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CASE REPORT

Eosinophilic cystitis as a rare cause of post-renal acute kidney injury in children: a case report

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ABSTRACT

Eosinophilic cystitis (EC) is a rare inflammatory disease of unclear etiopathology and various clinical presentations. We present a case of a 10-year old boy who was referred to our center because of acute kidney injury. The imaging diagnostic showed hydronephrosis, irregular thickening and infiltration of the posterior bladder wall. During cystoscopy, no ureter orifices were identified. Based on histopathological examination of bladder biopsy specimens, EC in an acute phase was diagnosed. To our knowledge the presented case is the first where EC led to post-renal acute kidney injury requiring hemodialysis. In the article we describe the diagnostic difficulties, therapy, clinical outcomes, and patient's follow-up.

KEY WORDS:

children, hemodialysis, acute kidney injury, eosinophilic cystitis.

INTRODUCTION

Eosinophilic cystitis (EC) is a rare inflammatory disease that affects all age groups, but more often adults, regardless of gender [1–6]. To date, less than 100 cases of EC in children have been described [1, 7].

The etiopathology of EC remains unclear. It is proposed that many factors, including allergy to medications and food, urinary tract infection, tuberculosis, parasitosis, vesical injuries, chronic irritation of the bladder wall as well as autoimmune disorders, may induce dysregulation of the immune system [1, 4, 8]. The underlying mechanism is related to the antigen-antibody complexes and IgE-mediated response resulting in mast cell degranulation and eosinophils' aggregation to the bladder wall [1, 8]. Further effects are inflammation, tissue remodeling and damage [8].

The clinical presentation of the disease may vary from frequency, dysuria, suprapubic pain, nocturnal enuresis, gross or microscopic hematuria, and urinary retention to formation of a bladder mass imitating bladder tumor [1, 2, 4, 5, 9–13].

Due to varying and non-specific clinical symptoms, diagnosis and proper treatment are often delayed. The case presented here is the first in which EC led to severe AKI requiring renal replacement therapy.

CASE REPORT

A 10-year-old boy was referred to the Department of Pediatric Nephrology (tertiary center) because of acute kidney injury (AKI). In the past three months, he had suffered from abdominal pain, initially on the left and then on both sides. His general condition was steadily getting worse; he felt weak and tired.

The diagnostics was initiated about a month after the first symptoms appeared. The outpatient ultrasound

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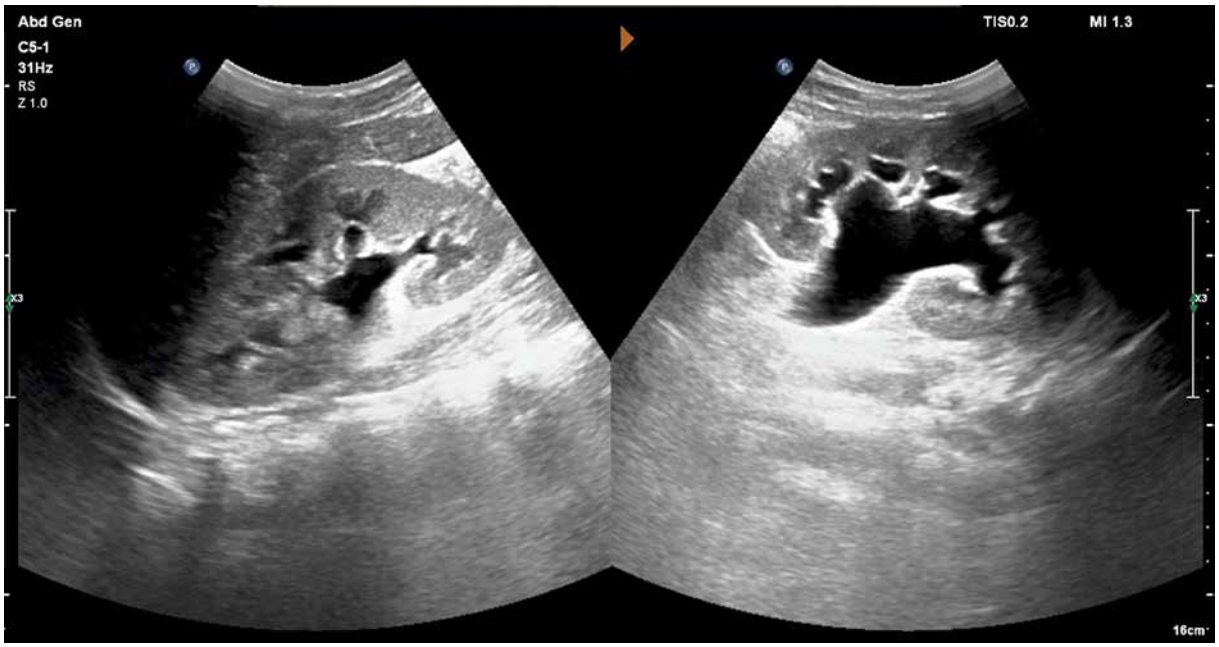

