SHORT COMMUNICATION

Contrast-enhanced ultrasound in detection and follow-up of focal renal infections in children

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Objective: Focal renal infections in children have to be diagnosed early in order to enable an appropriate antibiotic treatment. The purpose of this paper was to investigate the efficacy and clinical utility of intravenous renal contrast-enhanced ultrasound (CEUS) as an alternative imaging method for the diagnosis and follow-up of focal renal infections in children.

Methods: Fourteen children aged from 6 months to 17 years (mean 6.5 years) in whom focal renal infection was suspected were included in this retrospective study. All data were obtained from medical and imaging records of the patients.

Results: CEUS was performed for the diagnosis in all 14 children and then also for follow-up in seven children with renal abscess. In three children enhancement pattern was concordant with focal nephritis and in four children CEUS excluded focal renal infection and the diagnosis of pseudolesion was confirmed.

Conclusion: Renal CEUS was proven to be an efficient and self-sufficient imaging in diagnosis and further follow-up of focal renal infections in children. CEUS patterns of focal renal infections are described as well as relevant CEUS enhancement patterns important for differential diagnosis. Renal abscess follow-up algorithm with CEUS is suggested.

INTRODUCTION

Focal renal infections like focal nephritis and renal abscesses are not very common in children. However, they usually present with a non-specific and varying clinical presentation, which can result in prolonged antibiotic treatment and increased length of hospital stay.1,2 Renal abscesses can evolve from haematogenous spread of other localised infections or ascending urinary tract infection. Most frequently isolated pathogens in renal abscesses in children are Escherichia coli and Staphylococcus aureus.3 Conventional ultrasound is the first-line imaging method to detect renal structural lesions,4 but for final diagnosis, CT or MRI is often required. The latter are not optimal for the use in children due to ionising radiation exposure in CT and the need for sedation or general anaesthesia in MRI. On the other hand, contrast-enhanced ultrasound (CEUS) is a novel, real-time bedside, children-friendly imaging modality with high safety profile and many benefits in comparison with conventional imaging techniques.4–6

The purpose of this paper was to investigate the efficacy and clinical utility of intravenous renal CEUS as an alternative to CT or MRI for the diagnosis and follow-up of focal renal infections with particular attention to description of various enhancement patterns in children. Follow-up algorithm with CEUS is suggested to objectively monitor the focal renal infection and assess possible chronic renal parenchymal changes.

METHODS AND PATIENTS

Children in whom focal renal infection was suspected at our University Children’s hospital from January 2018 to February 2022 were included in the retrospective study. All data were obtained from medical and imaging records of the patients included in the study.

Clinical, laboratory and treatment data
Clinical data contained: prolonged fever, chills, pain (abdominal, flank), nausea and vomiting, diarrhoea, headache, changes in mental ability and smelly urine.

Documented laboratory data included: erythrocyte sedimentation rate (ESR) (mm/h), C-reactive protein (CRP) (mg/L), procalcitonin (PCT) (µg/L), white blood cell...
(WBC) count (x10⁹/L), haemoglobin (mg/dl), potassium and sodium levels (mmol/L), creatinine (mg/dl), blood urea nitrogen (mg/dl). Microbiology data included urine and blood cultures.

Treatment data included choice of antibiotics, mode of administration and duration of treatment (Table 1).

Renal ultrasound and intravenous contrast-enhanced ultrasound of the kidney

Conventional and colour Doppler ultrasound of the kidneys were performed in Aplio 500 US machine (Canon Medical System, Europe, B.V.) to evaluate the structural changes in kidney parenchyma and in the perirenal space. A focal nephritis was suspected, when an area of hypoechoic structural changes with diminished vascularisation usually without mass effect was seen. When a heterogeneous mass within the renal parenchyma, which usually causes mass effect, was seen, an early stage of renal abscess was suspected. Mature renal abscess typically appears as a well-defined hypoechoic mass with thick irregular walls or a capsule and increased through-transmission. It demonstrated internal echoes and/or hypoechoic fluid areas. Colour Doppler ultrasound showed increased peripheral vascularisation and lack of vascularisation in the central part of the abscess. In addition, the local extrarenal parenchymal extension of the collection was determined as subcapsular or perinephritic fluid collection and inflamed hyperechoic thickened perirenal fat. CEUS examinations of a kidney were performed on the same ultrasound machine using a 1.9–5.0 MHz convex or 7.5–12 MHz linear transducer. A child laid in the position (supine, prone, decubitus) where the renal changes were best seen. The second-generation ultrasound contrast agent (UCA) SonoVue® (Bracco, Milan, Italy) in a dose of 0.03 mL/kg for convex probe or 0.05 mL/kg for linear probe was injected by bolus through one of the arm veins followed by a 10 ml saline flush. Subsequent enhancement was recorded as a continuous cine loop for the first 60 s, then the shorter cine loops or still images were saved. Number of UCA applications depended on the visualisation of the lesion and

