

[Case Report]

## Utility of Positional Instillation of Contrast Cystography for Diagnosing Occult Vesicoureteral Reflux in Children: A Report of Two Cases

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**Abstract :** Positional instillation of contrast (PIC) cystography is effective for detecting occult vesicoureteral reflux (VUR), which can not be revealed by standard voiding cystourethrography (VCUG). We experienced two cases of young female patients; one had repeated urinary tract infection with a negative VUR on standard VCUG, and the other had findings suggestive of reflux hydronephrosis and intolerance of standard VCUG. They underwent PIC cystography, and occult VUR was detected in both cases. Both were successfully treated with simultaneous endoscopic injection therapy with dextranomer/hyaluronic acid. PIC cystography is useful for detecting occult VUR in children with negative VUR findings on standard VCUG or who are unable to tolerate standard VCUG.

**Keywords :** PIC cystography, VUR, VCUG, UTI, Children.

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### Introduction

Voiding cystourethrography (VCUG) is usually used to evaluate vesicoureteral reflux (VUR) in children with recurrent febrile urinary tract infection (UTI). Standard VCUG can usually be completed on an outpatient basis without general anesthesia, and it provides information on the vesical function and the urethral anatomy. VUR can be more easily detected during urinary voiding, and VUR is reportedly observed in 29–50% of children with febrile UTI in standard VCUG [1]. Rubenstein *et al* first introduced positional instillation of contrast (PIC) cystography in 2003 as a new approach to detecting “occult VUR” in patients with recurrent urinary tract infections (UTIs) after negative findings on standard VCUG [2]. PIC

cystography is performed in pediatric patients by cystoscopy under general anesthesia for the patients’ safety. It is not a common examination because it is an invasive procedure requiring general anesthesia and cystoscopy, and only a few reports in English have been reported from Japan [3]. In addition to the detection of occult VUR, PIC cystourethrography has the advantage of allowing the performance of simultaneous injection therapy in patients with occult VUR by the same anesthesia [3]. PIC cystography has disadvantages, however, such as the inability to evaluate bladder voiding function and urethral anatomy, in addition to requiring general anesthesia and expertise in pediatric cystoscopy.

We herein report two cases in which PIC cystography was effective for the diagnosis and treatment of

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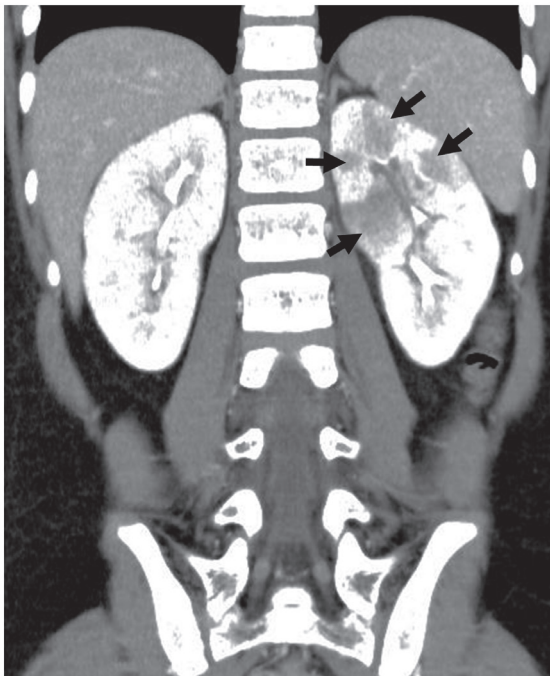
occult VUR.

## Case report

### Case 1

A case of PIC cystography was performed for suspected occult VUR due to repeated urinary tract infections within a short period. An eight-year-old girl (height 136.0 cm, weight 40.1 kg) visited our hospital due to a fever and headache. She had no history of urinary tract infection, but she was constipated. A blood test showed that her white blood cell (WBC) count was 11,400/ $\mu$ l, and her C-reactive protein (CRP) level was 28.7 mg/dl. Urinary culture showed *Escherichia coli* as the causative organism. Contrast-enhanced computed tomography (CT) showed multiple low attenuation areas in the upper pole of the left kidney, suggesting acute focal bacterial nephritis (AFBN) (Figure 1). Antibacterial drug therapy was performed with CTX and CEZ for three weeks, and her symptoms improved. She was subsequently discharged from the hospital.

