Chronic tubulointerstitial nephritis in a solitary kidney of a child with Noonan syndrome

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ABSTRACT

Noonan syndrome is a genetic disorder with involvement of many organ systems; facial dysmorphism and cardiovascular defects being the common abnormalities. Renal involvement is uncommon and abnormalities of the genitourinary system are usually limited to structural anomalies and cryptorchidism. We report a case of Noonan syndrome with chronic tubulointerstitial nephritis in a solitary kidney.

Key words: Chronic tubulointerstitial nephritis, Noonan syndrome, solitary kidney

Introduction

First described by Jacqueline Noonan in 1962, Noonan syndrome (NS) is a congenital genetic disorder with an estimated prevalence of 1 in 1000 to 1 in 2500 live births.[1] Renal anomalies include solitary kidney and collecting system duplication. Chronic tubulointerstitial nephritis associated with Noonan syndrome has not been reported in the literature. We report a case of chronic tubulointerstitial nephritis in a child with NS and a solitary kidney.

Case Report

We present a case of a 7-year-old male child who had been diagnosed with Noonan syndrome at 3 years of age due to the characteristic morphological features and a normal male karyotype. He was born out of a nonconsanguineous marriage and had a normal peripartum period but had delayed milestones. He had presented to us with complaints of fever for the last 15 days that was low grade and without any history of clinical localization of the source. He also had a history of hematuria for the 3 days associated with oliguria. There is no history of recurrent urinary tract infections of any history suggestive of any genitourinary tract involvement. There is also no history of any drug use or any indigenous medication use. History also does not suggest any obvious autoimmune disorder. There was no other significant relevant history. He was found to have abnormal renal function tests and was referred to our centre for further evaluation and care.

On examination, he had morphological abnormalities suggestive of Noonan syndrome. He had low set and posteriorly rotated ears, epicanthic folds, hypertelorism, ptosis, high-arched palate, abnormal dentition, depressed nasal bridge, webbed neck, widely spaced nipples, low posterior hairline, left-sided cryptorchidism, and skeletal deformities such as scoliosis, rocker bottom foot, cubitus valgus, and joint hyperextensibility. His height was 106 cm (less than the third percentile for age). The BMI was 12.3 kg/m^2. Cardiovascular examination revealed findings suggestive of atrial septal defect. He also had pedal edema, facial puffiness, and coarse crackles in bilateral lung bases.

The serum creatinine was 4.6 mg/dl and urea was 163 mg/dl. Sodium was 134 mEq/l and potassium was 4.5 mEq/l. Serum uric acid was 2.6 mg/dl and corrected calcium was 8.1 mg/dl. ABG was suggestive of mild metabolic acidosis. He also had normocytic normochromic anemia with hemoglobin of 8.6 g/dl and TLC was 11 300

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without neutrophilia. Two-dimensional echocardiography revealed an ostium secundum ASD of 15 mm in size with a left to right shunt without any evidence of pulmonary arterial hypertension or other cardiac abnormalities. Ultrasound of the abdomen showed nonvisualization of the right kidney and a 7.9 cm left kidney, with raised cortical echogenicity and loss of corticomedullary differentiation. A Tc99m-DMSA scan was also done that showed a normally situated left kidney with regular outline and normal cortical function without any cortical scarring along with the absence of the right kidney [Figure 1]. Urine examination showed 2+ albumin with 3–4 RBCs and 2–3 pus cells per high-power field. C3 was low with normal C4 and ANA was negative. ASO titer was <200 IU/ml. He was given four sessions of hemodialysis along with supportive care with parenteral antibiotics and nutrition. The urine output improved, he became dialysis-free. The serum creatinine stabilized at 2–2.5 mg/dl. In view of the short history and rapid onset of symptoms a plan to do a renal biopsy was done and showed interstitial fibrosis and tubular atrophy with dense lymphocytic infiltration in the interstitium [Figure 2]. After 2 months of discharge, the serum creatinine continues to be in the range of 2–2.5 mg/dl. His eGFR calculated by the Schwartz formula is 17 ml/min/1.73 m^2.

Discussion

First reported by a pediatric cardiologist named Jacqueline Noonan in 1962, the Noonan syndrome has an estimated prevalence of 1 in 1000 to 1 in 2500 live births.[1] It is a clinically and genetically heterogeneous condition characterized by congenital heart disease, distinct facial features, short stature, and many other potential comorbidities. Gene mutations (six identified till date) identified in individuals with the NS phenotype are involved in the Ras/MAPK (mitogen-activated protein kinase) signal transduction pathway, and currently explain ~61% of NS cases. Because of this genetic heterogeneity and the poor negative predictive value of mutational analysis, Noonan syndrome frequently remains a clinical diagnosis.[2] Scoring systems have been proposed for the diagnosis of NS. One of the scoring systems proposed by Van der Burgt *et al*. in 1994 takes into consideration only the clinical features and is useful in making a clinical diagnosis in the absence of genotype analysis.[3]