FIGURE 1. Ultrasound showing left hydronephrosis

of the abdomen revealed asymmetry of the kidneys (length of the right kidney was 88 mm, left kidney 101 mm) and left hydronephrosis (the renal pelvis anterior-posterior (AP) diameter was 19 mm); the bladder was full with smooth walls. Two weeks later the diagnosis was continued in a primary hospital. There were no significant changes in the sediment in urinalysis. The repeated ultrasound confirmed previous findings. The voiding cystourethrogram was within normal limits. The patient was discharged home with a recommendation to continue diagnostics and with a planned outpatient diuretic dynamic renal scintigraphy. Pending the results of scintigraphy, while staying at home, the boy started to get up at night to urinate. The pain became more severe, and analgesics were required every day (ibuprofen 200 mg and drotaverine 40 mg, each once or twice daily). A few days later dysuria with mild leukocyturia also appeared, and antibiotic therapy was started due to the acute cystitis diagnosis. The symptoms did not diminish, and when the boy did not urinate for 12 hours, he was presented to the Emergency Department (ED) in a primary hospital.

His past medical history: hypothyroidism treated with levothyroxine, grass pollen allergy, rash after administration of amoxicillin.

The family medical history included: kidney cancer in a distant family member and allergic asthma in a younger brother.

In the ED of the primary hospital, the physical examination revealed: mild dehydration due to decreased fluid intake, abdomen pain on palpation; blood pressure was normal. An indwelling catheter was inserted and only 30 ml of urine was obtained. Laboratory tests showed moderate peripheral eosinophilia (1.56×10^9/l, normal range below 0.8×10^9/l), elevated levels of serum creatinine (6.9 mg/dl), urea (128.8 mg/dl), and potassium (5.4 mmol/l), decreased serum sodium level (130.4 mmol/l), CRP within the norm. Urinalysis showed a trace of protein with normal sediment. The diagnosis of AKI was made and the boy was referred to our department (tertiary hospital). Laboratory tests confirmed the above disorders; calculated by the Schwartz formula, eGFR was 9.79 ml/min/1.73 m^2. Compensated metabolic acidosis was also found. The urinalysis showed mild leukocyturia, but the urine culture was negative. The ultrasound of the abdomen showed increased parenchymal echogenicity of both kidneys, left hydronephrosis (renal pelvis AP 24 mm, calyces 18 mm), and distended left ureter to 10 mm; the bladder was empty (Figure 1).

Because of dehydration, intensive intravenous fluid administration was started, after which diuresis occurred, and after a few days serum creatinine decreased to 2.24 mg/dl. Unfortunately, it was a temporary improvement, and after another few days, there was complete urinary retention and rapid deterioration of renal parameters, as well as hyperkalemia, being an indication for hemodialysis.

