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CASE REPORT

Clean intermittent catheterization reverses hydronephrosis in a child with congenital nephrogenic diabetes insipidus: a case report

Jianlin Xie,[1#] Jingde Wu,[1] Qingwei Zhang,[1] Yuanqi Guo,[1] Xiande Huang[2*]

[1]The First Clinical Medical College, Gansu University of Chinese Medicine, Lanzhou, China

[2]Department of Urology, Gansu Provincial Hospital, Lanzhou, China

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Background: *Congenital nephrogenic diabetes insipidus (CNDI) is most frequently caused by mutations in the AVPR2 gene. Patients exhibit persistent polyuria due to renal insensitivity to antidiuretic hormone. Chronic high urine output predisposes to bladder dysfunction and upper urinary-tract dilatation, notably hydronephrosis. Although pharmacotherapy can partially reduce urine volume, its capacity to reverse established hydronephrosis is limited. Clean intermittent catheterization (CIC), a mainstay in managing neurogenic bladder, warrants investigation regarding its utility in CNDI-associated hydronephrosis.*

Case Description: *A 9-year-old Chinese boy presented with lifelong polydipsia and polyuria, with a peak 24-h urine output of approximately 7100 mL. Renal ultrasonography demonstrated bilateral moderate hydronephrosis. Whole-exome sequencing identified a hemizygous nonsense mutation, AVPR2 c.968G>A (p.Trp323*); his mother was a heterozygous carrier of the same variant. After one month of standard therapy with hydrochlorothiazide and indomethacin, his daily urine volume decreased to approximately 3400 mL/d, but the hydronephrosis showed no improvement. A subsequent video urodynamic study revealed decreased bladder sensation, reduced compliance, and diminished detrusor contractility. In addition to the continued pharmacological regimen, clean intermittent catheterization (performed three times daily at home) was introduced. Follow-up ultrasonography one month later showed significant improvement in the bilateral hydronephrosis.*

Conclusions: *For pediatric CNDI patients with persistent incomplete bladder emptying and hydronephrosis despite pharmacotherapy, short-term clean intermittent catheterization can break the vicious cycle of "chronic urinary retention—elevated bladder pressure—upper urinary tract dilatation," representing a safe, effective, and readily implementable adjuvant intervention.*

Key Words: congenital nephrogenic diabetes insipidus, intermittent catheterization, individualized treatment, case report

Introduction

Congenital nephrogenic diabetes insipidus (CNDI) is a rare and genetically heterogeneous monogenic disorder, representing a distinct subtype of nephrogenic diabetes insipidus (NDI).[1] It results from mutations in either the AVPR2 or AQP2 genes.[2] Compared with NDI, CNDI is markedly less prevalent, accounting for approximately 10% of all NDI cases. Among individuals with CNDI, about 90% of cases are caused by mutations in the AVPR2 gene, inherited in an X-linked recessive manner, while the remaining 10% are due to AQP2 gene mutations, which follow either autosomal dominant or autosomal recessive inheritance patterns.[3] The overall incidence of CNDI is extremely low; a Canadian population-based study reported an incidence of X-linked CNDI in male

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[#]First author: Jianlin Xie

*Corresponding Author: Xiande Huang.
Email: huangxiande720@163.com

infants born in Quebec of approximately 8.8 per million.[4] The hallmark clinical features of this condition include polyuria with hyposthenuria and compensatory polydipsia, which may lead to complications such as growth retardation, developmental delay, and hydronephrosis.[5]

This report presents a retrospective analysis of a pediatric case of CNDI caused by a nonsense mutation in the AVPR2 gene (c.968G>A, p.Trp323*), confirmed by genetic testing. The patient exhibited classic symptoms of polyuria and polydipsia from early infancy, and imaging studies revealed bilateral hydronephrosis. Although standard pharmacological therapy (hydrochlorothiazide combined with indomethacin) significantly reduced urine output, it did not lead to improvement in hydronephrosis. However, following the addition of CIC, marked improvement in bilateral hydronephrosis was observed after one month of intervention. This case underscores the efficacy and safety of CIC as an adjunctive treatment in CNDI patients with concomitant hydronephrosis, offering valuable insights for the development of individualized clinical management strategies. This case report follows the CARE guidelines, please see the CARE checklist (Supplementary Material S1) for further details.[6]

