Smyrna Tıp Dergisi ***Araştırma Makalesi***

Comparison of Imaging Techniques in Detecting Renal Scars in Children with Recurrent Urinary Tract Infections
Tekrarlayan Idrar Yolu Enfeksiyonu Olan Çocuklarda Renal Skar Tespiti Icin Görüntüleme Yöntemlerinin Karşılaştırılması

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Summary

Objectives: Urinary tract infections (UTIs) are frequent and important cause of fever, bacteremia, sepsis and organ failure in children under 2 years of age. Severe infections that cause mortality and morbidity in recurrent urinary tract infections, risk factors, diagnosis and treatment for the prevention of acute and chronic renal insufficiency should be well known.

Materials and Methods: Between January 2005 and January 2010; 101 patients with recurrent urinary tract infection were evaluated retrospectively in our a pediatric nephrology clinic. Patients' data were obtained retrospectively from charts in the hospital archive. The age, gender, demographics, physical examination findings, laboratory results, and imaging studies were recorded.

Results: For 101 cases; 78.2% of them were female, 21.8% of them were male. In renal ultrasonography (USG) renal parenchymal damage was detected in 23.8% of the cases; vesicoureteral reflux (VUR) in voiding cystourethrography (VCUG) was detected in 38.6% and renal scars and activity loss in Tc-99m dimercaptosuccinic acid (DMSA) scintigraphy was detected in 70.3% of cases.

Conclusion: It has been determined that as the incidence and the degree of VUR increase, the frequency of renal scar increases. There was a positive correlation between VUR and renal scar. In addition, renal scintigraphy was the most sensitive imaging method in cases of recurrent urinary tract infections.

Key words: Recurrent urinary tract infection, renal scar, vesicoureteral reflux.

Özet

Amaç: İdrar yolu enfeksiyonu 2 yaş altı çocuklarda ateş, bakteriyemi, sepsis ve organ yetmezliğinin sık ve önemli bir nedenidir. Tekrarlayan idrar yolu enfeksiyonlarında mortalite ve morbiditeye neden olan ciddi enfeksiyonlar, akut ve kronik renal yetersizliğin önlenmesi için risk faktörleri, tanı ve tedavi iyi bilinmelidir.

Gereç ve Yöntem: Ocak 2005 – Ocak 2010 tarihleri arasında cocuk nefroloji polikliniğinde tekrarlayan idrar yolu enfeksiyonu tanısı ile izlenen 101 hasta retrospektif olarak değerlendirilmiştir. Bu hastaların tam idrar tetkiki, idrar kültürü, üriner sistem ultrasonografisi ,voiding sistoüreterogram ve Tc-99m DMSA sintigrafisi toplanmıştır.

Bulgular: 101 olgunun %78.2'si kız, %21.8'i erkek, %23.8 olguda üriner USG'de renal parankimal hasar, %38.6 olguda VCUG'de reflü, %70.3 olguda DMSA'da skar ve aktivite kaybı tespit edilmiştir.

Sonuç: VUR insidansı ve derecesi arttıkça renal skar sıklığının arttığı, VUR ile renal skar arasında pozitif korelasyon olduğu tespit edilmiştir. Ayrıca tekrarlayan idrar yolu enfeksiyonu olan vakalarda renal hasarı göstermede en duyarlı görüntüleme yönteminin renal sintigrafi olduğu saptanmıştır.

Anahtar Kelimeler: Tekrarlayan idrar yolu enfeksiyonu, renal skar, vesikoüreteral reflü

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Introduction

Urinary tract infections are the most common cause of bacterial infections, especially in children under 2 years of age (1). In addition to being seen 6 times more frequently in girls, acute pyelonephritis, renal parenchymal injury, recurrent urinary tract infections cause severe mortality and morbidity such as chronic renal insufficiency and hypertension in 10-64% of the cases (2).

The most common anomaly in urinary tract infections is vesicoureteral reflux with the ratio of 30-50%. In 30-40% of these cases renal scarring is developed (3,4). Therefore, it is very important and necessary to investigate VUR with voiding cystoureterogram in cases where urinary

tract infection is detected. Dimercaptosuccinic acid (DMSA) sintigraphy is the most sensitive imaging technique for renal parenchymal damage (5).

Urinary tract infections are still the most common cause of acute or chronic renal damage, despite improvement in diagnosis and treatment (6). The importance and necessity of imaging methods in early diagnosis was also emphasised.

Material and Methods

This study was carried out retrospectively on 101 cases with recurrent urinary tract infection diagnosed between January 2005 and 2010 in pediatric nephrology policlinic of an educational hospital and it was approved by its' ethic comittee.

The inclusion criteria for the study was urinary tract infections with clinical findings of urinary system such as at least two fires, vomiting, abdominal pain, dizziness, pollakiuria, costovertebral angle sensitivity and urinary tract infections with elevated acute phase reactors, detection of growth in urine culture examination, renal ultrasonography, voiding cystourethrography (VCUG) and Tc-99m dimercaptosuccinic acid (DMSA) scintigraphy. Exclusion criteria included renal units with renal agenesis, multicystic dysplastic kidney, urinary tract obstruction, urogenital malformation, and neurogenic bladder.