In the meantime, the result of a scintigraphy was obtained; it confirmed left kidney obstructive nephropathy with a relative function of 19.8% and the right kidney of 80.2%. The diagnostics were extended. CT urography showed enlargement of both kidneys, bilateral hydronephrosis, more severe on the left side, left megaureter (12 mm width) with the narrowed distal part of 50 mm length and a 6 mm contrast filling defect in its lumen; the bladder was empty. Ultrasound performed on the saline-filled bladder showed irregular thickening of the posterior bladder wall and a bladder mass of 4.5×2 cm. Magnetic resonance imaging (MRI) indicated high-cellular infiltration of the posterior bladder wall, which encompassed all the bladder wall layers and spread beyond the bladder, suggesting BKV (BK virus) infection or malignancy (Figure 2).

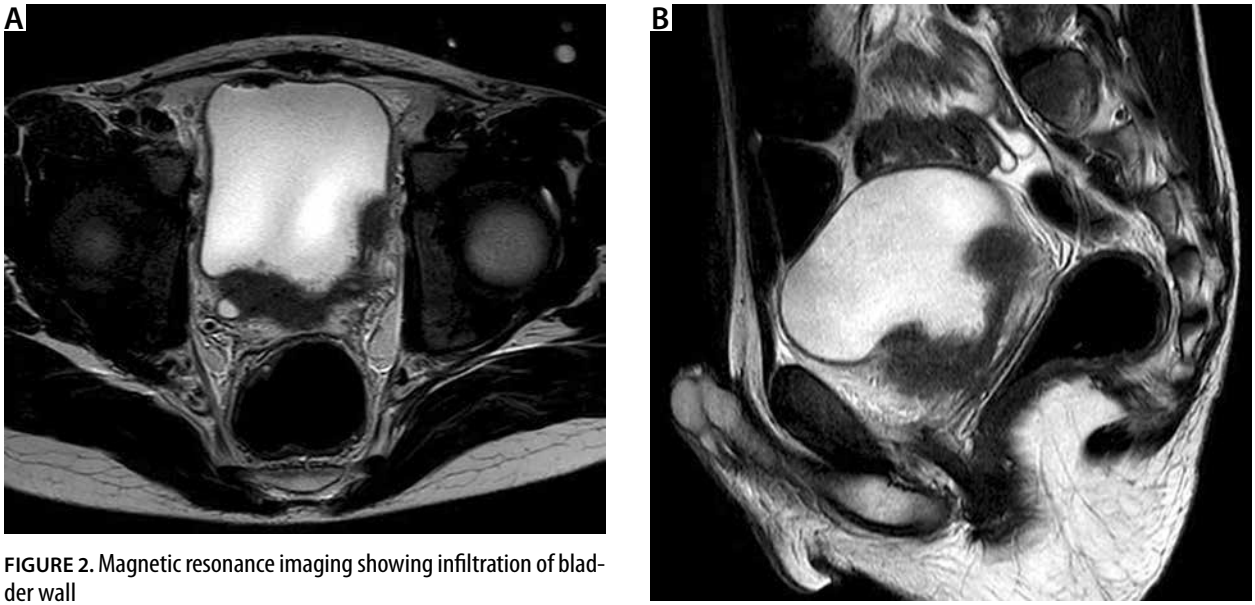

FIGURE 2. Magnetic resonance imaging showing infiltration of bladder wall

