International Journal of Nephrology and Renovascular Disease Dovepress

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ORIGINAL RESEARCH

Pediatric Acute Lobar Nephronia: A Case Series and Literature Review

Kfir Lavi[1], Adi Klein[1,2], Noy Shtein[1], Vered Schichter Konfino[1,2], Vered Nir[1,2]

[1]Department of Pediatrics, Hillel Yaffe Medical Center, Hadera, Israel; [2]Bruce Rappaport Faculty of Medicine, Technion–Israel Institute of Technology, Haifa, Israel

Correspondence: Vered Nir, Hillel Yaffe Medical Center, Hadera, 38100, Israel, Tel +972-4-6304331, Fax +972-4-6304186, Email veredn@hymc.gov.il

Introduction: Acute lobar nephronia (ALN) is a focal renal infection without liquefaction, historically regarded as rare in the pediatric population, yet recent literature suggests it may be under-diagnosed, which may result in the formation of renal abscess and future renal scarring.

Methods: The clinical presentation, investigations, treatment and long-term outcomes of 5 patients diagnosed with ALN was described and literature review was conducted by reviewing publications in PubMed using the keywords "acute lobar nephronia" and "pediatric".

Results: Three patients were males, aged 1 to 11 years. The primary complaint in all cases was fever, accompanied by significantly elevated inflammatory markers. Upon presentation, none of the patients exhibited pyuria on urinalysis, and all had sterile blood and urine cultures. Diagnosis was based on CT scans for three patients and renal sonography for two. Main findings included hyperechogenic renal parenchyma, and hypodense localized parenchyma. Treatment consisted of broad-spectrum intravenous antibiotics, administered for 7 to 12 days and additional 1 week course with amoxicillin-clavulanate, resulting in similar defervescence times across all patients. None of the patients demonstrated recurrence and none had renal pathology upon repeated renal sonography and upon DMSA scintigraphy.

Discussion: Clinical suspicion for ALN should arise in cases of abdominal pain and markedly increased inflammatory markers. It"s crucial to note that the absence of pyuria and negative culture results should not exclude ALN diagnosis, underscoring the need for a high index of suspicion in the pediatric population.

Keywords: acute lobar nephronia, culture negative, urinary tract infection, pediatric

Introduction

Acute lobar nephronia (ALN) was first described by Rosenfield et al. This term refers to focal renal infection without liquefaction.[1] Traditionally, ALN has been considered an intermediary condition between acute pyelonephritis and renal abscess.[2] However, recent doubts have been raised about this classification.[3]

Urinary tract infections (UTIs) are common in the pediatric population,[4] but ALN was previously thought to be relatively rare. However, a recent study revealed that nearly 20% of children hospitalized with their first episode of community-acquired febrile UTI were diagnosed with ALN.[5] This finding challenges the assumption that ALN is a rare condition and raises questions about its under-diagnosis.

The diagnosis of acute lobar nephronia (ALN) holds critical importance due to its potential to cause significant morbidity if untreated or if there is a delay in diagnosis. ALN poses diagnostic challenges, as its clinical features often overlap with those of other renal conditions.[5] Therefore, a thorough understanding of the epidemiology and clinical presentation of ALN is essential for ensuring timely and accurate diagnosis, especially in pediatric patients.

Presented here is a case series of pediatric patients diagnosed with ALN in 2023. We describe their clinical characteristics, diagnostic approaches, and treatment outcomes. By highlighting these cases, our aim is to contribute to

Received: 12 August 2024
Accepted: 3 December 2024
Published: 17 December 2024

the understanding of ALN in children and raise awareness of its potential under-diagnosis. Furthermore, we seek to emphasize that ALN can occur even in the presence of sterile urinary cultures.

Materials and Methods

This case series was conducted at Hillel-Yaffe Medical Center in Hadera, Israel. Patients" data were gathered retrospectively from medical records. We included all patients under 18 years of age who were clinically diagnosed or diagnosed using imaging with ALN between January and December 2023. There were no exclusion criteria. Literature review was conducted by reviewing publications in PubMed using the keywords "acute lobar nephronia" and "pediatric", we found 6 case studies and series reported between 2000 and 2023, along with only one recent review article concerning ALN in the pediatric population.[2,5–7]

The data, including demographics, clinical signs and symptoms, laboratory studies, microbiological studies, and imaging results, were collected retrospectively from the patients" medical records. All patients had scheduled follow-up with repeated renal sonography at 2 weeks after discharge and at 6 months after hospital discharge with dimercapto-succinic acid (DMSA) scintigraphy. The study was approved by the local ethics committee at Hillel-Yaffe Medical Center, Hadera, Israel (HYMC-16-24) and did not require patient consent, as the study involved a retrospective chart review of de-identified data, which did not require direct patient consent under the board's guidelines. Patient confidentiality was ensured by anonymizing all data prior to analysis. Patient consent was waived, and patient data confidentiality was maintained in accordance with the Declaration of Helsinki.