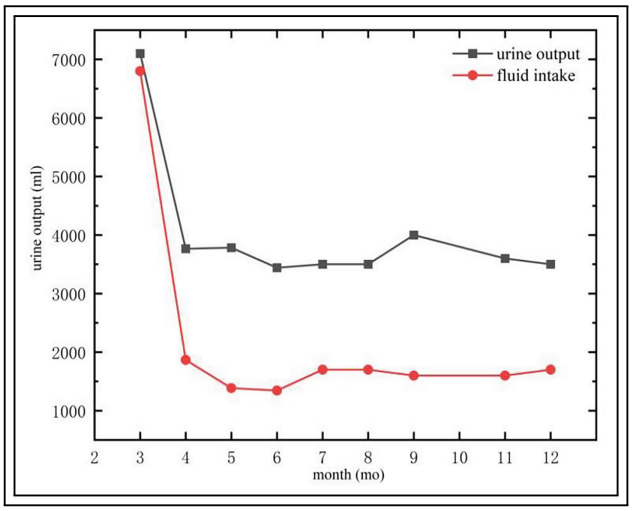

FIGURE 1. The changes in urine and water volume of the patient. Note: The March data represented the urine and water volume of the patients before they were treated by the team, while the data from April to December reflected the corresponding changes in the patients during their drug treatment. Data from April to May were the average of patient records, while data from June to December were estimated based on family recollections

Case Presentation

Patient information

A 9-year-old Chinese boy presented with symptoms of polyuria and polydipsia since early childhood. The patient had sought medical attention at multiple hospitals and was ultimately diagnosed with nephrogenic diabetes insipidus, although genetic testing was not performed. Upon admission, the patient's 24-h urine output exceeded 7100 mL, and his fluid intake surpassed 6800 mL (Figure 1). There was no family history of similar cases of nephrogenic diabetes insipidus, and the parents were non-consanguineous.

Inspection and verification

Through comprehensive physical examination and laboratory tests, we identified that the pediatric patient presented with hyperuricemia and hypokalemia, accompanied by significantly reduced urine osmolality and specific gravity. Ultrasonography revealed moderate bilateral hydronephrosis (with an empty bladder), The postvoid residual urine volume was 121 mL, while cranial MRI findings were unremarkable. To assess lower urinary tract function, we performed video-urodynamic studies (UDS). The key urodynamic parameters are summarized in Table 1. The study revealed markedly impaired bladder sensation, reduced bladder compliance, and weak detrusor contractility. The water deprivation test demonstrated no significant reduction in urine output or notable increase in urine osmolality. To establish a definitive diagnosis, whole exome sequencing was performed on both the patient and parents, which revealed a G>A point mutation in the AVPR2 gene, resulting in a Trp323* nonsense mutation (Figure 2), thereby confirming the diagnosis of CNDI.

Diagnostic assessment

A diagnosis of congenital nephrogenic diabetes insipidus caused by AVPR2 gene mutation was confirmed based on the patient's clinical manifestations and genetic testing results. The maternal carrier status of a heterozygous mutation at the same locus further supported the inheritance pattern. Initial management with hydrochlorothiazide and indomethacin led to significant reduction in urinary output and fluid intake compared to pre-treatment levels, though bilateral hydronephrosis persisted.

TABLE 1. **The key urodynamic parameters**

Parameter	Value
CC	529 mL
P_{detmax}@capacity	28 cmH_2O
$P_{det}Q_{max}$	N/A
Q_{max}	13 mL/s
PVR*	150 mL

Note. As the pressure catheter had been removed, the true value could not be recorded; the 150 mL is a visual estimate from the fluoroscopic image and was therefore not included in the official dataset. *The PVR represents an estimated approximation, as opposed to a direct quantitative measurement. N/A: Not applicable, as the parameter could not be obtained due to the child's inability to voluntarily initiate effective voiding while the pressure catheter was in place. Abbreviations: CC, Cystometric Capacity; P_{detmax}@capacity, Maximum Detrusor Pressure at Cystometric Capacity; $P_{det}Q_{max}$, Detrusor Pressure at Maximum Flow Rate; Q_{max}, Maximum Flow Rate; PVR, Post-void Residual Volume.

Therapeutic measures

Following the diagnosis, the pediatric patient was administered a combined therapy of oral indomethacin and hydrochlorothiazide. After one month of treatment, the patient's 24-h urine output decreased to approximately 3500 mL, and fluid intake was reduced to around 1600 mL (Figure 1). Post-discharge, the patient continued with the prescribed medication regimen and underwent regular follow-up assessments. The follow-up results indicated that urine output remained stable at approximately 3500 mL, with fluid intake maintained at 1700 mL. Renal ultrasound continued to demonstrate moderate bilateral hydronephrosis. Subsequently, given the patient's hydronephrosis, we instructed the child to perform at-home clean intermittent catheterization in addition to voluntary voiding. The catheterization frequency was set at three times daily: after morning voiding (around 7:00 AM), after noon voiding (around 12:00 PM), and after voiding before bedtime at night (around 10:00 PM). After one month of intermittent catheterization therapy, the patient's hydronephrosis showed significant improvement (Figure 1).

