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Best Regards,

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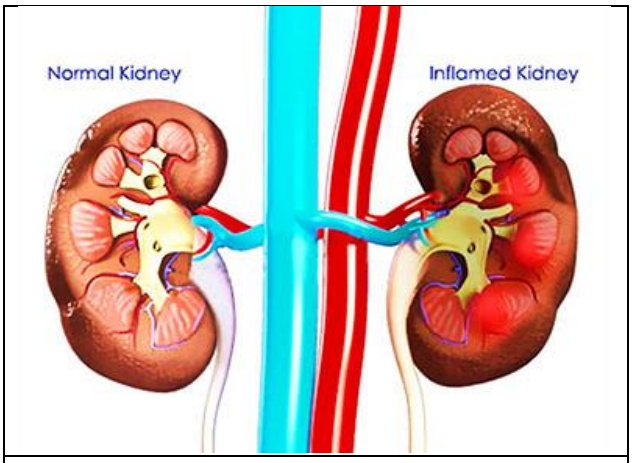
1. Assessment of the clinical importance of renal immune complex accumulation in children suffering from acute interstitial nephritis

Introduction: Acute kidney injury (AKI) is often caused by acute interstitial nephritis (AIN), which is histologically defined by the presence of inflammatory infiltrates and oedema in the renal interstitium. AIN is typically linked to a decline in renal function. AIN accounts for 0.87% to 15.7% of AKI in all children and 27% in adults, making it a rare cause of AKI in the paediatric population.[1] The etiology of various conditions that cause systemic inflammation, including immunoglobulin G4 (IgG4)-associated immune complex multiorgan autoimmune disease (MAD), inflammatory bowel disease, tubulointerstitial nephritis and uveitis (TINU) syndrome, and infectious diseases, can be caused by drugs.[2] Immune complex (IC) deposition in AIN was not frequently reported in prior literature. However, AIN showed evidence of IC deposition not only in the mesangial fields and in capillary loop but also in the tubulointerstitium.[1] The purpose of this study was to create a theoretical foundation for the diagnosis and treatment of AIN patients as well as to examine the relationship between IC deposition and clinical symptoms, pathological changes, and prognosis in paediatric AIN patients.



Acute interstitial nephritis

Methods: In this retrospective study, a total of 78 children with AIN were included. The non-IC group and the IC group were the two groups into which the patients were divided. The IC group was further divided into two subgroups: the extraglomerular (EG)-IC group and the intraglomerular (IG)-IC group. The primary intent was to compare the renal outcomes and clinical and histological characteristics between the groups.

Results: Drugs were the cause of 52 cases (66.67%), while infectious diseases were linked to 35 cases (44.87%). The children that had the IC, IG-IC, and EG-IC depositions were 22 (28.21%), 12 (15.38%), and 10 (12.82%), respectively. Comparing the IC group to the non-IC group, the IC group showed significantly higher levels of Scr, urine N-acetyl-β-D-glucosidase (NAG) enzyme, retinol-binding protein (RBP), neutrophil gelatinase-associated lipocalin (NGAL), a higher frequency of neutrophils, plasma cells, and eosinophils infiltrate, higher scores of interstitial inflammation (i), total inflammation (ti), and interstitial edema, and a lower level of estimated glomerular filtration rate (eGFR) ($p<0.05$, $p<0.01$). Plasma cell infiltration, interstitial inflammation (i), total inflammation (ti), and interstitial edema were all positively moderately linked with IG-IC deposition whereas the levels of RBP with EG-IC deposition. In children with AIN, interstitial fibrosis/tubular atrophy (IF/TA) was a risk factor for chronic kidney disease (CKD), whereas interstitial inflammation, EG-IC deposition, and interstitial edema were risk factors for acute kidney disease (AKD). (Table 1)

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	AKD		CKD 3-5 stage	
	P	HR(95% CI)	*P*	HR(95% CI)
Interstitial inflammation	0.019	15.534 (1.215~24.183)	0.155	8.378 (1.538~43.276)
IG-IC deposition	0.356	0.612 (0.297~9.066)	0.108	4.559 (1.113~9.357)
EG-IC deposition	0.024	0.759 (0.572~1.536)	0.267	2.165 (0.243~7.435)
Interstitial edema	0.036	3.582 (1.326~7.879)	0.195	0.858 (0.126~6.149)
IF/TA	0.572	0.813 (0.232~2.719)	0.033	6.052 (1.621~14.095)

AKD: acute kidney disease; CKD: chronic kidney disease; AIN: acute interstitial nephritis; IG-IC: intraglomerular immune complex; EG-IC: extraglomerular immune complex; IF/TA: interstitial fibrosis/tubular atrophy.