Results

Our case series comprised five pediatric patients diagnosed with ALN. All patients were admitted to the pediatric ward at Hillel Yaffe Medical Center during 2023. Three of the patients were males, with ages ranging from 1 to 11 years old with an average age of 7.0 years. Patient number 4 and 5 had a past history of febrile UTI, but none of the patients had congenital or acquired renal anomaly. The chief complaint for 100% of the patients was fever, with a duration of 1 to 2 days prior to presentation, accompanied by decreased appetite for 100% of the patients. Initial physical examinations revealed nonspecific signs, including weakness (40%) and pallor (60%), with 60% of the patients reporting abdominal pain upon arrival at the emergency department. Interestingly, only one verbal patient (20%) complained of dysuria, while the others did not report any urinary symptoms.

As shown in Table 1, upon presentation, all patients exhibited markedly increased inflammatory markers, with a mean white blood cell count of 24.66 × 10^3/uL and a mean C-reactive protein (CRP) level of 209.4 mg/L. Estimated

Table 1 Patients Characteristics, Laboratory Findings and Management

Case Number	Age (Years) / Sex	Chief Complaint	Additional Complaints	WBC Count (10^3/uL)	CRP (mg/L)	Isolated Organism	Imaging Modality	Treatment and Treatment Duration (Days)	Time to Defervescence (Days)
Patient 1	1 / male	Fever	Vomiting, Diarrhea	51.0	108.0	None	US - hyperechogenic parenchyma CT - hypodense localized parenchyma	Ampicillin + Amikacin / 12	4
Patient 2	11 / male	Fever, abdominal pain	Dysuria	12.4	15.6	None	CT - hypodense localized parenchyma	Piperacillin-tazobactam / 9	4
Patient 3	10 / male	Fever, abdominal pain	Flank pain, Vomiting	15.7	233.4	None	US - normal CT - nephromegaly, localized hypodense area	Ceftriaxone / 10	4
Patient 4	9 / female	Fever, abdominal pain	None	18.9	362.3	None	US - hyperechoic upper pole	Gentamicin / 7	3
Patient 5	4 / female	Fever	None	25.3	328.1	None	US - hyperechoic upper pole	Ampicillin + Gentamicin / 7	4

Abbreviations: ALN, acute lobar nephronia; UTI, urinary tract infection; CRP, C-reactive protein; IV, intravenous; CT, computed tomography; DMSA, dimercaptosuccinic acid; VUR, vesicoureteral reflux.

glomerular filtration rate (eGFR) was within normal limits for 100% of the patients. It is noteworthy that all patients had urinalysis negative for leukocytes and nitrites and none of the patients had positive urine or blood cultures, despite patients 4 and 5 having been treated before cultures were taken.

Since patients 4 and 5 had a history of febrile UTIs, ALN was initially suspected and diagnosed via sonography on the day of presentation. In contrast, the primary differential diagnosis for patients 1 and 2 was acute appendicitis, as they had no history of febrile UTIs or abdominal pain. ALN was diagnosed in these patients on their second day of presentation using a CT scan. Although patient 3 initially showed normal findings on sonography, a high index of suspicion ultimately led to the diagnosis of ALN through a CT scan.

Upon diagnosis, all patients were treated with broad-spectrum intravenous (IV) antibiotics. The duration of IV treatment ranged from 7 to 12 days. Clinical improvement, as measured by time to defervescence, occurred within 4 days for all patients, except for patient number 4, who improved after 3 days of IV treatment. Subsequently, all patients were treated with an additional 7 days of amoxicillin-clavulanate without experiencing any relapses. 3 patients attended first follow-up check-up and all had normal renal sonography. 2 of the patients who attended their second follow-up examination showed no abnormality upon DMSA scintigraphy.

Discussion

Our series includes five pediatric patients with ALN over a one-year period at a single medical center in Israel. In our series, the mean age of patients was 7.0 years, contrasting with the mean age of 1.86 years reported in the recent review article. Similarly, our case series showed a male predominance.[5,8,9] Like previously reported cases, all patients in our cohort were febrile at presentation and had poor appetite. However, only one verbal patient was able to describe dysuria, and neither the verbal patients nor their parents described urinary frequency.[5]

Laboratory anomalies at presentation tend to show dramatically increased inflammatory markers, with ALN reviews reporting mean white blood cell counts of 22.6 (±8.2) × 10^9/L and 18.86 (±8.7) × 10^9/L and mean CRP levels of 145.3 (mg/L).[3,5] This trend was also observed in our cohort, with a mean white blood cell count of 24.6 × 10^9/L and a mean CRP value of 209.5 mg/L, prompting further investigation into the source of infection.