The patient had a fever and pyuria appeared again at home on the 11th day after discharge from the hospital.



**Figure 1.** Coronal section of abdominal computed tomography reveals acute focal glomerulonephritis with multiple low attenuation areas in the left kidney (black arrow) in case 1.

A blood test showed that her WBC count was 19,600/ $\mu$ l, and her CRP level was 9.47 mg/dl. A urinary culture showed ESBL-producing *Klebsiella pneumoniae* as the causative organism in the second infection. Contrast-enhanced CT showed an area of low absorption at the same site as in the previous CT, suggesting recurrent UTI with AFBN. Antibacterial treatment with CMZ was again performed for 3 weeks, and her symptoms improved. She underwent standard VCUG during hospitalization with the insertion of a 5-Fr urethral catheter. It failed to detect the VUR, although the patient demonstrated a normal voiding function (Figure 2A), so occult VUR was suspected as the cause of the recurrence of febrile UTI within the short period. PIC cystography was then performed under general anesthesia, revealing the occult VUR (International Reflux Grade III) on the affected left side (Figure 2B). Subsequently, simultaneous endoscopic injection therapy was performed to prevent the VUR, and 0.5 ml of Dextranomer/hyaluronic acid (Dx/HA; Deflux<sup>®</sup>) was injected into the submucosa at the 6 o'clock position in the left ureteric orifice.

The total general anesthesia time was 80 minutes, including 34 minutes of operative time, and there were no complications during any of the operative procedures. Postoperatively, antibiotics were administered orally for three days to prevent a urinary tract infection. After endoscopic injection therapy, the patient showed an uneventful postoperative course without recurrence of UTIs or a decline in the renal function during twelve months after PIC cystography.

### Case 2

A case of PIC cystography was performed because VCUG could not be performed due to the patient's non-cooperative behavior. A 4-year-old girl (height 98.3 cm, weight 15.5 kg) was referred to our hospital under suspicion of left VUR due to a worsening grade of left hydronephrosis. Her hydronephrosis had first been found at the infant health examination, and she had been continuously followed up every year by a local pediatrician who suspected the development of reflux hydronephrosis. Her parents wished for her to undergo VCUG to exclude VUR, but the implementation of VCUG failed, because of her fear and non-cooperative behavior during the insertion of a 5-Fr urinary catheter.

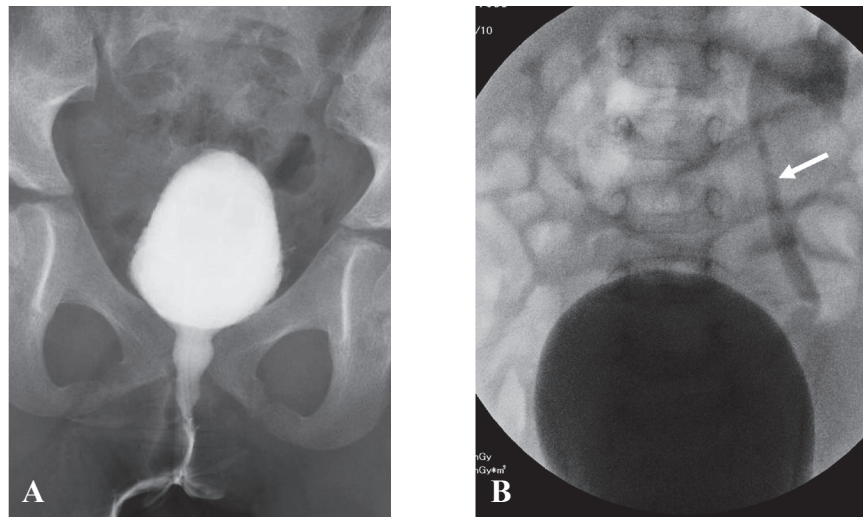
ter. PIC cystography was therefore performed under general anesthesia in the same way as in Case 1, and bilateral VUR (both International Reflux Grade II) was identified (Figure 3A, B). Simultaneous endoscopic injection therapy was performed to prevent VUR on both sides. Deflux was injected into the submucosa at the 6 o'clock position in the urethral orifice (0.4 ml on the right side and 0.3 ml on the left side).

