

Renal Scar Formation in Children with Recurrent Urinary Tract Infections

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Abstract

Background: Reports of renal scar formation in children even in the absence of vesicoureteral reflux necessitates studying other causes of this major complication. The present study mainly focuses on the role of recurrent urinary tract infections (UTI) in renal scar formation.

Methods: The records of 53 patients with recurrent UTI and the data on their regular follow up visits were reviewed. Renal scar formation was confirmed by dimercapto-succinic acid (DMSA) scan.

Results: DMSA scan, done at a mean age of 8.31 years, revealed renal scar formation in 12 cases (22.44%). Seventy-five percent of the patients with scar formation and 80.5% without scar were older than 3 years at the time of the first documented UTI. The etiologic organism was found to be *Escherichia coli* in 89.2% of the infections in the scar forming versus 78.8% in the non-scar forming group.

Conclusion: In the presence of normal urinary tract anatomy, recurrent UTI can be a significant cause of renal scar formation in children.

Keywords: Recurrent UTI; Renal Scar; DMSA Scan; VCUG

Introduction

Urinary tract infection (UTI) is a common disease among children which may lead to renal scarring with a risk of later hypertension and renal insufficiency. The major goal of treatment in UTI is prevention of these complications.¹ Previous studies showed that scar formation following UTI is almost always associated with vesicoureteral reflux, but recently dimercapto-succinic acid (DMSA) scan studies showed that scar formation even in the absence of reflux, makes it an independent entity from reflux.² Recurrent UTI is not well defined in the literature and its consequences in patients with normal urinary tract are not clear. In this study, the risk of renal scar formation in patients with recurrent UTI and normal urinary tract anatomy was evaluated.

Materials and Methods

The subjects of this retrospective study consisted of 53 patients with recurrent UTI. All of them had normal initial sonography and voiding cystourethrography (VCUG) with regular follow up visits to Motahari Nephrology Clinic affiliated to Shiraz University of Medical Sciences. Recurrent UTI was defined as at least two episodes of documented UTI in a 6-month period or three episodes in one year (at least in one occasion during the follow-up). UTI was documented either by one suprapubic urine culture (2 or more cfu/ml) or two midstream cultures (>100000 cfu/ml) with similar microorganism and related clinical symptoms. At least one of the two urine cultures was done in one laboratory and by one person in the clinic.

The patients' records were reviewed for the following data including age at first presentation, number of episodes of UTI, clinical presentations, radiological findings, and urine culture results. Scar formation in the kidneys was confirmed by DMSA scan as persistent cortical defect or thinning. DMSA scan was

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done in one center and was reported by one specialist. The scan was not done with a constant interval from UTI, but for those with more than one DMSA scan, the last one was considered in the study. All the patients were followed by one nephrologist. Statistical analysis was done using Fisher-Exact test and a p value of <0.05 was considered as significant.

Results

Among 53 patients with recurrent UTI and a mean age of 10.1 years (range 9 months to 16 years), all except one were female. The mean time of the follow-up was 4.9 years (range 3 months to 11 years). The mean age at first diagnosis of UTI was 4.8 years (range 6 months to 16 years). DMSA scan was done at a mean age of 8.31 years and scar was reported in 12 cases (22.4%) all of whom were all female; however, serial ultrasonographic studies were unable to show scar formation in patients with positive DMSA scan. Scar had mostly developed in the left kidney ($n=8$) and only one patient was affected bilaterally. All the scars were mild (not more than one scar in each kidney).

Eleven patients were less than 3 years old at the time of the first UTI, with scar formation in 27% as compared to 19% rate of scar formation in 42 patients with the first presentation at 3 years or older ($P=0.69$). At least, one episode of febrile UTI was documented in 16 patients, among whom 43.7% ($n=7$) had scar formation as compared to 13.5% in those without febrile UTI ($P=0.02$).

The etiologic organism was found to be *E. coli* in 91.6% of episodes of infection in the scar forming group vs. 78% in the non-scar forming group ($P=0.42$).

Hypertension or renal failure was not detected in any of the patients during the follow-up.

