Is Ureter Visualization Possible on Tc-99m DMSA Scintigraphy with Vesicoureteral Reflux Patients?

Vezikoüreteral Reflü'lü hastalarda Tc-99m DMSA Sintigrafisinde Üreter Vizüalizasyonu Mümkünmü?

Hasan Ikbal Atilgan[1], Murat Sadic[2], Meliha Korkmaz[2], Sinem Ozyurt[3], Gökhan Koca[2]
[1]Ministry of Health Kahramanmaras Necip Fazıl City Hospital, Division of Nuclear Medicine, Kahramanmaras,
[2]Ministry of Health Ankara Training and Research Hospital, Department of Nuclear Medicine, Ankara,
[3]Ministry of Health Sami Ulus Children Hospital, Division of Nuclear Mecicine, Ankara, Turkey

Özet

Amaç: 99mTechnetium- dimercaptosuccinic acid (99mTc-DMSA) normalde renal korteks tarafından akümüle olan bir radyoaktif madde olup üreter veya pelvikaliseal sistemde vizüalize olmamaktadır. Bu çalışmada 99mTc-DMSA Sintigrafisinde üreterleri vizüalize olan vakalar derlenmiştir. Gereç ve Yöntem: Çalışmaya ortalama yaşları 3.5 (min 2 ay-max 18 yaş) olan 18 hasta (5 kız, 13 erkek) dahil edildi. 99mTc-DMSA Sintigrafisinde18 hastanın 20 üreter ve/veya pelvisi görünür durumdaydı. İki hasta her iki üreterler vizüalize olmaktaydı. Tüm hastaların Vezikoüreteral Reflü (VUR) dereceleri, 99mTc-DMSA uptake'leri, Pelvikaliseal sistem durumları, Üre ve kreatinin seviyeleri ele alındı. Bulgular: Vizüalize olan üreterlerin 3 tanesinde pelvikaliektazi olması nedeniyle bu hastalar çalışmadan çıkarıldı. Geri kalan 17 üreterli hastanın değerlendirilmesinde 3 hastada konjenital megaüreter mevcuttu. 3 hastada Grade 3 VUR, 3 hastada Grade 4 VUR vardı. Grade 5 VUR ise 7 hastada (8 üreter) var idi ve bu hastaların bir tanesinde bilateral vizüalize üreter mevcuttu. Tartışma: Konjenital megaüreterli ve VUR olan hastalarda 99mTc-DMSA Sintigrafisinde üreterler vizüalize olabilmektedir. Bu hastalarda ileri görüntüleme modaliteleri önerilmektedir.

Anahtar Kelimeler

Vezikoüreteral Reflü (VUR); Megaüreter; 99mTechnetium-Dimercaptosuccinic Acid (99mTc-DMSA)

Abstract

Aim: Ureter or pelvicalyceal system is not be vizualized with 99mTechnetium- dimercaptosuccinic acid (99mTc-DMSA) which is accumulated by renal cortex normally. In this study the cases whose ureters are visible were reviewed with 99mTc-DMSA scintigraphy. Material and Method: 18 patients (5 females, 13 males) with median age 3.5 years (min 2 months-max 18 years) were included in this study. Twenty ureters and/or pelvis of 18 patients were visible in 99mTc-DMSA scintigraphy. In two patients's both ureters were visible. Vesicoureteral reflux (VUR) grade, 99mTc-DMSA uptake, renal size, status of pelvicalyceal system, urea, creatinine levels were evaluated in all patients. Results: Three of the visible ureters were actually due to pelvicaliectasis. These pelvicaliectasic patients were excluded from the study. In the evaluation of the remaining 17 ureters of patients, congenital megaureter was present in three patients. Grade 3 VUR was detected in three patients, grade 4 was in three patients. VUR is seen as grade five in eight kidneys of seven patients because one of these patients has bilateral vizualized ureter. Discussion: In patients with congenital megaureter and VUR, ureters can be visible with 99mTc-DMSA scintigraphy and further imaging modalities are recommended for these patients.