The age, gender, demographics, physical examination findings, laboratory results and imaging studies were recorded.

Suprapubic aspiration in neonatal period, midstream urinary catheterization and urinary catheterization in children up to 5 years, moderate urinary flow in children older than 5 years and catheterization methods in non-adaptable children were used in order to receive urine samples from patients in the clinic. In the mentioned clinic; it was performed routine cleaning of the skin with povidone iodine, followed by aspiration with 22G needle for suprapubic aspiration in neonates and young children. In older children; the way to give a medium-flow urine was described to them and a sterile coarse urine was provided. Some of the samples taken from the patients were sent to the laboratory for culture sowing and some were reserved for full urine analysis. Materials sent to the laboratory were cultured at 36-38 °C on a McKey agar medium and the reproduction was controlled every 24 hours. Pathogens were searched in the cases where reproduction was detected. The leukocyte esterase and nitrite tests were performed in the urine collected for complete urine screening. After centrifugation at 3,000 rpm for 3 minutes, the supernatant was poured onto the remaining 0.5 ml urine slide and the coverslips were closed and examined under a microscope.

Ultrasonography examinations were either performed using probes varying from 4 to 13 MHz, depending on the patient's size. Kidneys were routinely assessed for hydronephrosis, parenchymal echogenicity, parenchymal thickness, corticomedullary differentiation, lengths (by comparison with standards for age), and regularity of cortical outline.

Planar Tc-99m DMSA scintigraphy was performed using a standard protocol according to the European Association of Nuclear Medicine guidelines (7).

However, renal ultrasonography was performed during the treatment of all patients with recurrent urinary tract infection, voiding cystourethrogram was taken 6 weeks after the end of the treatment. Bladder catheterization for VCUG was performed with age-appropriate foley catheter. Reflux grading was performed using the radiographic international reflux rating system (8). If the contrast material was only in the ureter, grade 1; if there was reflux to the renal calyx and the ureter is not dilated, grade 2; ureter and renal pelvis were slightly dilated and kidney calices are not yet blinded, Grade 3; ureters were mildly curved, renal pelvis dilate and kidney calices are blind, Grade 4; ureters were folded at significant degrees, renal pelvis and calyces are highly dilated, it was evaluated as grade 5.

Simultaneous DMSA scintigraphy was performed with disease VCUG and control DMSA scintigraphy was performed 6 months after the first DMSA scintigraphy pathology. Findings that persisted on the second DMSA scintigraphy were accepted as renal scars and VUR and renal scar relation were investigated in the accordance with the findings.

For the statistical analyzes, Statistical Package Program for Social Sciences (SPSS) for Windows 10.0 program was used. The Mc Nemar test and Chi-square test were used to compare descriptive statistical methods (mean, standard deviation, frequency) as well as qualitative data when study data were evaluated. Results 95% confidence interval, $p<0.05$ was considered significant.

Results

The distribution of the demographic characteristics of the first urinary tract infection of 101 patients with recurrent urinary tract infection is shown in Table 1.

There was reproduction in 172 cases (4.1%) of 4195 urine cultures evaluated in the follow-up of 101 patients in 5 years. 84.8% E. Coli, 3.4% Enterobacter, 2.3% Proteus, 3.4% Pseudomonas, 4.6% MRSA (Methicillin Resistance Staphyloccus Aureus), 1% Klebsiella, 0.5% Enterococcus spp. were detected.

Ultrasonography of 101 patients' urinary system was performed. It was found that 77 patients (76.2%) were normal and 24 patients (23.8%) had pathology. Pathology was detected in 7 patients (6.9%) grade 1, 4 patients (3.9%) grade 2, 4 patients (3.9%) grade 3, 5 patients (4.9%) grade 4 hydronephrosis, 4 patients (3.9%) parenchymal pathology was found.

Table 1. *Demographic features.*

Age	Female	Male	Total
0-2 age	57(%56.4)	17(%16.8)	74(%73.2)
3-6 age	14(%13.8)	3(%2.9)	17(%16.8)
7-12 age	6(%5.9)	1(%0.9)	7(%6.9)
13-17 age	2(%1.9)	1(%0.9)	3(%2.9)
Total	**79 (%78.2)**	**22(%21.8)**	**101**

In the VCUG applied to all patients it was detected that 62 patients (61.3%) were normal and 39 patients (38.6%) were refluxed. Grade 1 in 3 patients, grade 2 in 5 patients, grade 3 in 8 patients, grade 4 in 10 patients, grade 5 reflux in 13 patients were detected.

When the results of DMSA taken twice with VCUG after 6 months later were evaluated together, it was detected that 30 patients (29.7%) were normal and 71 patients (70.3%) had scarring and activity loss.

Discussion

The most common infections of upper respiratory tract infections in childhood are urinary tract infections (1). Early diagnosis and correct treatment are the most important preventive measures for complications causing serious mortality and morbidity such as acute and chronic renal failure (2).