Table 1. Incidence of both CKD and AKD in children with AIN.

Discussion: In this investigation, the incidence of IG-IC and EG-IC deposition was 15.38% and 12.82%, respectively. In addition to confirming that IC deposition may be an early lesion in AIN and highlighting the significance of renal biopsy in an early stage of AIN, IG-IC and EG-IC deposition primarily showed positive correlations with acute renal tubular and kidney inflammatory lesions. Additionally, EG-IC deposition was a risk factor for AKD in AIN.[1] According to Wang H et al., the most prevalent immune reactants on the tubular basement membrane (TBM) in IF observations were IgG and C3.[3] This study found that IgM and C3 were the most common deposits in AIN, implying that IC deposition in AIN and autoimmune illness are not generated by the same mechanism.[1]

Conclusion: The current study concluded that drugs and infections were the primary causes of AIN in children. EG-IC deposition was a risk factor for the onset of AIN in children, and IG-IC and EG-IC deposition were strongly linked with glomerular and tubular damage, as well as severe clinical symptoms.

Children diagnosed with acute interstitial nephritis (AIN) were found to be at risk for both chronic kidney disease (CKD) and acute kidney disease (AKD), depending on their interstitial fibrosis/tubular atrophy (IF/TA), interstitial inflammation, and interstitial edema.

References:

1. Zhang P et al. Clinical significance of kidney immune complex deposition in children with acute interstitial nephritis disease. Ren Fail. 2023;45(2):2236234.
2. Joyce E et al. Tubulointerstitial nephritis: diagnosis, treatment, and monitoring. Pediatr Nephrol. 2017; 32:577–587.
3. Wang H et al. Tubular basement membrane immune complex deposition is associated with activity and progression of lupus nephritis: a large multicenter Chinese study. Lupus. 2018 Apr;27(4):545-555.

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2. Comparison of efficacy and safety of reterograde intrarenal surgery and antegrade flexible ureteroscopy for the treatment of impacted upper ureteric stones 1.5 cm or larger

Introduction: Impacted ureteral stones are defined as stones that have not moved in two months or that are not bypassable using contrast medium or a guidewire. Managing patients with severely impacted upper ureteric stones remains difficult.[1] Ureteterorenoscopy (URS), antegrade or retrograde, is the preferred choice for treating proximal ureter stones bigger than 1 cm, according to current European Association of Urology (EAU) urolithiasis recommendations. Shockwave lithotripsy (SWL) is the second approach. However, because of lower success rates and longer treatment times, SWL should not be used for bigger stones.[2] An alternative for managing upper ureteric stones is antegrade access through URS, which has the benefits of reaching the stone from a dilated system, preventing stone escape, and improving field of vision. On the other hand, this antegrade mode has disadvantages such as being more invasive due to renal puncture, requiring more radiation exposure, requiring longer hospital stays, and took more time during surgery. So, the authors performed a concept of puncturing in the lower calyx and dilatation up to 14 fr and thereby reducing the invasiveness of this surgery.[1] Moreover, they also compared the safety and effectiveness of retrograde intrarenal surgery (RIRS) and antegrade flexible ureteroscopy (FURS) in the treatment of large impacted upper ureteric stones of size 1.5 cm or larger.

Methods: A total of 61 patients with a single large impacted upper ureteric stone measuring ≥ 1.5 cm were included in this prospective analysis. The patients were divided into two groups. 31 patients receiving antegrade FURS along with JJ stent implantation were part of Group A. Thirty patients in Group B underwent RIRS treatment with JJ stent implantation. The two groups' stones were fragmented using holmium lasers. The study's primary outcome was to determine the stone-free rate (SFR) after two weeks. The secondary outcome comprised postoperative complications and intraoperative data, such as operating time, lithotripsy, and fluoroscopy times.

