ \mu\text{L}^{-1}$) and hematuria ($300\ \mu\text{L}^{-1}$).

Due to clinical suspicion of acute pyelonephritis, the patient was hospitalized under intravenous antibiotics (ampicillin and gentamicin) for 10 days. The first urine culture was polymicrobial and blood cultures were sterile. Initial renal ultrasound was normal.

At day 10 of hospitalization, the neonate presented fever for the first time. Repeated laboratory tests displayed a new increase of serum inflammatory parameters (leukocytosis $24\,500\ \mu\text{L}^{-1}$ and C-reactive protein 40 mg/L), once more associated with leukocyturia. At this point, urine culture was repeated and tested positive for *Enterococcus faecalis*, sensitive to ampicillin. She was then treated with ampicillin and amikacin for 10 days.

At day 19 of hospital admission, ultrasound displayed a new nodular lesion in the left kidney (middle third) with a diameter of $24\ \text{mm} \times 22\ \text{mm}$ (Figure 1) and subsequent increase to $27\ \text{mm} \times 21\ \text{mm}$ on day 23. There was no mention of renal calculi and the right kidney appeared normal. A renal magnetic resonance imaging (MRI) was performed on day 23 revealing a nodular lesion in the left kidney with internal areas of water-like signal intensity and apparent rim enhancement after contrast (Figure 2).

Given the suspicion of a malignant lesion or a renal abscess, she was transferred to our tertiary unit on day 27. Urinary catecholamines and tumor markers were

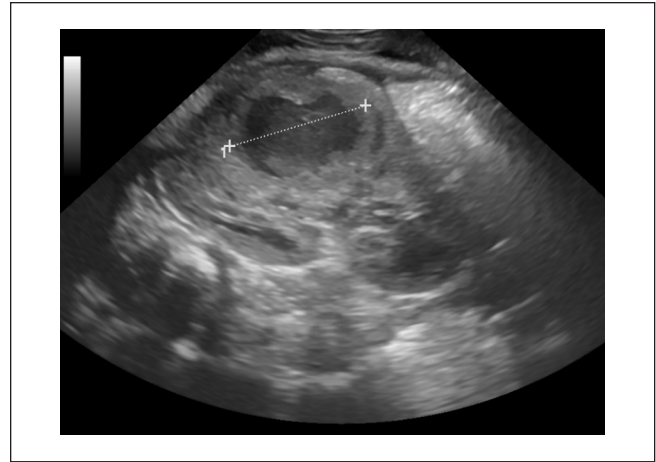


Figure 1. Renal ultrasound performed on day 19 of hospital admission showing a nodular heterogeneous lesion in the left kidney (middle third) with a diameter of $24\ \text{mm} \times 22\ \text{mm}$.

within normal range. Percutaneous renal biopsy revealed an inflammatory cell infiltrate with predominance of lymphocytes/plasma cells and sheets of foamy lipid-laden macrophages, with no signs of malignancy and negative detection of microorganisms by *Periodic acid-Schiff* and *Ziehl-Neelsen* staining. The diagnosis of XPN was confirmed by histopathological examination. Culture of resected tissues was sterile.

Renal scintigraphy with MAG3 demonstrated a slightly hypo-functioning left kidney (42.7% vs 57.3%), without signs of obstruction. An abdominopelvic computed tomography (CT) scan was performed and excluded extension of the inflammatory process to neighboring structures. In collaboration with the department of Pediatric Surgery, a conservative management was decided due to the characteristics of the lesion—unilateral, focal, and noninvasive. Furthermore, ampicillin and cefotaxime had already been initiated in our institution before establishing a definitive diagnosis, with an apparently optimal clinical response. This systemic antibiotic therapy was kept for 7 weeks, with gradual decrease of lesion size and subsequent calcification (Figure 3). The clinical evolution was favorable, and this patient was discharged under antibiotic prophylaxis (cefaclor). Voiding cystourethrography performed 5 months later excluded vesicoureteral reflux. The study of neutrophil function (*Burst-test* and *Phagotest*) and the lipid profile were unremarkable. Periodic renal ultrasounds have been normal (except for the previously described scarring lesion) and episodes of urinary tract infection were never reported at 3 years of follow-up.

