Case Report

Interstitial nephritis: Two pediatric cases with atypical radiological features

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ABSTRACT

Interstitial nephritis (IN) is a relatively rare entity in children and adolescents that can be caused by a range of disorders including infection, medications, inflammatory bowel disease, and sarcoid. There is no proven therapy for this condition. We present 2 cases of biopsy-proven interstitial nephritis, of which 1 case was with granulomatous features that presented with unusual sonographic findings of discrete mass lesions in the kidney parenchyma bilaterally. Although a precise cause could not be identified in either case, 1 patient progressed to end-stage kidney disease (ESKD) and the other is in the early stages of treatment. We suggest that recognition of the atypical imaging features of interstitial nephritis may enable early recognition of this condition and avoid confusion with neoplastic or infectious processes.

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Introduction

Interstitial nephritis (IN) is a relatively rare disorder in pediatrics that can be caused by a wide range of infections (eg, mycoplasma), prescription drugs, and autoimmune disorders (eg, sarcoidosis and inflammatory bowel disease; Ref. 1). In a subset of cases, a discrete cause cannot be identified and they are characterized as idiopathic. The diagnosis is established by kidney biopsy demonstrating interstitial edema and infiltration with inflammatory cells including neutrophils, eosinophils, and plasma cells [1]. Granulomatous interstitial nephritis (GIN) is a subtype of IN accounting for 0.9%-5.9% of cases that also occur in association with numerous medications, infections, and autoimmune disorders [2]. The prognosis of IN depends on the cause, extent, and duration of the disease [3]. Prompt withdrawal of a causative medication is generally associated with a good outcome, whereas poorer outcomes are seen in cases with diffuse inflammation, increased neutrophil infiltration, the presence of granulomas, and extensive fibrosis [1-3].

Renal biopsy remains the gold standard for diagnosis of all forms of IN, including GIN [3]. IN is characterized radiographically by increased kidney size and diffuse increased
Table 1 – Laboratory data.

|                      | Patient 1         | Last follow-up | Patient 2         | Last follow-up |
|----------------------|-------------------|----------------|-------------------|----------------|
| Presenting           |                   |                | Presenting        |                |
| Creatinine           | 1.28              | 4.75           | 2.4               | 2              |
| BUN                  | 22                | 122            | 37                | 28             |
| Urine protein: creatinine ratio | 1.82 | 2            | 0.8               | 4.6            |
| Albumin              | 1.9               | 4.6            | 8.4               | 9.8            |
| Ca                   | 5.7               | 7.7            |                   |                |
| QuantiFERON          | Indeterminate (A) |                |                   |                |
| ANA                  | <40               |                |                   |                |
| ANCA                 | <1:20             |                |                   |                |
| DsDNA                |                   |                |                   |                |
| ACE                  |                   |                |                   |                |
| ASLO                 |                   |                |                   |                |

Echogenicity on ultrasound (US) imaging [1,3]. In cases of sarcoidosis-related GIN, there can be pseudotumoral masses that are histologically consistent with the granulomatous lesions [4]. In pediatric patients, presentation of IN with mass-like lesions on US is exceedingly rare. There is a single case report describing GIN in a child with sarcoidosis who had mass-like lesions on computerized tomography (CT) and US imaging [5]. We present 2 cases of children with IN, of which one was with GIN, who presented in the last 2 years and in whom US imaging revealed striking bilateral mass-like lesions without diffusely increased echogenicity. We highlight the importance of early recognition and timely diagnosis with a kidney biopsy in these cases because of the risk for progression to end-stage kidney disease (ESKD).

Case reports

Case 1 is a 17-year-old white male with a history of autistic spectrum disorder, Crohn’s disease, and pulmonary embolism. He had history of chronic iron-deficiency anemia of unclear etiology and he was treated with intravenous iron infusions. For his Crohn’s disease, he received weekly infusions of adalimumab for 1 year. The antibody was discontinued when he was noted to have an elevated serum creatinine and low serum calcium level, 1.28 mg/dL and 5.7 mg/dL, respectively (Table 1). He was referred for a second opinion evaluation because of the abnormal renal function. Testing for sarcoidosis and TB was negative.

A renal ultrasound revealed bilateral, discrete hypovascular echogenic mass-like lesions (Fig. 1a) that were also visualized on axial T2-weighted MRI images (Fig. 1b). A percutaneous kidney biopsy demonstrated IN with widespread interstitial fibrosis and tubular atrophy (Fig. 1c).

He was treated with high-dose corticosteroids for the IN with a partial response. In June 2015, he had worsening of his kidney function and was diagnosed with pulmonary emboli. He was placed on enoxaparin. Over the next 2 years, his kidney function gradually deteriorated, complicated by hypertension. Despite retreatment with steroids in January 2016, his serum creatinine level continued to increase (2.39 mg/dL). His BUN and serum creatinine rose to 120 mg/dL and 4.5 mg/dL, respectively, and he was started on hemodialysis in June 2017. He received a kidney transplant from a living donor in July 2017 and is currently doing well without evidence of disease recurrence.