Results: Compared to Group A, Group B had a considerably shorter operational time. (Table 1). Group A had a considerably higher percentage of SFR (90.3%) than Group B (70%) ($p = 0.046$). There were not any significant differences in bleeding between the groups under study ($p = 0.238$). When compared to an antegrade approach, urosepsis demonstrated a considerably larger percentage associated with a retrograde approach ($p = 0.024$).

Variable	Group A Antegrade FURS (N=31)	Group B RIRS (N=30)
Operative time, min, mean (SD)	93.55±7.58	64.40±7.16
Fluoroscopy time, s, mean (SD)	254.84±46.82	112.33±20.29
Lithotripsy time, min, mean (SD)	35.68±2.71	35.20±2.87
Complications n (%)		
Bleeding (<150 cc)	3 (9.7)	0 (0)
Sepsis	0 (0)	5 (16.7)
Haematuria	3(9.7)	2(6.7)
Stone free rate, n/N (%)	28/31(90.3)	21/30 (70.0)
Auxiliary treatment (ESWL), n/N (%)	3/31 (9.7)	9/30 (30)
VAS Score, n/N (%)		
1–3	29/31 (93.5)	30/30 (100)
4–6	2/31 (6.5)	0/30 (0)

Table 1. Operational and post-operative data.

Discussion: Compared to the antegrade FURS group, the RIRS group had a shorter operating period in this investigation. After two weeks, SFR was higher in the antegrade URS group than in the RIRS group (90.3% vs. 70%).[1] According to Güler Y et al., the antegrade URS had the shortest operation time, while the RIRS group had the shortest hospital stay. The VAS scores of the LU group were the highest, while those of the RIRS group were the lowest. The antegrade URS, LU, and RIRS groups had success rates of 97.4%, 97.5%, and 83.7%, respectively.[2] The operating time was substantially less in the retrograde URS group than in the antegrade miniperc URS group, according to Elgebaly et al., there was a greater stone-free rate in the antegrade group compared to the reterograde group.[3]

Conclusion: The current study concluded that antegrade FURS was a safer and more efficacious treatment option than RIRS for large impacted upper ureteric stones measuring 1.5 cm or greater.

Antegrade FURS appears to be a viable operation for the therapy of large impacted upper ureteric stones (≥1.5 cm), and it has a high success rate and a low risk of complications.

References:

1. Mohey A, et al. Comparative study between antegrade flexible ureteroscopy and reterograde intrarenal surgery in the management of impacted upper ureteric stones 1.5 cm or larger. World Journal of Urology. 2023 Nov; 3:1-6.
2. Güler Y, et al. Comparative evaluation of retrograde intrarenal surgery, antegrade ureterorenoscopy and laparoscopic ureterolithotomy in the treatment of impacted proximal ureteral stones larger than 1.5 cm. Cent European J Urol. 2021;74(1):57-63.
3. Elgebaly O, et al. Antegrade mini-percutaneous flexible ureteroscopy versus retrograde ureteroscopy for treating impacted proximal ureteric stones of 1-2 cm: A prospective randomised study. Arab J Urol. 2020 Aug 23;18(3):176-180.

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3. Association between polar vasculosis and the progression of diabetic kidney disease (DKD) in type 2 diabetes

Introduction: Diabetes kidney disease (DKD) is one of the most serious microangiopathies associated with diabetes. Mesangial enlargement and nodular sclerosis are the two common structural alterations that can be seen in the glomeruli in early-stage DKD with albuminuria or normoalbuminuria, according to previous research.[1] DKD pathophysiology involves abnormal angiogenesis, and the growth of additional vessels, known as polar vasculosis, is observed as an early kidney lesion in DKD. While the precise anatomy of polar vasculosis remains unclear, a study employing three-dimensional image reconstruction indicates that these veins are angiogenesis linking peritubular capillaries, afferent arterioles, anastomosed glomerular capillaries, and efferent arterioles. It has been suggested that the development of polar vasculosis may lower the intraglomerular pressure, even if its purpose is still uncertain. However, there are few research examining the relationship between polar vasculosis and the long-term kidney prognosis in DKD.[2] The purpose of this study was to evaluate the relationship between the development of diabetic kidney disease (DKD) in individuals with type 2 diabetes and polar vasculosis.