| Number of children | 3 | 7 | 4 |
|-------------------|---|---|---|
| Age (years)       | 4–9 (avg. 6) | 0.5–12 (avg. 5.5) | 0.5–17 (avg. 8.6) |
| Gender            | Three girls | Two boys, five girls | One boy, three girls |
| Symptoms          | Fever, chills, pain in the abdomen and flank pain, smelly urine, vomiting, diarrhoea, headache | Fever, chills, pain in the abdomen and flank pain, smelly urine, vomiting, diarrhoea, headache, changes in mental status, photophobia | Fever, chills, pain in the abdomen and flank pain, smelly urine, vomiting, diarrhoea, headache |

### Laboratory at admission

| CRP (mg/L) | 13–228 (avg. 97) | 39–478 (avg. 245) | 31–144 (avg. 89) |
| WBC (x10⁹/L) | 6.3–19.9 (avg. 12.3) | 13–32.7 (avg. 20.7) | 6.2–28.6 (avg. 17.6) |
| First urinalysis | Few to numerous bacteria, protein, nitrates, WBCs | Few to numerous bacteria, protein, WBCs | Few to numerous bacteria, protein, WBCs |
| Urine culture | 2x E. coli | 2x E. coli, 2x E. faecalis | 3x E. coli |
| Blood culture | All sterile | All sterile | All sterile |

### Treatment

| Intravenous antibiotic (duration: weeks) | All 1 | 1.5–7 (avg. 3.6) | 0.5–1 (avg. 0.8) |
| Oral antibiotic treatment (duration: weeks) | 2–3 (avg. 2.3) | 2–7 (avg. 3.7) | 0–1 (avg. 0.8) |
| Total duration of antibiotic (weeks) | 3–4 (avg. 3.3) | 6–9 (avg. 7.3) | 0.5–2 (avg. 1.4) |

### CEUS findings

| Description | Hyponenhanced focal area(s) with slow washout comparable to normal renal parenchyma | 3x subcapsular (nonenhanced subcapsular areal with hyperenhanced capsula and perirenal tissue changes), 3x parenchymal (non-enhanced areals in renal parenchyma with or without hyperenhanced capsula), 1x combination | Similar enhancement pattern of focal lesion as normal kidney parenchyma |
| Perirenal fat inflammation | 1x yes, 2x no | 5x yes, 2x no | No |

**CEUS**, contrast-enhanced ultrasound; **CRP**, C-reactive protein; **PCT**, procalcitonin; **WBC**, white blood cell.
child’s cooperation, but in order to thoroughly scan the whole kidney with focal infection and also contralateral kidney in venous phase, usually two applications of UCA were applied.

Based on the CEUS enhancement the type of focal kidney infection was identified as: (1) focal nephritis—hypoenhanced area in renal parenchyma with slow washout comparable to normal renal parenchyma washout (Figure 1), (2) early stage of abscess—hypoenhanced area with nonenhanced part (Figure 2a), (3) mature abscess—non-enhanced central part with hyperenhanced capsule (Figure 2b), (4) subcapsular abscess with boundary between the avascular non-enhancing subcapsular collection and the enhancing renal parenchyma (Figure 3a), and (5) perinephritic changes including perinephritic fluid (non-enhanced part) and hyperenhanced inflammatory changed perinephritic fat. The same enhancement of focal lesion detected on conventional ultrasound as the surrounding normal renal parenchyma indicated parenchymal pseudolesion (Figure 4).

Prior to the CEUS examination, written informed consent was obtained from all children’s parents. All the examinations were conducted following the Helsinki Declaration.

RESULTS
During the study period, there were 14 children (11 girls and 3 boys) with suspected focal renal infection, aged from 6 months to 17 years (mean 6.5 years). Renal CEUS was performed for diagnosis in all children and then also for follow-up in seven children.

Demographic, clinical, laboratory, treatment data, and CEUS findings were presented in Table 1.

In three cases, risk factors for bacteraemia were present; first child was suffering from pneumonia caused by Mycoplasma pneumoniae during hospitalisation and later immunodeficiency disorder was diagnosed, second presented influenza infection and pneumonia, and third was diagnosed with peritonitis and appendectomy was performed at the beginning of the hospital stay. Three children had suffered from antecedent urinary tract infections. Vesicoureteral reflux was diagnosed in three of the observed patients. All children had normal potassium, sodium, blood urea nitrogen and creatinine levels on admission. ESR was done in four patients and it was elevated in all of them, values ranging from 46 up to 113 mm/h. In 9/14 patients, causative organisms were isolated from urine (E. coli in seven, Enterococcus faecalis in two). All blood cultures were negative.

