Case Report

Spontaneous resolution of infantile nephrotic syndrome

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ABSTRACT

Congenital nephrosis is a rare disease with universally accepted poor prognosis; despite developments in the pathogenesis and management, these children are always a challenge to the caregivers and families. Reported here, is a case of a 6-month-old female infant with infantile nephrotic syndrome, who went into spontaneous resolution within a week without therapy and remained asymptomatic for the following 2 years.

Saudi Med J 2003; Vol. 24 (1): 91-93

A nephrotic syndrome in the first year of life is very uncommon; nonetheless it is defined as proteinuria leading to clinical symptoms fairly early after birth. It is called Congenital Nephrotic syndrome (CNS) if it starts after birth or Infantile Nephrotic syndrome if it presents after 3 months of life.[1] There are many types of CNS but Finnish type is considered to be the most common,[2] that, presents within first month of life. Other types are diffuse mesangial sclerosis and associated with various malformation syndromes like Deny's Drash syndrome or Galloway Mowat syndrome. The secondary types are caused by congenital viral infections like cytomegalovirus, rubella, and toxoplasmosis for example.[3-5]

Case Report. A 6-month-old female infant was admitted to the King Fahd Hospital of the University, Al-Khobar, Kingdom of Saudi Arabia, with a history of eyelid swelling, blood in urine and irritability for 2 days duration. She was born to a G2P0+one Saudi female, who had one stillbirth, at 40 weeks of gestation by cesarean section due to failure to progress. She was thriving and developing adequately until 10 days prior to admission, when she contracted upper respiratory tract infection followed by gastroenteritis. Over the next few days, she developed decreasing frequency of urination and 2 days prior to presentation she started to have blood in the urine. She had no history of fever, skin rashes, and easy bleeding tendency. Family history was noncontributory.

Physical examination revealed an irritable infant with moderate periorbital edema, mild dehydration, without pallor or jaundice. Vital signs showed temperature 37°C, respiratory rate 40 per minute, heart rate 140 per minute, blood pressure was 117/62 mm Hg (>95th percentile for age), which was found to be normal on repeat measurements. The head, eye, ear, nose and throat revealed normal anterior fontanel, chest had equal bilateral air entry with no adventitial sounds, and the cardiovascular system had a normal first and 2nd heart sound with no murmurs. Abdomen was distended with positive shifting dullness, no organomegaly or

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Received 15th June 2002. Accepted for publication in final form 9th September 2002.

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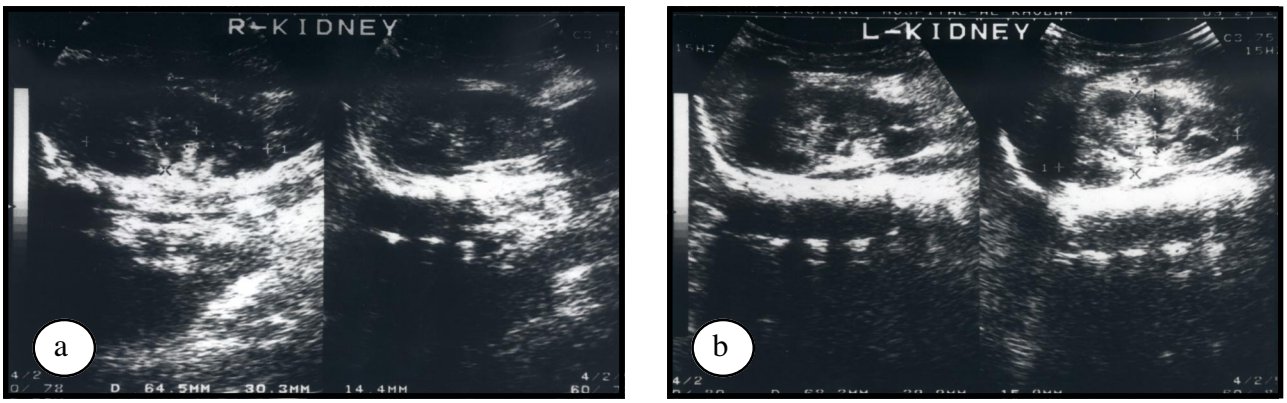

Figure 1 - Bilateral renal sonogram at presentation showing enlarged echo-dense kidneys **a)** right kidney measured 6.4 cm x 3 cm x 1.6 cm **b)** left kidney was 6 cm x 3 cm x1.6 cm.

Table 1 - Clinical follow-up data.