Case 2 is an 18-year-old black male admitted for a hypertensive crisis, BP 180/120 mm Hg. He had a history of constipation and gastroesophageal reflux. He presented with dizziness, weakness, and headache for 2 days prior to admission. There was no prior history of renal disease, UTI, gross hematuria, abnormal urinalysis, or edema. Testing for sarcoidosis and TB was negative. A renal ultrasound showed bilateral hypovascular echogenic mass-like lesions (Fig. 2a). There was no diffuse increased echogenicity. The lesions were also seen in axial T2-weighted MRI images (Fig. 2b). A kidney biopsy showed GIN (Fig. 2c). IgG4-related tubulointerstitial nephritis was excluded [6]. He was started on prednisone 1 mg/kg per day and mycophenolate mofetil was added to his regimen to facilitate resolution of the interstitial inflammation. He developed a UTI 1 week after discharge and was treated with amoxicillin. At his last follow-up, his BUN and serum creatinine concentrations were 24 mg/dL and 1.9 mg/dL, respectively (Table 1).

Discussion

We present 2 cases of IN in pediatric patients, of which 1 was with GIN that presented with impaired kidney function in the absence of evidence of glomerular disease. In both cases, a renal ultrasound revealed striking evidence of discrete mass-like lesions distributed heterogeneously throughout both kidneys without diffusely enhanced echogenicity. The findings were confirmed by MRI. The differential diagnosis of multiple bilateral solid renal lesions in pediatric patients includes nephroblastomatosis, angiomyolipomas, and lymphoma. In both cases, the age of the patients spoke against nephroblastomatosis and the echogenicity of the lesions against angiomyolipomas or lymphoma. Finally, in the setting of Crohn’s disease, granulomatous renal inflammation is a consideration. The appearance of IN as echogenic mass-like lesions is
Fig. 1 – (a) Ultrasound image of the kidney in Case #1. (b) Axial T2-weighted MRI images through the abdomen in Case #1 showing multiple bilateral T2 hyperintense renal lesions. (c) Histopathology illustrating inflammation and fibrosis in the interstitium in Case #1 (PAS stain, 10x magnification, bar 50 μm).

Fig. 2 – (a) Ultrasound image of the kidney in Case #2. (b) Axial T2-weighted MRI images through the abdomen in Case #2 showing multiple bilateral T2 hyperintense renal lesions. (c) Histopathology illustrating granulomas in the interstitium in Case #2 (PAS stain, 20x magnification, bar 50 μm, arrows indicate granulomas).
exceedingly rare and it is not on the standard list of possible causes of this ultrasound finding.

GIN represents a subset of IN, which is most commonly caused by drug exposure and has also been linked to numerous infections and autoimmune disorders [2]. Medications linked to the GIN include antibiotics (eg, penicillins, cephalosporins, fluoroquinolones, vancomycin, and doxycycline), nonsteroidal anti-inflammatory drugs, diuretics, allopurinol, and antiepileptics drugs [2]. The third most common cause of GIN is autoimmune disorders such as systemic lupus erythematosus, Sjögren syndrome, ANCA-associated vasculitis, Crohn’s disease, and most commonly, sarcoidosis. The fourth category is immunologic diseases such as common variable immunodeficiency [2].

IN and GIN in particular can present with flank pain and hematuria, nonspecific symptoms such as malaise, anorexia, nausea, and vomiting, or with no symptoms or signs other than newly detected renal dysfunction [1–3]. There is a hypersensitivity syndrome that was once commonly associated with IN. However, this pattern was linked to drug-induced cases and found to have a fairly low incidence even among this subgroup of IN. In a large series of 128 patients, in which 71% of them had drug-induced IN, the triad of fever, rash, and arthralgia was present in only 10% with a low incidence of each individual symptom as well [3]. The presentation in our 2 cases was nonspecific with few symptoms suggestive of kidney disease.

The exact cause of IN in these 2 cases has not been definitively established. The renal histopathology has been thought to provide some clues. In 12 patients with GIN, Viero et al noted that necrotic granulomas were observed in certain infections, while noncaseating granulomas were more common in sarcoidosis and drug-related cases of GIN [2]. The inflammatory infiltrates are dominated by macrophages and T cells, but neutrophil predominance is possible in infectious processes [1,2]. Tomlinson et al have claimed that TNFα plays a key role in pathogenesis of GIN and that the majority of idiopathic cases might in fact represent sarcoidosis with no extrarenal lesions [7]. We speculate that in Case #1, the IN was a complication of his Crohn’s disease or a reaction to the anti-TNF antibody, adalimumab. This is supported by isolated cases linking IN with Crohn’s disease [1,2] and the contribution of antecedent drug exposure to this renal disease entity. The etiology of the GIN in patient 2 remains elusive.

The most common treatment for IN is corticosteroid therapy, but in the absence of case-control series or clinical trials there is a disagreement on its efficacy. Moreover, while there is some evidence to support the addition of mycophenolate mofetil as a steroid-sparing agent in patients with IN [8], there are no data regarding the use of this immunosuppressive agent in GIN. Despite treatment and retreatment with high-dose steroids, Case #1 displayed delete progressive worsening of his renal disease and required dialysis treatment and then kidney transplantation for ESKD. The response to corticosteroids and mycophenolate mofetil in Case #2 remains to be determined. Our experience with these two cases is too limited to make any comment on optimal treatment of GIN.

We highlight the unexpected sonographic appearance of the renal parenchyma in these 2 cases of IN. The mass-like lesions noted in Case #1 were initially thought to suggest a malignant process. This may have delayed performance of a kidney biopsy and recognition of the underlying IN. We hope that increased awareness of this unusual imaging manifestation of IN, including an adolescent with GIN, will prompt earlier diagnosis and treatment of this condition and lead to better long-term outcomes.

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