Keywords

Vesicoureteral Reflux (VUR); Megaureter; 99mTechnetium-Dimercaptosuccinic Acid (99mTc-DMSA)

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Corresponding Author: Murat Sadic, Department of Nuclear Medicine, Ministry of Health Ankara Training and Research Hospital, Ankara, Turkey.
T.: +90 3125953608 F.: +90 3125953856 E-Mail: mdmuratsadic@gmail.com

Introduction

Vesicoureteral reflux (VUR) which is the reverse flow of the urine from bladder to the ureter or renal pelvis causes urinary system infections and renal scars in children [1]. It is usually mild or moderate and heals spontaneously, but in very rare cases it persists and causes pyelonephritis, renal scars and even renal failure [2]. Voiding cystourethrography (VCUG), radionuclide cystography and voiding urosonography are used for the diagnosis of VUR [3]. VCUG is the most commonly used method for the diagnosis [4]. 99mTechnetium-dimercaptosuccinic acid (99mTc-DMSA) is used in the diagnosis and follow up of pyelonephritis in VUR patients. Size, number, morphology, anatomic localization and functional capacity of the kidneys can be determined with 99mTc-DMSA scintigraphy [5]. 99mTc-DMSA scintigraphy is the most sensitive method with high specificity for the detection of renal paranchymal hypoactive/defective regions [6]. Diffusely decreased uptake of 99mTc-DMSA or hypoactive regions are seen in the presence of pyelonephritis. 99mTc-DMSA is filtered in the glomeruli and then reabsorbed by proximal renal tubular epithelial cells via megalin- and cubilin-mediated endocytosis [7]. In normal urological system, 99mTc-DMSA is only accumulated by renal cortex and ureter or pelvicalyceal system can not be vizualized with this agent.

Dilatation of collecting system is seen due to VUR, obstruction and urinary tract infections (UTI). Acute UTI may cause dilatation of the ureter beside the pelvicalyceal system. Increase in ureteral dilatation is correlated to grade of VUR [8]. Congenital wide ureters can also be observed and named as megaureter. Megaureter was first described by Caulk in a patient with wide ureter and normal pelvicalyceal system [9]. In case of ureter dilatation due to VUR and megaureter, ureter can be visualized by 99mTc-DMSA scintigraphy and up to date, only one case was presented with visibly dilated ureter [10]. In this study the cases of 99mTc-DMSA scintigraphy in which the ureters are visible were evaluated.

Material and Method

3251 patients were referred to our nuclear medicine clinic for the evaluation of renal parenchymal scars and split function between July 2007 and April 2013. VUR history was present in 894 (27%) of 3251 patients. Twenty ureters and/or pelvis of 18 patients were visible with 99mTc-DMSA scintigraphy. These 18 patients (5 females and 13 males) ranging in age from 2 months to 18 years (median age: 3.5) were included in this study. Patients were evaluated according to age, gender, urea and creatinine levels, kidney size, pelvic dilatation, 99mTc-DMSA uptake ratios and hypoactive/defective regions.

After written informed consents were obtained from their parents, 99mTc-DMSA scintigraphies were taken. Dosage of 99mTc-DMSA was arranged in relation to the weights of patients and was injected intravenously between 800 µCi and 5 mCi (27.2-170 MBq). The images were taken 3-4 hours after the injection of the radiopharmaceutical with low energy high resolution parallel hole gamma camera (General Electric GE, Millenium MG, USA) in 140 keV±%20 peaks. Anterior, posterior and posterior oblique static images were obtained. Relative uptakes of the kidneys were calculated quantitatively and hypoactive/defective regions were recorded. A kidney uptake of 45–55 % of the total renal activity was considered as normal (symmetrical renal split function). VUR grades were noted according to their previous VCUG. Size of the kidneys and diameter of the pelvis were calculated by ultrasonography (USG) [Table 1].