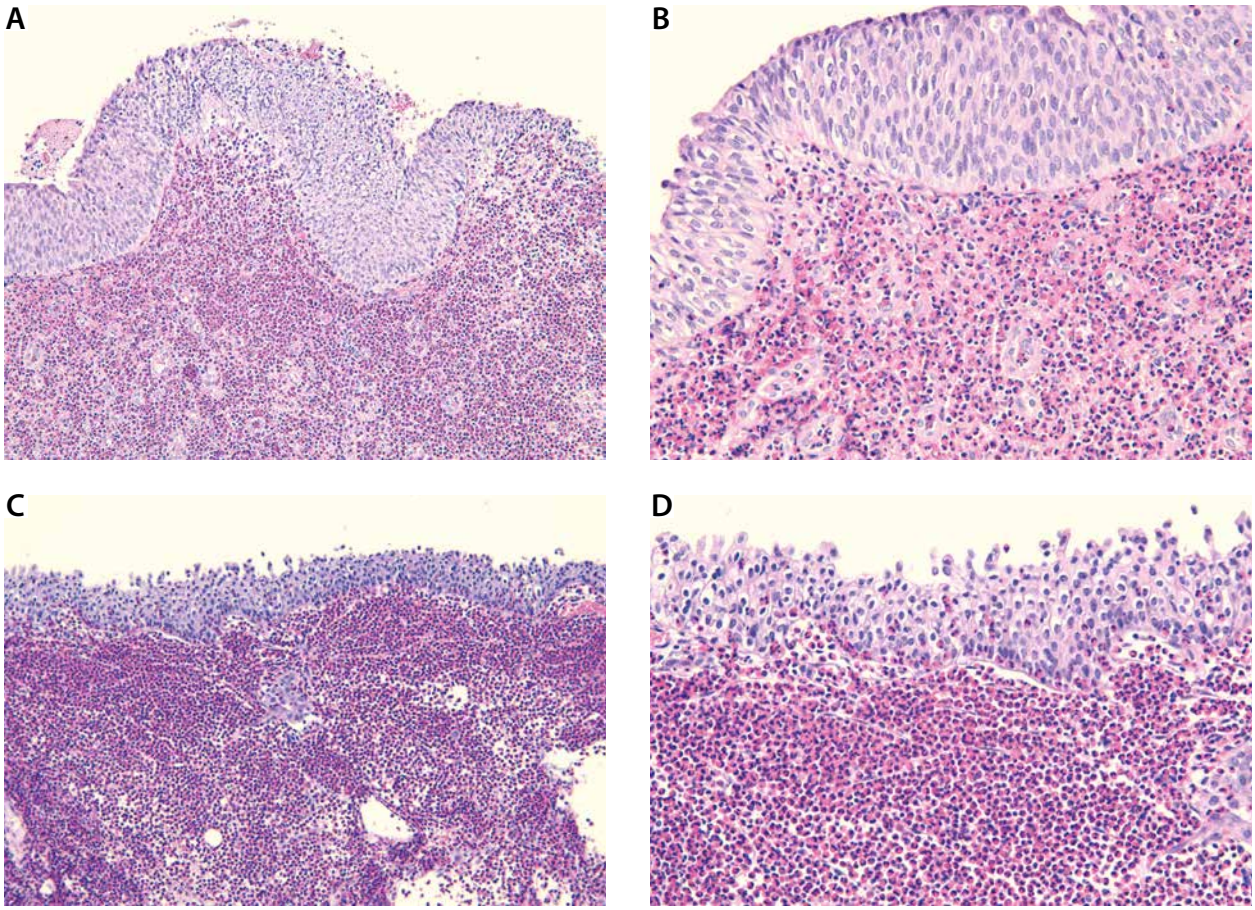

FIGURE 3. Eosinophilic cystitis in histopathological examination: specimens taken during cystoscopy (**A, B**) and open bladder biopsy (**C, D**)

During cystoscopy, no ureters orifices were identified. Bladder biopsy specimens were taken. Pending the result of the histopathological examination and the BKV test, bilateral nephrostomy was performed, after which the renal function gradually improved and after two days full recovery was achieved. BKV infection was finally ruled out. Specimens taken during cystoscopy showed eosinophilic cystitis; no dysplastic or neoplastic changes were identified. Because of strong suspicion of malignancy, open biopsy of the bladder wall was performed. Histopathological examination revealed numerous eosinophilic infiltrates in the bladder wall and urothelial papillary hyperplasia; eosinophilic cystitis in an acute phase was diagnosed (Figure 3).