Methods: 811 type 2 diabetes patients with biopsy-proven DKD and proteinuria (≥0.15 g/g creatinine [g/day]) were included in this retrospective analysis. For categorical analyses, baseline eGFR was categorized as G1-G2 (≥60 mL/min/1.73m^2) and G3a–G5 (<60 mL/min/1.73m^2) based on the classification of chronic kidney disease (CKD). The Japanese Society of Nephrology's updated definition of chronic kidney disease (CKD) classified baseline urine protein excretion as 0.15–0.49 g/g creatinine (g/day) and ≥0.5 g/g creatinine (g/day). The relationship between polar vasculosis and other renal abnormalities was investigated. The endpoint was the development of DKD, which was defined as a combination of starting renal replacement therapy and experiencing a 50% reduction in estimated glomerular filtration rate (eGFR) from the beginning of the study.

Results: Polar vasculosis was found in 677 (83.5%) of the patients. In multivariate logistic regression analysis, vascular lesions, age, eGFR, hemoglobin A1c, glomerulomegaly, subendothelial widening of the glomerular basement membrane, glomerular class in the Renal Pathology Society classification ≥IIb, vascular lesions were positively linked with polar vasculosis whereas, interstitial fibrosis and tubular atrophy (IFTA) were negatively associated with polar vasculosis. Progression of DKD was seen in 322 of 677 and 79 of 134 individuals with and without polar vasculosis, respectively, after a median follow-up of 5.2 years. A Kaplan–Meier analysis revealed a correlation between polar vasculosis and decreased cumulative occurrences of DKD development. (Figure 1) Polar vasculosis was linked to a decreased risk of DKD progression, independent of eGFR or proteinuria subgroups, according to multivariate Cox regression analyses. Examining all-cause mortality prior to DKD progress as a competitive event did not alter these relationships between polar vasculosis and improved kidney outcome.

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Discussion: Multivariate Cox regression analyses in this study revealed that polar vasculosis was linked with a decreased risk of DKD development, regardless of eGFR or proteinuria subgroups. Examining all-cause mortality prior to DKD progress as a competitive event did not alter these relationships between polar vasculosis and improved kidney outcome.[2]

According to Saito et al., multivariate Cox regression analysis revealed that a high degree of proteinuria, a low starting eGFR, and severe interstitial inflammation were all poor prognostic variables.[3]

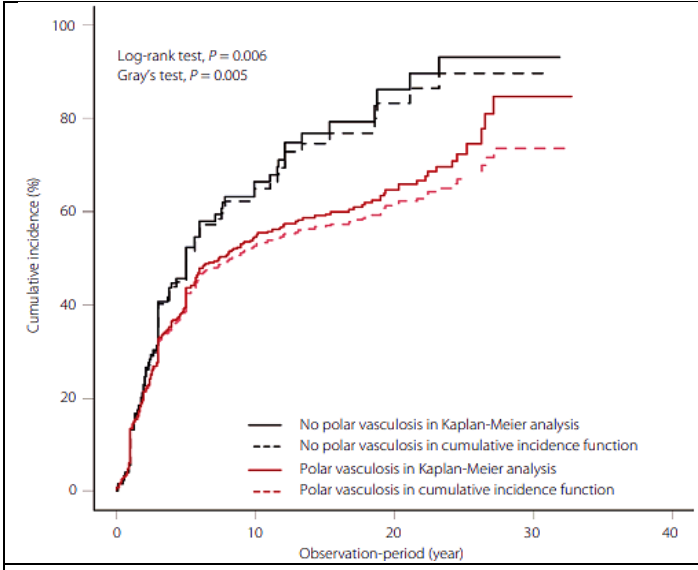

Figure 1. Cumulative incidence of the progression of diabetic kidney disease (DKD) in 677 individuals with polar vasculosis (red lines) and 134 patients without (black lines)

Conclusion: The current study concluded that polar DKD vasculosis was linked to less advanced IFTA and improved renal outcomes in type 2 diabetes with proteinuria.