The total general anesthesia time was 74 minutes, including 37 minutes of operative time, and there were no complications during the PIC cystography. Postop-

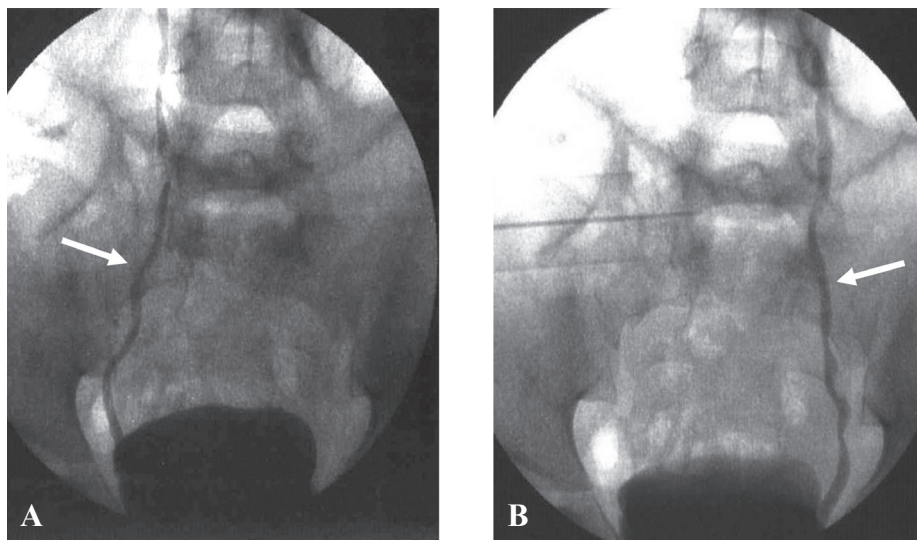
eratively, antibiotics were administered orally for three days to prevent urinary tract infection. Subsequently, no urinary tract infection occurred, and renal ultrasonography showed improvement of the left hydronephrosis one year after the PIC cystography (Figure 3A, B).

#### Standard VCUG

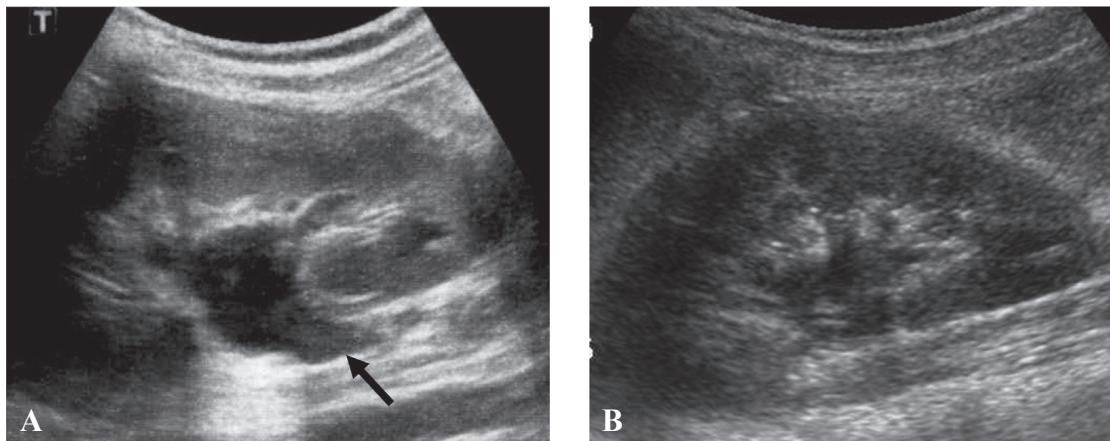
Standard VCUG was performed according to the protocol described by Johnin *et al* [4]. After the insertion of a 5-Fr non-balloon urethral catheter, we



**Figure 2.** Standard voiding cystourethrography showed negative findings for VUR with a normal voiding function (A), although PIC cystography showed positive findings for the VUR (white arrow) on the left side (B) in case 1.



**Figure 3.** PIC cystography showed positive findings for bilateral VUR (white arrows) on both the right (A) and left side (B) in case 2.



**Figure 4.** Ultrasonography showed left hydronephrosis extending into the extra-pelvic area (black arrow) (A), and the improvement of hydronephrosis was shown one year after PIC cystography (B) in case 2.

performed VCUG via the gradual injection of the estimated cystic volume of contrast medium (30% urographin®,  $25 \times [\text{age}+2]$  ml) in the supine position, using a drip infusion technique from a height of 80 cm. Images were then obtained of the antero-posterior and lateral views during urinary voiding. In both cases, 3–5 ml of Lidocaine jelly was used as a local anesthesia during urethral catheter insertion.