Discussion

Xanthogranulomatous pyelonephritis is a rare diagnosis that accounts for 0.6% of histological reports of chronic pyelonephritis.⁸⁻¹⁰ The first descriptions by *Schlagenhauser* date from 1916 but the initial pediatric cases were documented

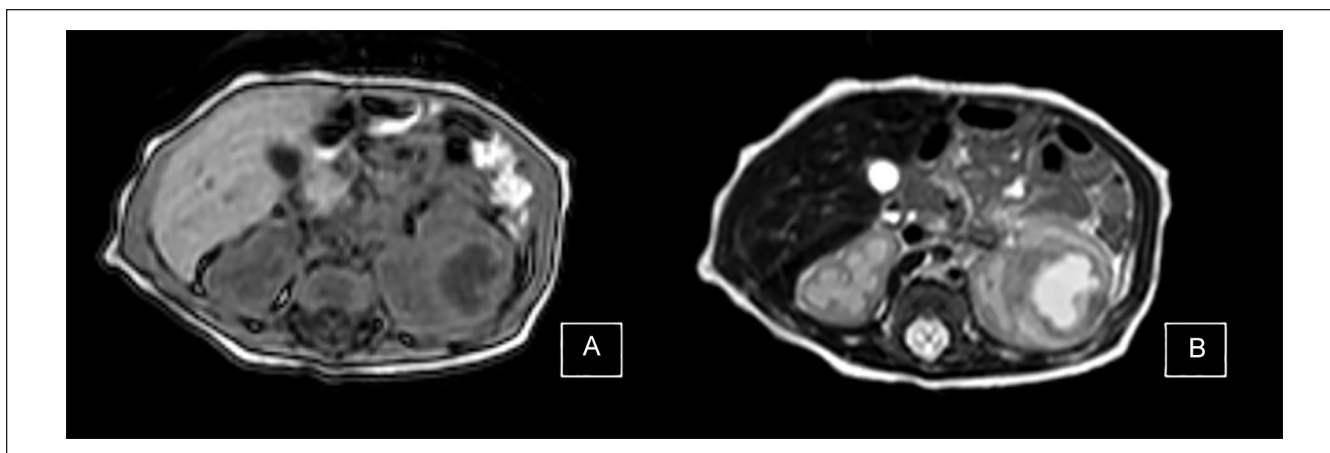


Figure 2. Renal MRI performed on day 23 of hospital admission revealing a nodular lesion in the left kidney with internal areas of water-like signal intensity and apparent peripheral enhancement after contrast. The results of this MRI raised the suspicion of a renal neoplasm or abscess (A: T1-weighted image; B: T2-weighted image).
Abbreviation: MRI = magnetic resonance imaging.