Table 1. Ultrasonographic findings of the patients

Patient no	Age	Visible side	Renal size (Visible side)	Renal size (Nonvisible side)	Pelvicalyceal system (Visible side)	Pelvicalyceal system (Nonvisible side)
1	11 months	Left distal ureter	Decreased	Increased	Normal	Normal
2	10	Left whole ureter	Normal	Normal	Normal	Normal
3	6	Right whole ureter	Decreased	Normal	Increased	Normal
4	1	Left whole ureter	Normal	Normal	Normal	Normal
5	2	Right 1/2 distal ureter	Decreased	Normal	Increased	Normal
6	10 months	Right whole ureter	Normal	Normal	Normal	Normal
7	3	Left whole ureter	Increased	Agenetic	Increased	Agenetic
8	9	Bilateral whole ureter	Bılateral Increased		Increased	Increased
9	18	Left whole ureter	Normal	Normal	Increased	Increased
10	5	Left whole ureter	Increased	Normal	Normal	Increased
11	4	Right distal ureter	Increased	Decreased	Normal	Normal
12	7	Left whole ureter	Decreased	Normal	Increased	Normal
13	13	Right whole ureter	Normal	Decreased	Normal	Normal
14	2 months	Right whole ureter	Normal	Agenetic	Normal	Agenetic
15	2	Bilateral whole ureter	Right decreased, left increased	-	Increased	Increased

Results

Twenty ureters and/or pelvis of 18 patients were visible in 99mTc-DMSA scintigraphy. In two patients both ureters were visible. Proximal part of the three ureters of three patients were visible with 99mTc-DMSA scintigraphy, yet it was realized that these were due to the dilatation of renal pelvis resembling the ureter with 99mTechnetium mercaptoacetyltriglycine (99mTc MAG3) and/or USG imaging. These three patients were excluded from the study. Remaining 17 ureters had congenital megaureter or VUR. Three of the ureters were dilated and visualized due to congenital megaureter [Figure 1] and the remaining 14

ureters were due to VUR [Figure 2, 3].

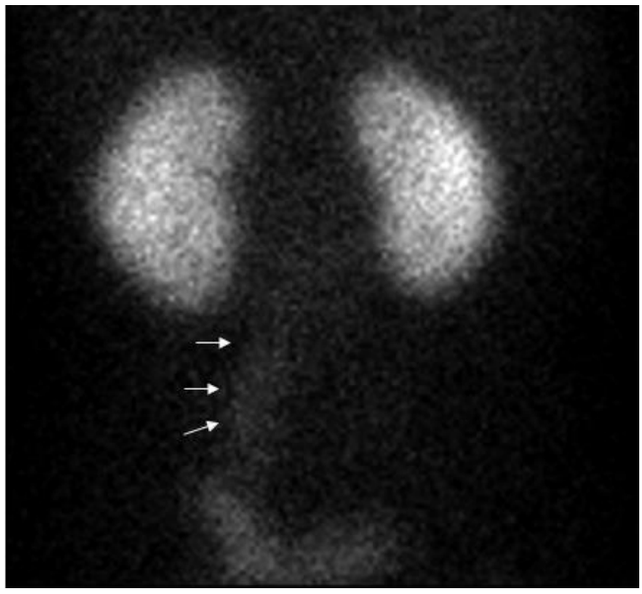

Figure 1. Posterior 99mTc-DMSA image. One year old boy, left ureter is visible.

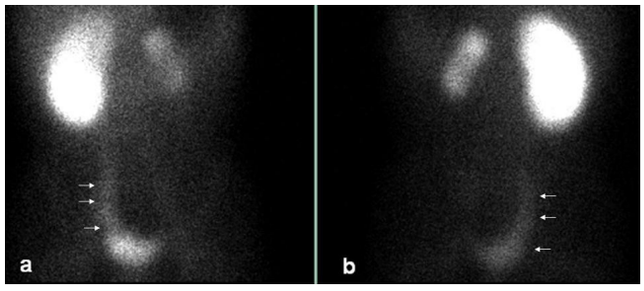

Figure 2. Anterior (a) and posterior (b) 99mTc-DMSA image. Four years old boy, right ureter is visible. Contralateral kidney is small, has hypoactive region and low grade 99mTc-DMSA uptake.