Renal abnormalities have been described in 10–11% of cases and are usually not of much clinical significance. These include solitary kidneys and duplication of the collecting system.[4,5] The spectrum of renal failure in Noonan syndrome is largely unknown and information is limited only to case reports. Martin *et al*., reported a case of a 20-year-old male patient with clinical diagnosis of SLE with renal insufficiency.[6] Lopez *et al*., also reported a 5-year-old female child with Noonan syndrome who had presented with nephrotic range proteinuria with active urinary sediments with renal dysfunction and ANA and ds-DNA positivity. The renal biopsy in this case had shown finding of diffuse proliferative glomerulonephritis.[7] There is one more reported case of Noonan syndrome with SLE and Class I lupus nephritis in an 11-year-old male patient.[8] There are many other case reports with autoimmune disorders in association with Noonan syndrome, but renal involvement was not present in these cases.[7] There is one more case reported by Tejani *et al*., of

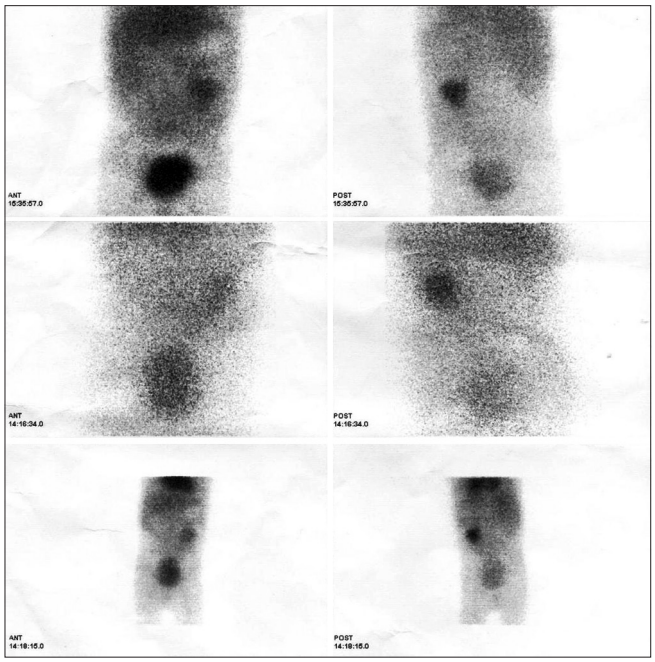

Figure 1: Tc99m-DMSA scan of the patient which shows normally situated left kidney with regular outline, normal cortical function, and without any evidence of scarring along with nonvisualization of the right kidney

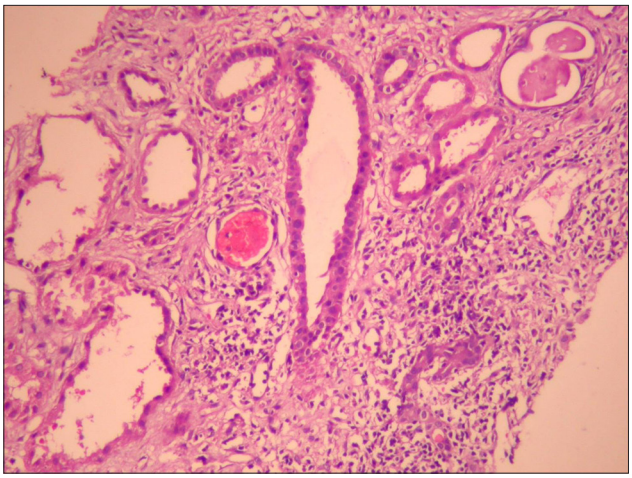

Figure 2: Interstitial fibrosis and tubular atrophy. A dense lymphocytic infiltrate is seen in the interstitium. An RBC cast is identified in one tubule (H and E, ×10)

an infant who had Noonan syndrome along with advanced renal failure and who had renal dysplasia with cystic disease.[9] The most common genitourinary abnormality seen in NS is cryptorchidism that is seen in up to 80% of boys and orchiopexy is required in many cases.[10]

The Noonan Syndrome Support Group (NSSG) is a nonprofit organization committed to providing support, current information, and understanding to those affected by NS. It has given some guidelines for managing cases of NS. The following guidelines were given pertaining to renal and genitourinary issues: (1) All individuals should have a kidney ultrasound at the time of diagnosis; a repeat test may be needed depending on initial findings. (2) Individuals may be at increased risk of urinary tract infections if a structural abnormality is present. (3) Antibiotic prophylaxis may be considered for hydronephrosis and/or recurrent urinary tract infection. (4) Orchiopexy should be performed by the age of 1 year if testicles remain undescended at that time.[2]

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