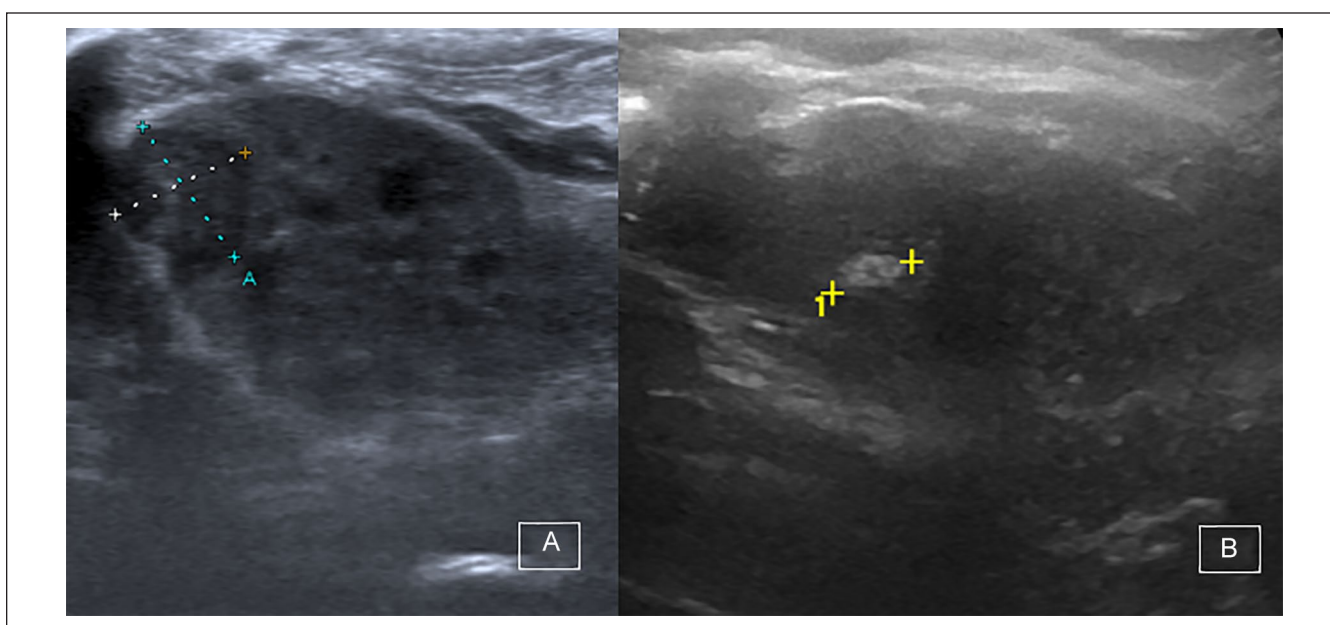


Figure 3. (A) Renal ultrasound performed after 1 month of treatment with ampicillin and cefotaxime, showing a nodular heterogeneous hypoechoic lesion with a diameter 16 mm × 13 mm × 12 mm and (B) renal ultrasound performed 6 months after discharge revealing a calcification with a diameter of 7 mm.

almost 50 years later by *Avnet* and *Friedenberg*.⁸⁻¹⁰ Since then, there have been approximately 283 published cases in pediatric literature, mainly case reports and small case series.^{1,11} Neonatal cases are exceptionally rare, and the youngest age of presentation varies from 21 days in English literature and 48 days in Japanese literature.^{12,13} In our patient, a nodular lesion was detected by ultrasound at the age of 37 days; however, the first urinary tract infection was diagnosed at 18 days of life.

The pathogenesis of XPN is not yet clarified. The most consensual etiologies are obstruction and chronic infection

of the urinary tract. Most infections are caused by *Proteus mirabilis* and *Escherichia coli* but other causative organisms have been isolated (*Staphylococcus aureus*, *Klebsiella*, and *Pseudomonas*).^{2,14} In a published case series, 33% had polymicrobial cultures; urine cultures may be sterile in 25% of cases.^{2,14} Other factors may be implicated on pathogenesis such as chronic renal ischemia, lymphatic obstruction, altered renal metabolism, malnutrition, and host immune defects. The fact that this entity can occur at any age, including the neonatal period, raised the possibility of a prenatal origin and suggested that obstruction (eg, through

congenital urinary anomalies) might play a greater role in pathogenesis than chronic infection.^{2,14} In the presented case, no underlying urogenital malformations or immunological defects were detected, and urolithiasis was never reported. Concerning possible infectious organisms, one culture tested positive for *E faecalis*, which is an atypical etiological agent.