#### *PIC cystography*

PIC cystography was performed according to the modified protocol described by Rubenstein *et al* [2]. An 8 Fr. cystoscope was inserted into the bladder under general anesthesia, and the outflow portion of the scope was placed to face the ureteral orifice. A contrast medium (30% urographin®) was then dripped from a height of 80 cm under fluoroscopy. In both cases, the contrast agent was sprayed directly from the outflow portion of the rigid cystoscope at a site 0.5–1 cm from the ureteral opening. No direct injection was performed by inserting the cystoscope tip into the ureter. About 40 ml of 30% urographin® was used in both cases during PIC cystography. Images were obtained in antero-posterior views.

#### *Endoscopic injection therapy*

Dextranomer/hyaluronic acid (Dx/HA; Deflux®) was injected under a cystoscopic view using a long needle inserted through the operating channel of the cystoscope and advanced into the submucosa at the 6 o'clock position of the ureteric orifice. Deflux® was

then injected until the formation of mucosal protrusion was noted.

### **Discussion**

Patients with recurrent febrile UTI are more likely to have VUR than a single onset of febrile UTI, and they are therefore indicated for VCUG [5, 6]. Standard VCUG is widely performed as an excellent test that can be completed on an outpatient basis, and it provides information on the bladder and urethral anatomy. It is also possible to examine the bladder function during voiding. However, VCUG cannot be performed in cases where urethral catheter insertion is difficult. It has also been reported that the detection rate of VUR by VCUG is 29–50% in UTI patients [1]. When VUR can not be detected by standard VCUG or when catheter insertion is too difficult to perform, a renal radioimmunoassay or voiding ultrasound is sometimes used to detect VUR. PIC cystography was first introduced by Rubenstein *et al* [2] as a novel technique for detecting occult VUR that evaded detection by standard VCUG despite repeated UTI, noting that the sensitivity, specificity and accuracy of PIC cystography for the detection of the VUR were 100%, 87% and 91%, respectively; the sensitivity was higher than with standard VCUG. Edmondson *et al* reported that PIC cystography demonstrated occult VUR in 32 of 39 (82%) patients who had recurrent UTIs with negative findings on standard VCUG [6]. Palmar *et al* suggested that PIC cystography was effective in detect-



ing new contralateral VUR in cases of preoperatively unilateral VUR [7]. Rubenstein *et al* suggested that VUR is caused by insufficient valve mechanism at the ureterovesical junction, related to short submucosal ureteral length, weak detrusor support or periureteral diverticulum, and PIC cystography is thought to be more sensitive to insufficient valve mechanism than standard VCUG, as cystoscopy directly faces the ureteral orifice [2]. Most authors recommend the simultaneous endoscopic injection therapy with Deflux® for newly detected VUR during PIC cystography [7–9]. Hagerty *et al* reported that the incidence of febrile UTI was significantly decreased after endoscopic injection therapy of Dx/HA in pediatric patients with occult VUR [8]. PIC cystography is not yet commonly performed worldwide, probably because it is an invasive procedure requiring general anesthesia and expertise in pediatric cystoscopy. Another disadvantage of PIC cystography is the inability to evaluate the voiding function of the bladder.

The major advantages of PIC cystography are the detection of occult VUR that cannot be detected by standard VCUG and the performance of simultaneous injection therapy to prevent VUR under the same anesthesia. In addition to its utility for detecting occult VUR, we used PIC cystography to examine the VUR in Case 2, who was suspected to have reflux hydronephrosis, but the patient showed serious non-cooperative behaviors and was therefore unable to tolerate standard VCUG. We then performed PIC cystography and obtained PIC-VUR, after which simultaneous endoscopic injection therapy was performed for VUR, resulting in an improvement of the reflux hydronephrosis.

### Conclusions

Although PIC cystography is associated with some disadvantages, such as the need to perform cystoscopy under general anesthesia in pediatric patients, it may be useful for detecting occult VUR in children with recurrent UTIs and negative VUR findings on standard VCUG or in patients who are unable to tolerate standard VCUG due to behavioral or mental issues.

### Ethical Approval

Informed consent to publish this paper was obtained from the patients and their parents.

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### Conflicts of Interest

The authors declare no conflicts of interest in association with the present study.

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