Urinary tract infections are the most common cause of chronic renal failure in Turkey (9). Urinary tract infections are also six times more common in girls, and urine evaluation in girls who have fever gain importance one more time (6). In the study, 78.2% of the cases were identified as female gender.

Gram (-) bacteria, especially E. coli, are the most frequently isolated pathogenic agents described in the literature. E. coli is responsible for 80-90% of acute urinary tract infections (10). Consistent with the relevant literature, E. coli was the most frequently isolated strain in the study.

VUR, a common anomalous urinary system seen in children, can cause a wide range of clinical conditions ranging from spontaneous healing to recurrent pyelonephritis attacks and kidney scarring. In many clinical trials, the relationship between SCI, VUR and renal scarring has been demonstrated. One of three UTI patients has a VUR, and one of three VUR patients has a renal scar (11). The incidence of VUR varies among races in patients in whom UTI is detected. While Gelfand et al. found the VUR frequency to be 32% (12), Mahyar et al. was found as 39.2% (13). The highest VUR rates range from 41% to 63% in the US, England and Italy, with the lowest rates being 6-12% in African-American children and 10% in Jamaican children (14,15). The incidence of VUR in the study was found to be 37.6%, similar to this data.

In the study of Caino and his colleagues, describing the relationship between renal scarring and VUR; it was reported that presence of renal scars in VUR cases was 67% and presence of renal scars in non-VUR cases was 16% (16). In the presented study, the presence of renal scar was detected as 100% in VUR cases and 19% in non-VUR cases. Lee et al. reported that VUR increases renal scarring risk in children and that VUR grade and renal scarring don't correlate (17). Peru et al. reported that renal scar ratio increased as VUR grade increased; 37.1% of renal scar ratio in grade 1 VUR patients and 61.5% of renal scar in patients with grade 4-5 VUR (18). In the presented study, the renal scar frequency increased as the VUR grade increased and the renal scar frequency of grade 1-5 VUR was 33.3%, 40%, 50%, 60%, 84.6%.

USG is the most preferred method of imaging in the diagnosis of UTI. In this context, the American Academy of Pediatrics 2011 guidelines recommend USG imaging after UTIs developed in children 2-4 months of age. Bush et al. 99 of the 512 UTI patients with normal USG were found to have renal scars on the DMSA scintigraphy, and they concluded that USG was not sensitive enough to detect renal damage (19). In another meta-analysis; USG was found to have a sensitivity of 37-100% and a specificity of 65-99% because USG was dependent on personal interpretation when USG compared with DMSA scintigraphy (20). In another study, the sensitivity, specificity, positive predictive value, and negative predictive value for USG in the detection of renal scarring was found as 57.1, 89.6, 40.8 and 94.4%, respectively (21). In the study, it was determined that the sensitivity of USG to detecting renal scar was 33.8% and it was low. On the other hand; statistically significant correlation was found between findings of renal ultrasonography and voiding cystourethrogram ($p<0.01$). As the USG grade increases, the amount of reflux and VCUG grade increases.

Statistically significant correlations were also found between VCUG findings and DMSA findings ($p<0.01$). As vesicoureteral reflux grade increases, the frequency of renal scarring and loss of activity increases.

In addition, VCUG could detect developing renal damage in 71 of 101 patients which is 54.9% of the patients and ultrasonography could detect 33.8%. In other words, voiding of 46.5% of the patients with renal damage and ultrasonography of 66.2% were found normal.

Table 2. *Comparation of renal ultrasonography (USG) and voiding cystourethrography (VCUG) findings*

USG (n)	**Normal**	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Other**	**Total**
VCUG (n)							
Normal	60	1	0	0	0	1	**62**
Grade 1	2	0	0	0	0	1	**3**
Grade 2	2	1	0	0	1	1	**5**
Grade 3	4	2	1	0	0	1	**8**
Grade 4	6	1	1	1	1	0	**10**
Grade 5	3	2	2	3	3	0	**13**
Total	**77**	**7**	**4**	**4**	**5**	**4**	**101**

Chi-square test =145.51 *p=0.001*

Table 3. *Comparation of voiding cystourethrography (VCUG) and Tc-99m dimercaptosuccinic acid (DMSA) scintigraphy findings*

DMSA (n)	**Normal**	**Loss of activity**	**Renal Scarring**	**Total**
VCUG (n)				
Normal (n)	26	22	14	**62**
Grade 1 (n)	1	1	1	**3**
Grade 2 (n)	1	2	2	**5**
Grade 3 (n)	1	3	4	**8**
Grade 4 (n)	1	3	6	**10**
Grade 5 (n)	0	2	11	**13**
Total (n)	**30**	**33**	**38**	**101**

Chi-square test:62.39 *p:0.001*

Conlusion

In conclusion, it was concluded that DMSA is the most sensitive imaging technique for showing renal damage in children who have urinary tract infections that is detected with clinical and laboratory findings, where ultrasonography and voiding cystourethrography are important factors in determining risk factors, but ultrasound and voiding can be detected normal even if renal damage is present.

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