In individuals with proteinuria, the presence of polar vasculosis was related with improved renal outcome.

References:

1. Oda Y, et al. Significant polar vasculosis in a patient with a 30-year history of type 2 diabetes. Endocrinology, Diabetes & Metabolism Case Reports. 2019 Nov 12;2019:19-0092.
2. Shimizu M, et al. Polar vasculosis is associated with better kidney outcome in type 2 diabetes with biopsy-proven diabetic kidney disease: A multicenter cohort study. Journal of Diabetes Investigation. 2023 Nov;14(11):1268-78.
3. Saito A, et al. Clinicopathological features and outcomes of diabetic kidney disease with extracapillary hypercellularity: a Japanese single-center experience. Clinical and Experimental Nephrology. 2020 Jun;24:509-17.

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4. A rare case of uretero-iliac artery fistula

Introduction: A fibrous and inadequately vascularized uretero-vascular adhesion is the result of persistent inflammatory processes that lead to uretero-iliac artery fistulae (UIAF). Patients with a history of pelvic radiation, surgery, or chronic ureteral stenting are frequently affected. This is a potentially fatal illness that typically manifests as massive gross hematuria along with acute anaemia and hemorrhagic shock.[1] A patient's diagnosis may be delayed if they frequently have sporadic symptoms and negative results from their initial scan. Hemorrhagic shock is frequently present at the time of fistula diagnosis; hence, immediate multidisciplinary treatment is necessary.[2] Endovascular stent implantation was used to treat this fatal case, and the suggested causes for fistula formation are examined.

Case presentation:

A 70-year-old man presented to a urology clinic for examination of extensive hematuria. He reports that over the past three months, the hematuria has been happening sporadically, sometimes with large clots and no discomfort. After stopping for a few weeks, the hematuria would start again. He was able to urinate during this period with a good stream, but according to the report, the urine was very red. According to the patient's medical history, another urologist treated the patient's left ureteral calculi endoscopically more than ten years ago. At that point, the patient sustained left ureteral damage, for which he was sent to a sizable tertiary facility for final care. He had endoscopic surgery, but he was unable to provide an accurate record of the events that occurred. For ten years after his full recovery, the patient had no symptoms. In addition, he previously had a slight obstruction of the left ureteropelvic junction (UPJ), which did not require treatment. A standard gross hematuria work-up, including urine cytology, urine culture, office cystoscopy, computed tomography (CT) with and without intravenous contrast (Figure 1), and 3D reconstruction, was performed upon presentation to the local urologist.

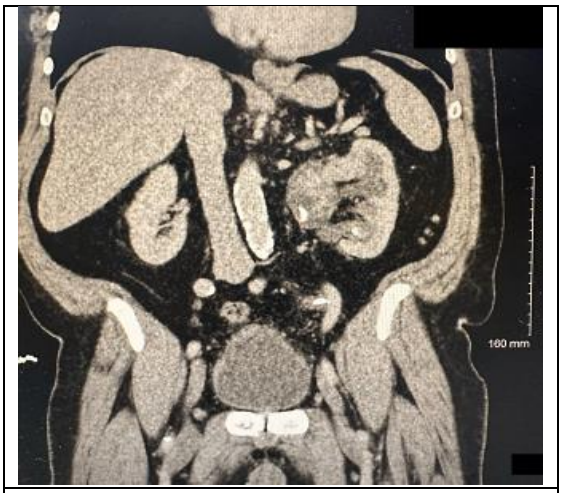

Figure 1. An indwelling left ureteral stent near the iliac artery is seen in the coronal view of a CT scan performed with and without intravenous contrast.