Preoperative diagnosis remains challenging, especially on focal form, as differential diagnosis vary from inflammatory processes (renal or perinephric abscess, focal or diffuse nephritis, renal tuberculosis, Wegener granulomatosis disease, sarcoidosis) to frequent renal neoplasms (clear cell carcinoma, Wilms tumor). Symptoms of XPN are nonspecific and the most frequent include a palpable flank or abdominal mass with associated pain, fever, general malaise, weight loss, and rarely lower urinary tract symptoms, or gross hematuria.⁶

Laboratory tests may show mild anemia, leukocytosis, thrombocytosis, and increased inflammatory markers. Ultrasound imaging typically demonstrates enlargement of the entire kidney and hypoechoic renal areas of calyceal dilatation and parenchymal destruction, with or without calculi. These results are virtually impossible to distinguish from a renal neoplasm or abscess;^{2,6} CT and MRI scans are thought to be more sensitive imaging modalities and can be helpful evaluating perinephric collections and invasion to neighboring structures. These radiological methods usually reveal a well-defined nodular lesion with a peripheral enhancement (due to compressed renal parenchyma or granulation tissue) and hypodense round areas attributed to enlarged calyces or abscess cavities of pus and debris (“bear-paw sign”). However, the role of MRI on focal form is still uncertain due to insufficient data and its usefulness on diagnosis seems to be dependent on the number of foamy macrophages in the lesion.^{3,6,7}

In our case, the patient was presumptively misdiagnosed as a renal abscess or neoplasm based on symptoms and initial radiologic assessment. The definite diagnosis was only established after percutaneous renal biopsy, by the presence of lipid-laden foamy macrophages (the hallmark finding of XPN). Nuclear renal scans frequently demonstrate nonfunction or poor function of the affected kidney.¹

The management of XPN depends on the patient’s disease status and dissemination. Total nephrectomy is the gold-standard in diffuse XPN. The prognosis after surgery is excellent, the risk of mortality is low and recurrence on the healthy contralateral kidney has never been reported. Nevertheless, a long-term follow-up is necessary due to the risk of urinary tract infections and hypertension.^{1,6,11}

The main controversies reside in the treatment of focal XPN. Options include partial nephrectomy and conservative management (percutaneous drainage and/or broad-spectrum antibiotics). In the past, most cases of focal XPN underwent surgical exploration because of the resemblance to malignant lesions. Nowadays, an elevated index of suspicion is crucial to avoid an unnecessary nephrectomy and allows preoperative

diagnosis by image-guided biopsy or intraoperative biopsy.^{6,15} Collaboration of oncology departments to exclude the possibility of renal neoplasms may be necessary, as it occurred in our center.

Aside from the diagnostic challenges, it also remains difficult to select the cases of focal XPN in which a nonsurgical approach should be considered. It seems plausible that focal, noninvasive lesions, apparently responding to systemic antibiotic therapy, might be good candidates to conservative management. Some authors used 3 stages to classify lesions according to invasion of neighboring structures: stage I (nephritic), stage II (peri-nephritic), and stage III (para-nephritic).¹⁶ Huang and Chen and Rasoulpour et al described good outcomes with medical management on stages I and II.^{17,18} There have been other successful reports with nonsurgical approaches of focal XPN on pediatric literature, from as young as 2 years old.¹⁹⁻²⁴ Although most cases are unilateral, a favorable evolution with prolonged systemic antibiotic therapy on bilateral focal XPN had also been stated.²⁵ In some reports, treatment with antibiotics was combined with percutaneous local drainage.^{19,26} It is consensual that the choice of systemic antibiotic therapy should be tailored according to the causative organism. There are no clear guidelines regarding duration, though prolonged treatment is often required as well as a long-term follow-up.³

Our case reinforces the notion that medical management may be an option to preserve renal function in non-invasive focal XPN. The selection of broad-spectrum antibiotics in our institution was made according to age and the isolated organism. Prolonged antibiotic therapy was necessary until full resolution of the lesion. This patient was closely monitored after discharge and prognosis has been favorable.

In conclusion, neonatal reports of XPN are extremely rare. The authors intend to highlight the importance of a high index of suspicion of XPN to allow preoperative diagnosis. Histopathological assessment is mandatory to confirm XPN and exclude other pathologies mimicked by focal and unilateral renal lesions. Our case follows a series of other pediatric reports with optimal evolution under conservative management, which seems to be a beneficial nephron-sparing approach in selected patients.

Authors’ Note

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Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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