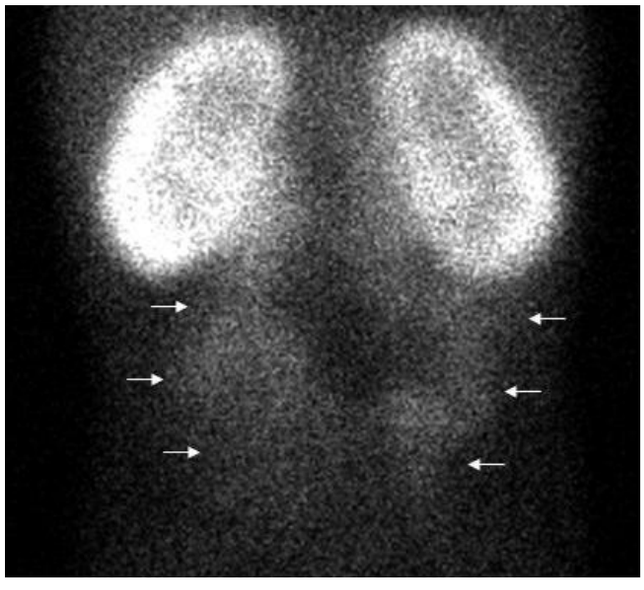

Figure 3. Anterior 99mTc-DMSA image. Nine years old boy, bilateral ureter is visible. The patient has also pelvicaliectasis and neurogenic bladder.

Four ureters of two patients, six right ureters and seven left ureters were visible. In two patients both ureters were visible [Figure3], the distal parts of the two and whole part of the four right ureters, the distal part of the one and whole part of the six left ureters were visible with 99mTc-DMSA imaging. [Table 2]. VUR is seen in grade three in three kidneys, grade four in three kidneys, grade five in eight kidneys with seven patients. Three patients had megaureter and VUR wasn't observed [Figure 4].

Six of the patients had elevated urea and creatinine levels. These six patients all were in the wholly visible ureter group on right or left.

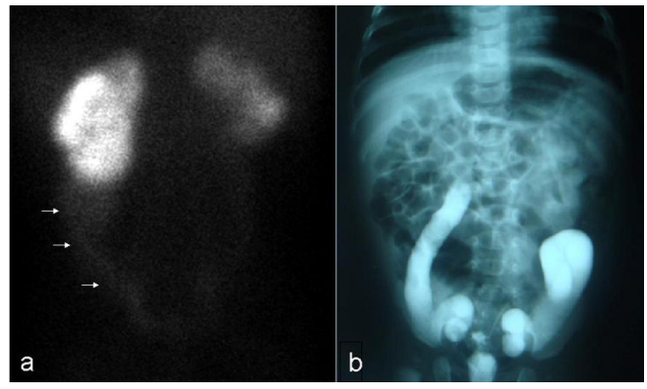

Figure 4. Posterior 99mTc-DMSA image and(A), VCUG(B). Two years old boy, bilateral ureter is visible. In VCUG, grade 5 VUR in left kidney and grade 4 in right kidney.

Two patients had solitary kidney due to renal agenesis. Both had grade 5 VUR in their solitary kidney [Figure 5].