Discussion

The main long term consequence of UTI is renal scarring which may lead to hypertension and end stage renal disease.⁴ An association between vesicoureteral reflux (VUR) and renal damage was found in 1960,⁵ and later on some studies showed scar formation to be almost always associated with VUR.² Although we can not deny the role of vesicourethral reflux as a major risk factor for development of renal scar, the fact that some studies have reported renal scar formation

even in the absence of vesicourethral reflux^{1,4} indicates that the role of other causative factors as the type of microorganism or total episodes of recurrences should be considered.

As reported in previous studies^{1,5} and confirmed by the present study, there is a direct relationship between episodes of UTI and renal scar formation. Febrile UTI is expected to lead to scar formation more than afebrile episodes. This was also documented in the present study.

Blumenthal argues that there is a sex difference in the cause of renal scarring.⁵ Reflux nephropathy is seen mostly in male patients with congenitally abnormal kidneys; however, the most severe damage is expected in females with recurrent urinary tract infections.⁵ In this study, it was observed that all the patients with recurrent UTI and normal urinary tract anatomy were females except one. Similar to previous studies,⁶ the age of presentation of the first UTI was not predictive of scar formation in our patients. The aim of imaging in UTI is to detect conditions that must be corrected to avoid the forthcoming deterioration of kidney function, or to prevent recurrent infections and long-term kidney damage.⁷ In 1985, Smellie, et al. reported renal scar formation in 5-20% of cases with acute pyelonephritis through IVP.³ Later, scar formation following acute pyelonephritis was reported to be 37%, using DMSA scan as a diagnostic tool.² Although DMSA scan is the gold standard for the diagnosis of renal scar formation, there is still controversy on the optimal imaging for the detection of scarring.⁸ In this experiment, serial ultrasonographic studies were unable to show any scar formation in patients with positive DMSA scan probably due to the small size of the scars and lower sensitivity of sonography. As with previous studies,^{9,10} *E. coli* was found to be the predominant uropathogen with no difference between the scar forming and non-scar forming groups.

It is concluded that even in the presence of normal anatomy, recurrent UTI can be a significant risk for renal scar formation in children. Therefore, with the prevention of recurrent UTI, the rate of this major complication will be reduced.

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References

- 1 Clarke SE, Smellie JM, Prescod N, Gurney S, West DJ. Technetium-99m-DMSA studies in pediatric urinary infection. *J Nucl Med* 1996; **37(5)**:823-8. [8965153]
- 2 Jakobsson B, Berg U, Svensson L. Renal scarring after acute pyelonephritis. *Arch Dis Child* 1994; **70(2)**:111-5. [8129430]
- 3 Smellie JM, Ransley PG, Normand IC, Prescod N, Edwards D. Development of new renal scars: a collaborative study. *Br Med J (Clin Res Ed)* 1985; **290(6486)**:1957-60. [3924325]
- 4 Schlager TA. Urinary tract infections in children younger than 5 years of age: epidemiology, diagnosis, treatment, outcomes and prevention. *Pediatric Drugs* 2001; **3(3)**:219-27. [11310718] [doi:10.2165/00128072-200103030-00004]
- 5 Blumenthal I. Vesicoureteric reflux and urinary tract infection in children. *Postgrad Med J* 2006; **82(963)**:31-5. [16397077] [doi:10.1136/pgmj.2005.036327]
- 6 Mingin GC, Hinds A, Nguyen HT, Baskin LS. Children with a febrile urinary tract infection and a negative radiological workup: factors predictive of recurrence. *Urology* 2004; **63(3)**:562-5. [15028458] [doi:10.1016/j.urology.2003.10.055]
- 7 Johansen TE. The role of imaging in urinary tract infections. *World J Urol* 2004; **22(5)**:392-8. [15290204] [doi:10.1007/s00345-004-0414-z]
- 8 Christian MT, McColl JH, MacKenzie JR, Beattie TJ. Risk assessment of renal cortical scarring with urinary tract infection by clinical features and ultrasonography. *Arch Dis Child* 2000; **82(5)**:376-80. [10799427] [doi:10.1136/adc.82.5.376]
- 9 Zmysłowska A, Kozłowski J, Zielińska E, Bodalski J. Urinary tract infections in children under three years of age *Pol Merkur Lekarski* 2003; **14(82)**:319-21. [12868192]
- 10 Ronald A. The etiology of urinary tract infection: traditional and emerging pathogens. *Dis Mon* 2003; **49(2)**:71-82. [12601338] [doi:10.1016/S0011-5029(03)90001-0]