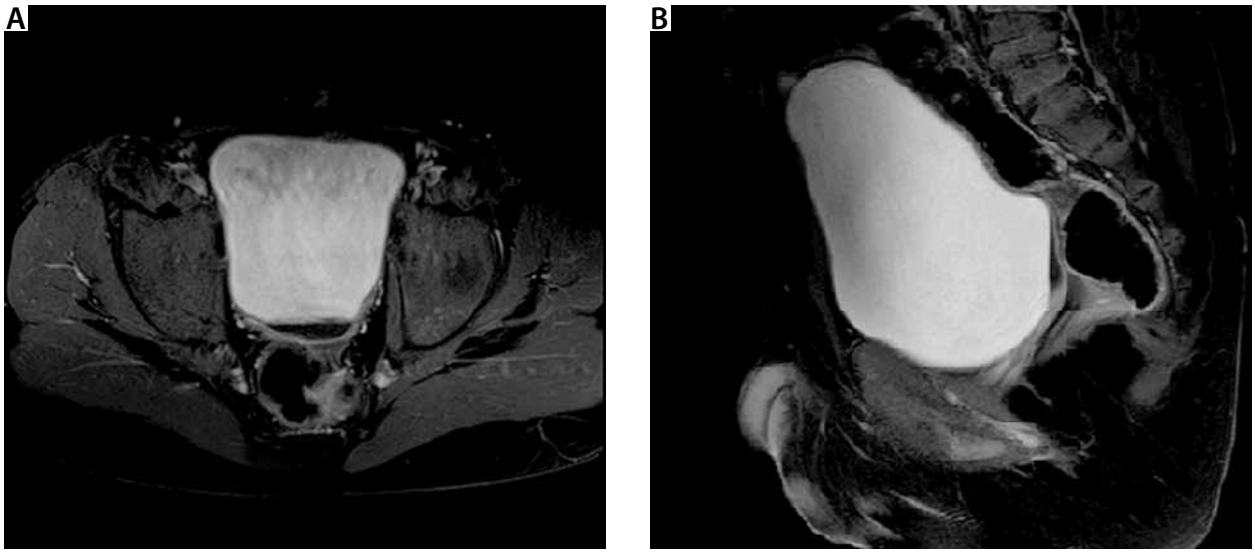

FIGURE 4. Follow-up magnetic resonance imaging after 3 months

Therefore, treatment including oral prednisone (1.5 mg/kg b.w./24 hours) and oral antihistamine (cetirizine 5 mg twice daily) was started. The ultrasound after 4 weeks showed partial regression, and the dose of prednisone was gradually reduced. After nephrostomy removal in the 10th week of therapy, no disturbances in the urinary passage were noted. Follow-up MRI after 3 months revealed almost complete resolution of the bladder mass. There was also a significant improvement in the scintigraphic image after 6 months (relative function of the left kidney improved to 38%, and the renogram curve was nearly normal) (Figure 4).

DISCUSSION

Eosinophilic cystitis is a rare disease with various etiology and symptomatology, which can significantly delay diagnosis. EC in children may present with frequency, dysuria, suprapubic pain, nocturnal enuresis, gross or microscopic hematuria, and urinary retention [1, 9, 10, 14–17]. In later stages, massive infiltration of the bladder wall may form a mass imitating bladder tumor [2, 12, 13, 18–21]. Uncommon manifestations include oliguria and acute kidney injury [22, 23], and even intraperitoneal bladder perforation [24].

In laboratory tests, a complete blood count can reveal peripheral eosinophilia in about 40–50% of patients [4, 6, 7]. Erythrocytes, leukocytes, and proteinuria are the most common findings in urinalysis, while urine culture is negative in most cases [1, 4, 6, 7].