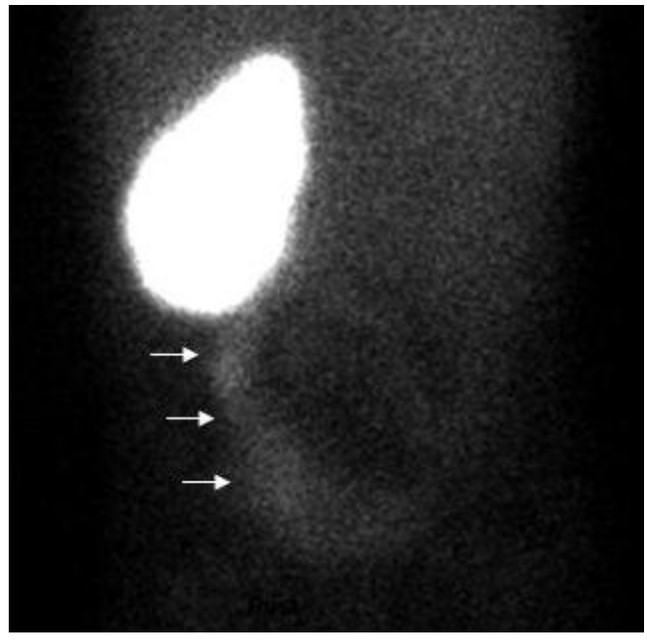

Figure 5. Posterior 99mTc-DMSA image. Three years old boy, left ureter is visible and right kidney is agenetic.

Six of the kidney sizes were large, six were in normal size and five were small. Eight of the pelvicalyceal system on visible side were in normal size, five of the pelvicalyceal system were dilated. Additionally, pelvicalyceal systems of the patients who have bilateral visualized ureter were dilated in both kidneys.

Eight kidneys had hypoactive/defective regions and/or low grade 99mTc-DMSA uptake, five kidneys had normal cortical functions. Additionally, cortical functions were normal beside dilated pelvicalyceal system in the bilateral visualized ureter patient, but the other patient who has bilateral visualized ureter had bilateral hypoactive/defective regions and right kidney has

Table 2. Demographic, biochemical and VCUG findings of the patients

Patient no	Age	Gender	Urea Level (mg/dL)	Creatinine level (mg/dL)	Visible side	VUR grade
1	11 months	Boy	25	0,5	Left distal ureter	3
2	10	Girl	42	1,42	Left whole ureter	3
3	6	Girl	34	1,35	Right whole ureter	3
4	1	Boy	27	0,6	Left whole ureter	Megaureter
5	2	Boy	30	0,62	Right 1/2 distal ureter	4
6	10 months	Girl	7	0,4	Right whole ureter	4
7	3	Boy	33	0,74	Left whole ureter	Megaureter
8	9	Boy	27	0,9	Bilateral whole ureter	Bilateral 5
9	18	Girl	69	1,32	Left whole ureter	5
10	5	Boy	24	0,77	Left whole ureter	Megaureter
11	4	Boy	26	0,81	Right distal ureter	5
12	7	Girl	42	1,41	Left whole ureter	5
13	13	Boy	32	1,28	Right whole ureter	5
14	2 months	Boy	18	0,59	Right whole ureter	5
15	2	Boy	40	0,67	Bilateral whole ureter	Left VUR 5, Right VUR 4

Table 3. Side and part of the visible ureter with the 99mTc-DMSA, uptake ratios of the same side of the kidney are shown.

Patient no	Visible side	DMSA uptake of kidney (%) (Side of visible ureter)	DMSA uptake of kidney (%) (Side of nonvisible ureter)
1	Left distal ureter	18	82
2	Left whole ureter	52	48
3	Right whole ureter	3	97
4	Left whole ureter	50	50
5	Right 1/2 distal ureter	11	89
6	Right whole ureter	31	69
7	Left whole ureter	100	0
8	Bilateral whole ureter	Left 53, Right 47	
9	Left whole ureter	57	43
10	Left whole ureter	92	8
11	Right distal ureter	90	10
12	Left whole ureter	20	80
13	Right whole ureter	76	24
14	Right whole ureter	100	0
15	Bilateral whole ureter	Left 85, Right 15	

low grade 99mTc-DMSA uptake [Table 3].