Variables	04/06/00	11/06/00	19/06/00	17/07/00	20/11/00	26/02/01	10/09/01
Weight	7.8 kg	-	7.2 kg 25th % ile	8.1 kg 50th % ile	10 kg 50-75th % ile	11 kg 75th % ile	12.5 kg 75th % ile
Height	62 cm	-	62 cm 5th %ile	70 cm 5th %ile	70 cm 5th %ile	74 cm 10th %ile	82 cm 25th %ile
Serum albumin	1.6 g/dl	4.1 g/dl	3.6 g d/l	3.4 g/dl	-	3.8 g/dl	-
Urinary protein to creatinine ratio	15710/43 (365)	-	-	26/16 (1.6)	-	-	-
Urinary protein	4+	Negative	Negative	Negative	Negative	Negative	Negative
Serum creatinine	0.4 mg/dl	0.3 mg/dl	0.3 mg/dl	-	-	-	-

% ile - percentile

tenderness. She had normal female genitalia with labial edema. Extremities had 2+ pitting edema as well. Investigations revealed normal renal function, urea in the blood 7g/dl, and creatinine 0.4mg/dl. Total protein was 4g/dl with serum albumin 1.6gm/dl. Serum cholesterol was 261mg/dl and serum tri-glycerides were 237 mg/dl. Urinalysis had a pH of 6.0, >100 red blood count/high power field, 2-5 white blood count/hpf. Urinary protein was >300mg/dl. Serum C 3 was 115mg/dl (88-201), negative antinuclear antibodies titer. Serology for TORCH was negative, and chromosome analysis revealed 46XX karyotype. Initial spot protein to creatinine ratio was 365 (normal <0.2). Her renal ultrasound showed bilaterally enlarged echo-dense kidneys, right kidney measured 6.4 cm x 3 cm x 1.6 cm and left was 6 cm x 3 cm x 1.6 cm. **(Figure 1a & 1b)**

In view of the above results she was started on captopril and intravenous human albumin followed by furosemide, but within a week she had resolution of proteinuria and edema also resolved. Then, all the therapy was discontinued, and patient was followed closely **(Table 1)**.

Discussion. Congenital and infantile nephrotic syndrome is a group of disorders, resulting in either end stage renal insufficiency within the first 2-3 years or death. There are occasional reports of spontaneous resolution at varying ages after onset of nephrosis.[6,7] This report is to remind us that this poor prognostic disease can rarely result in complete resolution of renal dysfunction. Congenital nephrosis syndrome, of Finnish type is the most common variety, presenting in the neonatal period with edema, heavy proteinuria and hypo-albuminemia. It is an autosomal recessive disease. Its gene has been localized to chromosome 19q13:1,[8,9]

which, is known as nephrin coding gere gene. Various mutations in this gene have been found in non-finnish CNS patients. Prenatal diagnosis is available by checking the alpha-fetoprotein level in serum, or in the amniotic fluid by 16-18 weeks of gestation.[10] Diffuse mesangial sclerosis (DMS) often presents after the first few months of life or as late as 2-3 years of age. It's a rare disease with no ethnic or racial predilection, but its occurrence in the same family suggests autosomal recessive inheritance as well.[11] Two important associations with malformation syndromes are Denys-Drash syndrome (DDS), which is male pseudo-hermapheroditism, various genitourinary tract abnormalities, glomerulopathy causing nephrosis and Wilms' tumor (WT). Denys-Drash syndrome is caused by mutations in WT1 gene localized to chromosome 11p13.[12-14] The treatment includes bilateral nephrectomies for the risk of WT prior to renal transplantation. The disease does not recur in the transplant graft. The 2nd one is Frasier Syndrome[15] presenting as intersex with focal segmental glomerulosclerosis and characteristic tumor is gonandoblastoma instead of wilms'. It is also associated with WT1 gene mutations. Gallway Mowat syndrome where microcephaly and various other CNS abnormalities are associated with congenital nephrosis. Idiopathic nephrotic syndrome is exceedingly uncommon in the first year of life. Secondary nephrotic syndrome due to infections like cytomegalovirus, toxoplasmosis and syphilis are known and need appropriate treatment of underlying cause. The current management of CNS per infantile nephrotic syndrome (INS) include 1. Providing adequate nutrition. 2. Reduction of proteinuria by medications like Angiotensin converting enzyme inhibitors (Captopril) and nonsteroidal anti-inflammatory drugs (Indomethacin). 3. Intravenous albumin substitution, 4. Optimizing growth and development. 5. Avoiding complications of nephrotic syndrome like infections, thrombosis, thyroid dysfunction and bone related problems. 6. There is no role of Corticosteroids or other immunosuppressive agents in therapy of CNS and INS 7. Establishing dialysis till patient receives renal transplantation.

Acknowledgments. I am thankful to Dr. Hatim Turkistani and Dr. Bassam Al-Awary for their assistance in preparing the Arabic abstract and to Dr. Abdul Latif Al-Faraidy for his editorial comments.

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