Based on the literature, the most common complication of EC in the general population is dilatation of the upper urinary tract (27%), while unilateral dysfunctional kidney (1.5%) and renal insufficiency (1.5%) are very rare [7]. Among pediatric patients with a detected bladder mass causing hydronephrosis and elevated serum creatinine, the renal function improved after enabling proper urine drainage by inserting an indwelling catheter, clean intermittent catheterization [6], or double JJ-stent placement [12]. Unilateral nephrostomy was required in three patients [6, 12, 23]. To the best of our knowledge, this is the first pediatric case where EC led to severe AKI requiring dialysis and bilateral nephrostomy.

During the diagnostic process, we faced several challenges. Initially, drug toxicity was taken into consideration. Peripheral eosinophilia and frequent intake of non-steroid anti-inflammatory drugs might be possible factors inducing AKI in the mechanism of acute tubulointerstitial nephritis.

The diagnosis in the present case was delayed for many reasons. The outpatient ultrasound and the ultrasound performed in the primary hospital did not show changes in the bladder wall. Different technical and non-technical factors may affect the detection of bladder wall lesions. Presumably, the infiltration which affected the left ureter drainage was localized intramurally or was too small to visualize at this stage. Also in our center, the first ultrasound and CT scans were performed on an empty bladder, which made it difficult to fully visualize its walls. However, complete urinary retention with a rapid deterioration of renal function, which was transient in nature, and complete remission of AKI after bilateral nephrostomy pointed to an obstructive cause. It was confirmed by further imaging and cystoscopy.

Differential diagnoses included primarily vesical rhabdomyosarcoma, followed by other malignant lesions such as urothelial carcinoma, leiomyosarcoma, lymphoma [3, 12, 18, 20] as well as non-malignant lesions, i.e. solitary fibrous tumor, leiomyoma, or cystitis caused by a polyoma-BK virus and other infectious agents [2, 18, 25]. Cystoscopy with tissue sampling for histopathological examination or whole layer bladder biopsy is required for the final diagnosis [2, 7, 13, 22, 26]. In cases in which the bladder mass was noted submucosally at cystoscopy, or in order to reinforce the accuracy of diagnosis when neoplasm in strongly suspected, open biopsies were per-

formed [2, 21]. Adequate deep biopsies are needed in order to study the muscle involvement; otherwise, the diagnosis can be missed [1, 17]. Recently, an ultrasound-guided needle biopsy including all the layers of the bladder wall has been proposed as a new feasible method [27]. However, it may not be relevant in all patients, for example in the present case due to the lesion localized in the posterior wall of the bladder. Only the histopathological examination established the diagnosis, including in our case.

As EC is a very rare condition in children, there are no guidelines regarding therapy and follow-up. The management depends on the clinical presentation and symptom severity. It ranges from observation and supportive care to removal of potential allergens, medications, and rarely surgical procedures [6, 13, 20, 28]. In most patients, corticosteroids and antihistaminic drugs are used, and antibiotics if the urine culture is positive [4, 6, 13, 20, 25].

Recurrence of the disease may occur in 30% of patients [5, 6]. In recurrent or refractory cases, cyclosporine A or azathioprine therapy might be an option [4, 5, 25, 29, 30]. Due to potential relapses, patients should be monitored with a frequency depending on the obtained effects. Fortunately, regardless of delay in the proper diagnosis of our patient, the treatment brought excellent results. The boy is still under our care.

CONCLUSIONS

Eosinophilic cystitis presents various clinical manifestations, but severe AKI requiring dialysis has not been described before. The bladder wall infiltration and thickening caused by EC may mimic a bladder tumor and might be a very unusual cause of post-renal acute kidney injury. The definitive diagnosis is based on the result of histopathological examination. Proper diagnosis and treatment result in a good clinical outcome. However, due to disease recurrence risk, patients need longer follow-up.

DISCLOSURE

The authors declare no conflict of interest.

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