Follow-up and outcomes

During the 5-month follow-up period, although pharmacological treatment effectively controlled urine output, vigilance against complications such as hydronephrosis remains imperative. Therefore, it is recommended to regularly monitor the child's hydronephrosis status and implement timely interventions as needed. This case underscores the importance of early genetic diagnosis for CNDI. Furthermore, in the treatment of cases complicated by hydronephrosis, the combination of CIC with foundational pharmacotherapy represents an effective comprehensive management strategy.

Discussion

CNDI is a rare genetic disorder characterized by renal insensitivity to arginine vasopressin (AVP), resulting in the inability to concentrate urine, which leads to polyuria, polydipsia, and an increased risk of dehydration.[7,8] The primary therapeutic objective at present is to manage urine output rather than to

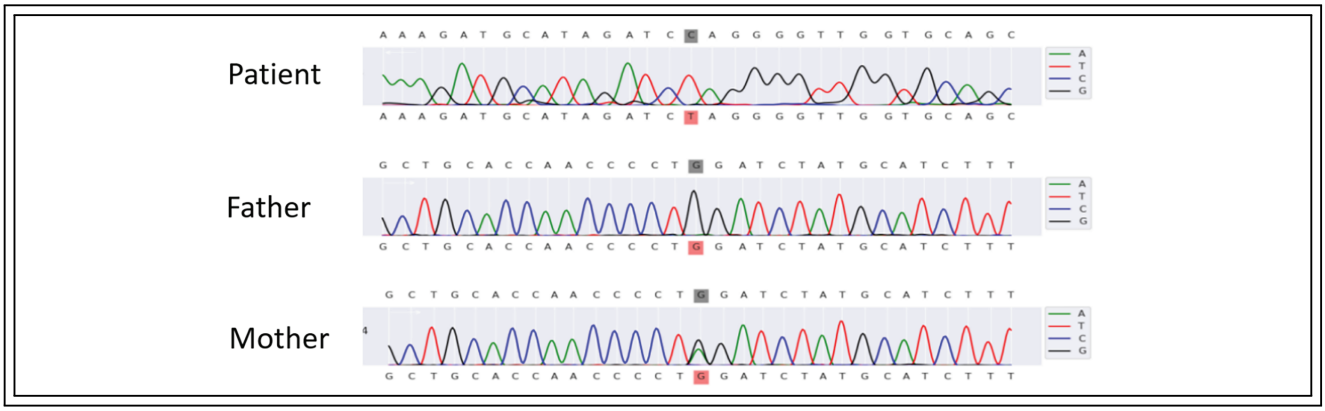

FIGURE 2. Result of arginine vasopressin receptor 2 (AVPR2) sequencing. The sequence chromatogram of AVPR2 in the patient and his parents

address the underlying etiology. Treatment strategies must be tailored to individual patient profiles, taking into account factors such as genotype, age, severity of symptoms, and the presence of comorbidities.[9] Current standardized treatment protocols encompass fluid replacement therapy, the adoption of a low-sodium and low-protein diet to minimize fluid shifts, and the use of combination pharmacotherapy.[10] However, despite adherence to the standard treatment protocols recommended by clinical guidelines, the majority of patients continue to exhibit urine output exceeding normal thresholds.[11]

In this case, the child showed significant improvement in urine output and fluid intake after standardized pharmacological treatment compared to the pre-treatment period, though the urine volume remained above normal levels. Ultrasound examination of the urinary tract (with the bladder non-distended) revealed that bilateral hydronephrosis had not improved. Video urodynamic studies indicated decreased bladder sensation, reduced bladder compliance, and weakened detrusor contraction. Therefore, the core pathological mechanism of hydronephrosis in this child can be explained as follows: long-term chronic bladder overdistension has led to a transient structural remodeling of the bladder wall. Initially, this presents as compensatory hypertrophy of the detrusor muscle. Over time, persistent overstretching results in degeneration of muscle cells and interstitial fibrosis, causing the bladder to enter a decompensated state characterized by low compliance and diminished contractility. During this stage, pathological elevation of intravesical pressure during the storage phase, combined with significant residual urine due to weak contraction, collectively leads to sustained high bladder pressure. This ultimately induces and maintains the hydronephrosis.