A fluorescence in-situ hybridization (FISH) was performed, and it was positive. The patient underwent a transurethral prostate biopsy, random bladder biopsies, selective ureteral cytology, and cystoscopy for operational evaluation after the FISH test showed a positive result. It was discovered that the patient had an abnormally large left looping ureter at the time of the above-mentioned operation. (Figure 2) There was no malignancy discovered during the diagnostic ureteroscopy. A stent was inserted and later taken out. Again, the left selective ureteral cytology yielded no conclusive results. After one month, the patient still had gross hematuria and was referred to a tertiary care hospital for further examination. A second cystoscopy with bilateral retrograde pyelograms, a negative left ureteral biopsy, and the implantation of a left stent were all part of the work-up at the hospital. After the treatment, the patient recovered well and showed no signs of hematuria.

After two weeks, the hematuria significantly increased, and the patient was again admitted to the hospital. Six packets of blood were needed for the transfusion because the patient's hemoglobin levels had decreased significantly. Following that, he was moved to a Level 1 trauma facility that offered interventional radiology treatments. An arteriogram revealed the presence of a uretero-iliac artery fistula with a characteristic blush on the left in-looping ureter after vascular surgery was advised. After that, the patient was brought back for an emergency iliac artery graft stent placement. The patient was discharged with no further hematuria. After a month, a CT scan of his abdomen and pelvis revealed several non-obstructing stones on the left side, minor prostatic lobar hypertrophy with nodular soft tissue thickening, and a slight improvement in the left UPJ obstruction. There is still work to be done to determine the cause of the positive FISH result and the inconclusive cytology. The patient's tertiary urologist and local urologist are still actively monitoring the patient.

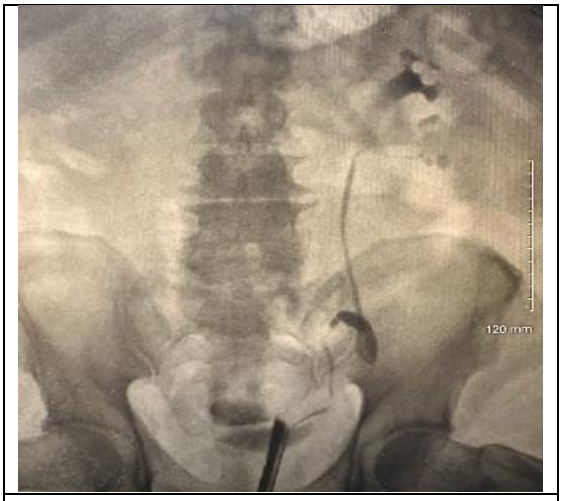

Figure 2: The left looping ureter is shown in the first intraoperative retrograde pyelogram.

Discussion: Vascular surgery was done in the present case, and a stent was implanted after CT angiography (CTA) with contrast confirmed the ureteroiliac artery fistula with a typical blush visible on the left in-looping ureter.[2] Leone L, et al. demonstrated that endovascular therapy using a vascular endoprosthesis was the most appropriate course of treatment, while angiography can be helpful in confirming the diagnosis.[1] According to Ghouti C, et al., there were no definitive recommendations for the management of UAF that would enable patients to be treated routinely. Endovascular stent-assisted mini-invasive surgery was a rapid, reliable, and effective treatment, especially for patients with several surgical comorbidities.[3]

Conclusion: CT angiography (CTA) with contrast was the ideal technique for the diagnosis of a ureteroiliac artery fistula. In this case, the patient report showed a negative CTA at first, followed by a positive CTA after a follow-up examination. Endovascular stent implantation was used for treatment.

Vascular surgery must be performed to diagnose and treat the ureteroiliac artery fistula.

References:

1. Leone L, et al. Uretero-iliac artery fistula: a challenge diagnosis for a life-threatening condition: monocentric experience and review of the literature. International Urology and Nephrology. 2019 May 1;51:789-93.
2. Urwin B, et al. Uretero-iliac Artery Fistula: A rare, life-threatening condition. Urology Case Reports. 2023 Nov 1;51:102584.
3. Ghouti C, et al. Uretero-arterial fistula: Six new cases and systematic review of the literature. Progrès en Urologie. 2021 Sep 1;31(10):605-17.