Focal renal infection was demonstrated by renal CEUS in 10 children; in 3 enhancement pattern was concordant with focal nephritis (Figure 1) and in 7 with renal abscess (parenchymal or subcapsular) (Figure 2 and Figure 3). In four children, CEUS excluded focal renal infection, the diagnosis of pseudolesion was established; in two cases, the pseudolesion represented atypical Columna Bertini and two pseudolesions were hyperechoic compared to normal renal parenchyma on conventional ultrasound (Figure 4).
Multiple follow-up CEUS were performed in seven children with renal abscesses. Three to four follow-ups were performed to evaluate the dynamics of abscess maturation and regression: the first follow-up after 7–9 days, the second follow-up after 22–28 days, the third after 1–2 months, and in one child after 9 months to evaluate chronic changes after abscess healing (Figure 2b–c, Figure 3b). Other children were followed-up only by ultrasound and Doppler.

All patients with focal renal infection were initially treated with intravenous antibiotics and completed the treatment with oral drugs. Total treatment duration ranged from 3 to 9 weeks (mean 6 weeks), depending on the type of focal infectious lesion.

However, no chronic changes like signs of renal parenchyma scars, thinned renal cortex or perfusion defects at the site of the abscess were found on follow-up examinations after treatment.

DISCUSSION

Clinical applicability and utility of CEUS in the diagnosis and monitoring of focal renal infections in children was investigated. All patients in our series presented similar clinical symptoms and elevated inflammatory markers. By the use of CEUS, clinically relevant imaging data of pathomorphological and structural changes in renal parenchyma and perirenal tissue in all of the children were obtained. All children with focal renal infection were promptly treated with broad-spectrum antibiotics and a complete resorption of lesions was achieved.

Renal CEUS was recognised as a problem-solving method in the evaluation of renal focal lesions and a promising method in microvascular renal perfusion evaluation, like in acute pyelonephritis or other causes of renal perfusion disorders (in the settings of renal artery stenosis, renal infarction, including smaller and polar areas as well as cortical necrosis). Most of the data regarding renal CEUS are based on studies of adults. There are only a few reports of using UCA in renal tumour or inflammation pathology in children. However, there are no papers evaluating CEUS in a subset of children with focal renal infections.

In our study, CEUS was performed as a continuation of the conventional ultrasound examination, particularly in cases presenting on ultrasound as an indeterminate solid or mixed lesion. The knowledge of distinct CEUS enhancement patterns of renal and perirenal space in different pathological entities helps in differential diagnosis. With CEUS, it is possible to confirm focal renal infection and to differentiate between focal nephritis and different stages of renal abscess. This has an impact on the antibiotic treatment duration, which is considerably longer in renal abscess. The possible differential diagnostic option in children with focal renal infection, particularly in the early stage of abscess formation, is Wilms tumour, which has a more non-homogeneous hyperenhancement of tumour tissue, usually with multiple non-enhanced areas of necrosis, various sizes and shapes. A focal nephritis has to be differentiated from renal cell carcinoma which is hypoenhanced, but has fast washout, while in inflammatory lesions there is slow washout on delayed images. On the other hand, CEUS can exclude focal renal infection by diagnosing pseudolesion, which has a similar enhancement pattern as normal kidney parenchyma, and direct the investigation searching for other infectious foci.

CEUS has been shown as a highly sensitive diagnostic imaging modality for detecting and monitoring renal scars in children with reflux nephropathy. Findings included hypoenhancing areas in the renal parenchyma of different shapes (wedge-shaped areas, areas of flattening), irregularity of the outer renal contour, and the parenchymal thinning. CEUS was proven to be an objective follow-up
method regarding inflammation of renal tissue and its repARATION in our small cohort. Suggested follow-up timing, according to our experience, is 7–10 days after the diagnosis, then after 3–4 weeks and 6–8 weeks, depending on clinical response to treatment. Only if parenchymal changes are seen on the last CEUS, another follow-up CEUS should be performed 3–6 months after the last examination to evaluate for possible chronic parenchymal changes. Due to a timely diagnosis and treatment, the outcome was excellent without the need for interventional (percutaneous drainage) or surgical treatment.

Although CEUS has many above-mentioned advantages, there are possible limitations to its use such as poor display of the entire kidney or poor depiction of the focal lesion by native ultrasound (obese patient, bowel gas interposition, poor child co-operation). Another limitation of this method is the off-label use of intravenous (obese patient, bowel gas interposition, poor child co-operation). Another limitation of this method is the off-label use of intravenous

CONCLUSION

Renal CEUS is an efficient, safe, children-friendly imaging method for timely diagnosis of focal renal infections, their objective follow-up during antibiotic treatment, and objective evaluation of potential chronic changes of renal parenchyma. It has proven to be a self-sufficient method and thus has a high potential to replace CT or MRI in the assessment and monitoring of focal renal infections in children.

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