ALN typically results from ascending infections and is frequently associated with underlying vesicoureteral reflux (VUR).[1,10,11] Thus, in the vast majority of ALN cases, urinalysis demonstrates pyuria, and urinary cultures are positive, with most cases attributed to E. coli.[5] However, some reported cases showed no growth in urinary cultures, with some attributing the lack of growth to previous antibiotic treatment.[6,7,12] In our cohort, none of the patients had pyuria on urinalysis upon presentation, while only two of the patients were pre-treated with antibiotics before culture sampling. Negative urine culture in this condition can be explained by improper sampling techniques, although less likely as a pattern in these patients can be seen, and low bacterial load on the urine sample that is taken. While hematogenous origin of infection is possible, none of our patients had a positive blood culture, which similarly can be explained by low bacterial burden. Additional reason why blood cultures were negative can be that in our patients, blood cultures were drawn only once before IV antibiotics initiation.

The "gold standard" for definitive ALN diagnosis is considered to be computed tomography (CT) scan showing poorly defined, localized, renal hypodensity.[2] As renal sonography is more readily available imaging modality several studies have suggested that the diagnosis of ALN can be made by demonstrating nephromegaly, focal renal mass or focal loss of corticomedullary differentiation.[13] A recent study even described the use of point-of-care ultrasound examination for diagnosing ALN in the pediatric emergency department.[14] Although ALN diagnosis with renal sonography seems promising, the pitfalls of this modality should be interest for further research, demonstrated in one of our cases in which renal sonography failed to yield the diagnosis. Up to this point, studies have shown that renal sonography is highly sensitive and specific for nephromegaly as compared to CT scan.[5] Thus, it is recommended that pediatric patients with suspected ALN should undergo renal sonography, followed by CT if suggestive signs are found. Our suggestion, based on our patient that had normal renal sonography and abnormal CT scan, that when there is high index of suspicion, CT scan should be performed even with normal renal sonography.

The recommended therapeutic regimen for ALN is not widely agreed upon, as IV antibiotic courses are guided by local patterns of pathogen resistance. While studies suggest that longer durations of IV treatment are more effective in

preventing persistent infection and progression to renal abscess formation,[15] there is no conclusive agreement on the duration of IV antibiotic treatment, with treatment durations ranging from one week to three weeks.[5–8] In our study, all patients were treated with broad-spectrum IV antibiotics, with treatment durations ranging from 7 to 12 days, all showing similar responses as measured by time to defervescence. An additional 7 days course of oral antibiotics with amoxicillin-clavulanate was administered to all patients. None of the patients demonstrated any clinical signs suggesting persistent infection or relapse. These findings support a shorter IV treatment course; however, the effectiveness of short antibiotic course still needs to be examined in larger samples and with longer patient follow-up.

A prospective study in the pediatric population demonstrated an increase in the incidence of renal scarring, as shown by DMSA scintigraphy 6 months following ALN, regardless of the duration of treatment.[16] Thus, DMSA scintigraphy is routinely recommended for patient follow-up. In our sample, all the patients had a recommendation for scintigraphy 6 months after the therapeutic course; 2 of our patients who continued their follow-up had normal DMSA scintigraphy. Further research and follow-up are required in pediatric and the adult population to determine the long-term outcomes of ALN patients as reports about the long-term outcomes in the pediatric population are lacking.

This case series has several limitations. This study was conducted in a single hospital and the data was collected in a retrospective manner, which likely led to incomplete data collection. In addition, there are small number of cases, which precludes statistical analysis.

Conclusion

Diagnosing pediatric ALN can be challenging due to non-specific symptoms, particularly in non-verbal patients. Fever and abdominal pain, along with elevated inflammatory markers, should raise suspicion for ALN. Importantly, sterile urine cultures should not rule out the diagnosis. This underscores the need for a high index of suspicion, especially when encountering pediatric patients with negative urine cultures.

In conclusion, timely recognition of ALN is crucial to prevent morbidity. Clinicians should remain vigilant, especially when faced with fever, abdominal pain, and elevated inflammatory markers, even in the absence of positive urine cultures. Further research is needed to refine management strategies for pediatric ALN.

Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The authors have no conflicts of interest relevant to this article to disclose.

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