Therefore, considering the patient's condition, we adjusted the subsequent treatment plan. While maintaining the original pharmacotherapy, we instructed the child to implement a combined regimen of voluntary voiding and at-home CIC. After one month of CIC, a follow-up urinary tract ultrasound revealed a significant improvement in bilateral hydronephrosis compared to the pre-catheterization status (Figure 3). As an adjunctive therapy, CIC played a crucial role in markedly ameliorating the patient's bilateral hydronephrosis in this case. The necessity of personalized treatment is further validated here, particularly when the improvement in hydronephrosis with pharmacotherapy alone is suboptimal, highlighting the significant value of CIC. However, this

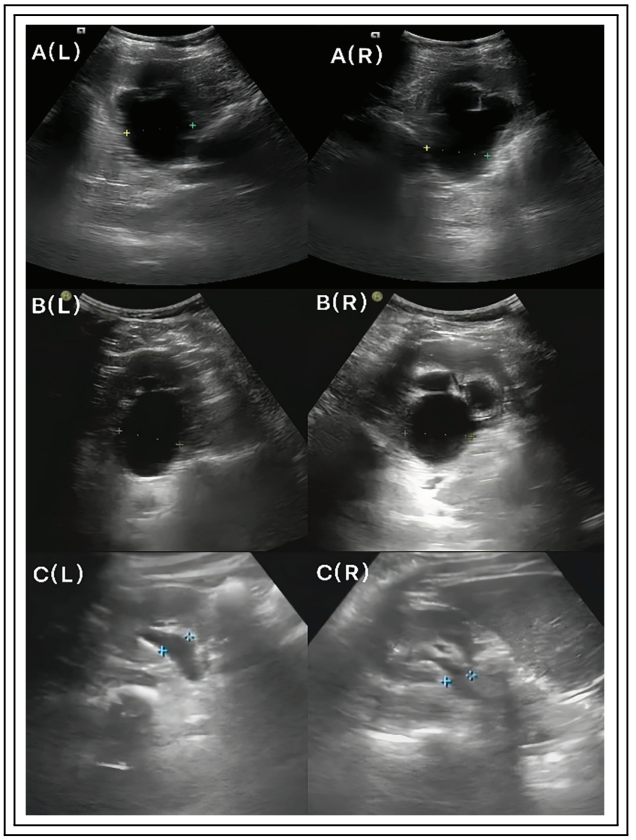

FIGURE 3. The B-ultrasound images of the kidney. (**A**) The kidney when the patient did not receive treatment in our department. The anterior-posterior diameter of the left kidney was 39 mm, and the anterior-posterior diameter of the right kidney was 37 mm. (**B**) The kidney after drug treatment. The anterior-posterior diameter of the left kidney is 31 mm and the anterior-posterior diameter of the right kidney is 33 mm. (**C**) The kidney after clean intermittent catheterization (CIC). The anterior-to-posterior diameter of the left kidney is 13 mm, and the anterior-to-posterior diameter of the right kidney is 11 mm. Abbreviations: L, Left; R, Right

report has several inherent limitations. First, as a single-case study, the generalizability of its findings is limited, particularly for CNDI patients with different genotypes, ages, or comorbidities. Second, the retrospective nature of data collection, which relied partly on family recall for fluid intake and output records (Figure 1), may introduce recall bias. Furthermore, the assessment of post-void residual urine was based on visual estimation from fluoroscopic images during urodynamic evaluation rather than standardized ultrasonographic measurement (Table 1), which may affect the accuracy of this parameter. Future

large-sample, prospective, and standardized follow-up studies are warranted to further validate the efficacy of CIC in CNDI patients complicated with hydronephrosis and to clarify its indications and optimal treatment duration.

In summary, the management of CNDI is expected to remain centered on individualized and precision medicine in the near term. Building upon current research advancements, future developments in pharmacological chaperone therapy and gene-based interventions hold significant promise for providing more effective and targeted treatment options for patients with this condition.[12]

Conclusions

This case demonstrates that in pediatric patients with congenital nephrogenic diabetes insipidus who continue to exhibit polyuria, low bladder compliance, and elevated post-void residual urine volume despite pharmacological treatment, short-term CIC can break the vicious cycle of "bladder overdistention → high-pressure state → hydronephrosis." Although bladder wall remodeling may gradually improve over time, potentially allowing for reduction or even discontinuation of CIC in the future, this intervention remains indispensable at the current stage.

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Author Contributions

Jianlin Xie: manuscript writing and data analysis. Jingde Wu: data collection and data analysis. Qingwei Zhang: data analysis. Yuanqi Guo: literature search and reference collection. Xiande Huang: supervision and guidance. All authors reviewed and approved the final version of the manuscript.

Availability of Data and Materials

All data supporting the conclusions of this article are included within the article and its supplementary material. Additional information can be obtained by reasonable request to the corresponding author.

Ethics Approval

Ethical approval for this study was obtained from the Ethics Committee of Gansu Provincial Hospital (Approval No. 2025-802). This study obtained dual written informed consent from both the minor patient and his/her legal guardian. The patient consented to participate in the study, and the guardian consented to the publication of any potentially identifiable information or images.

Conflicts of Interest

The authors declare no conflicts of interest.

Supplementary Materials

The supplementary material is available online at https://www.techscience.com/doi/10.32604/cju.2026.075856/s1.

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