Discussion

VUR is graded into five grades (grade 1-5) according to the severity the dilation and tortuosity of ureter and pelvicalyceal system in case reflux reaches the kidney [11]. VUR is the most common cause of antenatal hydronephrosis for 40% of intrauterin cases [12]. 30% of the children with attack of acute pyelonephritis had also VUR [13]. In our study, VUR is seen in grade five in eight kidneys with seven patients, grade four in three kidneys, grade three in three kidneys. VUR influences the diameter of the ureter, but ureters may be widened without VUR in case of UTI. Bacterial infection may cause smooth muscle dysfunction in ureteral wall and so UTI may cause dilatation of the ureter [8]. In long standing ureters widen excessively and tortuoused in high grade VUR cases. By USG examination, findings of pelvic and/or calyceal dilatation, ureteral dilatation, pelvic and/or ureteral wall thickening are to be considered as warning for VUR. Normal appearing urinary tract normally does not usually coexist with VUR [12]. VUR may effect the growth of kidneys. In unscarred kidneys as well as most of the kidneys with moderate scarring, normal growth is expected. Growth is impaired in case of severe scarring with little functioning parenchyma and dilate ureters. In unilateral VUR cases, the abnormal kidney growth is impaired and the opposite normal kidney may get larger to compansate the excretion function [14]. First studies about VUR were based on intravenous urography. Later on, these were replaced with 99mTc-DMSA scintigraphy due to its high sensitivity for the detection on renal defects [15]. In our study, eight patients had abnormal 99mTc-DMSA imaging with hypoactive/defective regions and/or low grade activity accumulation. And also, one of the patient in bilateral visualized group had bilateral hypoactive/defective regions and his right kidney has low grade 99mTc-DMSA uptake.

Congenital dysplastic kidneys may be seen with dilated and tortuous ureter in case of high grade VUR [16]. VUR related congenital dysplasia is seen as dilated ureter and pelvicalyceal system with abnormally thin parenchyma and loss of corticomedullary differentiation in USG examination. 99mTc-DMSA imaging varies in these cases, as asymmetrical uptake of activity with small kidney around dilated pelvicalyceal system may be seen in severe cases [17]. In antenatal diagnosed dysplastic kidney, two normal neonate renal USG can exclude significant abnormalities and so VCUG is not needed in the evaluation of VUR [18]. VCUG is indicated for the first examination of VUR in boys, inadequate visualization of the bladder of kidney and specific request for for urethral or bladder imaging [19]. When renal developmental abnormalities are recognized prenatally, VCUG is indicated 4-6 weeks after birth [20].

99mTc-DMSA scintigraphy is used for the diagnosis and follow up of pyelonephritis with detecting the renal cortical defective/hypoactive regions and calculate the differential renal functions. 90% of 99mTc-DMSA is bound to plasma proteins and 0%-5% to red blood cells. 40-50% of injected activity is taken by the kidney within 3-4 hours of injection and 6%-9% of the dose is present in the blood at 14 hours after injection [21]. In normal conditions, 99mTc-DMSA is concentrated only by the cortex and pelvicalyceal system and ureters are invisible.

Megaureter is the presence of enlarged ureter with or without dilatation of the upper collecting system and is possibly caused by congenital (primary) or abnormalities of bladder or urethra [22]. Diameter of normal ureter is almost always smaller than 5 mm [8]. Zelenko et al. defined the normal ureter diameter in ureterolithiasis patients by comparing the symptomatic and asymptomatic kidneys with unenhanced helical computed tomography. They described that in 96% of patients; normal ureter diameter was less than 3 mm with 6.6% of the patients' ureter less than 3 mm and mentioned that 3 mm should be considered

as upper limit of normal size for nonobstructed ureters [23]. If megaureter is not due to VUR, diuresis renography is indicated [24]. In our cases, three of the patients had megaureter and don't have VUR. In three cases, the proximal part of the ureter seemed widened, but in their USG and/or 99mTc MAG3 images, extremely dilated pelvicalyceal system were observed. Two of 15 patients had only one kidney and their left kidney was agenetic. Pelvicalyceal system on the visible side was dilated in eight kidneys of six patients in USG and other patients' pelvicalyceal system was not dilated.

In conclusion, ureters may become visible with 99mTc-DMSA scintigraphy in patients with congenital megaureter and VUR, more even so in high grade VUR. Ureter visualization with 99mTc-DMSA scintigraphy should urge the clinician to perform further imaging methods like VCUG to define the grade and therapy of the patients even if 99mTc-DMSA scintigraphy is normal.

Disclosure

The authors stated that they had no interests which might be perceived as posing a conflict or bias.

Competing interests

The authors declare that they have no competing interests.

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