Signature: © Pol J Radiol, 2016; 81: 465-468
DOI: 10.12659/PJR.898088

Polish Journal of Radiology
www.PolRadiol.com
CASE REPORT

Received: 2016.02.17
Accepted: 2016.03.13
Published: 2016.09.29

Sonographic Diagnosis in a Rare Aetiology of Neonatal Scrotal Swellings: A Case Report of Congenital Nephrotic Syndrome

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Shabnam Bhandari Grover[1ABDEF], Nishith Kumar[1ABDEF], Hemal Grover[3BEF], Dinesh Kumar Taneja[1BDE], Amit Katyan[1DEF]

[1] Department of Radiology and Imaging, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India
[2] Department of Pediatric Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India
[3] At time of study: Radiology Resident Deputed to Department of Radiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, from Institute of Nuclear Medicine and Allied Sciences, Delhi, India, currently, Research Associate Department of Neuro Radiology, New York Medical University, New York, NY, U.S.A.

Author's address: Shabnam Bhandari Grover, Department of Radiology and Imaging, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India, e-mail: shabnamgrover@yahoo.com

Summary

Background: Common etiologies of scrotal swelling in neonates include hydrocoele, inguinal hernia and testicular torsion; less common is epididymo-orchitis. Congenital nephrotic syndrome (CNS), a rare entity, is known to present as progressive renal failure and its leading presentation with scrotal involvement has not been reported.

Material/Methods: We report a rare case of CNS with primary clinical presentation as scrotal cellulitis and epididymo-orchitis. In this neonate, scrotal and abdominal ultrasound examination was performed and the laboratory data were obtained.

Results: Sonography revealed bilaterally enlarged echogenic kidneys, testis and epididymis with echogenic peritoneal fluid tracking into both scrotal sacs. Laboratory data revealed proteinuria and severe depletion of serum IgG. Culture of the peritoneal fluid showed gram-negative organisms. A final diagnosis of CNS, complicated with peritonitis tracking into the scrotal sacs was arrived at.

Conclusions: CNS may have a rare presentation with distracting symptoms of scrotal cellulitis and epididymo-orchitis, as seen in our patient. However, diligent use of abdomino-scrotal sonography, supported by relevant laboratory data can clinch the accurate diagnosis.

MeSH Keywords: Congenital Nephrotic Syndrome • Epididymo-Orchitis • Neonate • Scrotal Swelling • Ultrasound

PDF file: http://www.polradiol.com/abstract/index/idArt/898088

Background

Congenital nephrotic syndrome (CNS), a rare entity, is defined as a form of disease presenting either at birth or within the first three months of life [1–5]. The prognosis of CNS is significantly poorer than infantile and childhood forms of nephrotic syndrome (NS) [2]. The disease has a genetic etiology, frequently by mutations in the NPHS1 gene and is mostly reported from Finland with scattered reports from other regions such as Western Europe, North America, Turkey and Brazil [3,4,6]. A MEDLINE search did not reveal any case from India. The characteristic presentation of CNS is early onset, rapidly progressive renal failure with frequent complications of infections and thrombo-embolic events [1]. The primary presentation of CNS with scrotal involvement has not been reported so far. The leading causes of neonatal scrotal masses are hydrocoele, inguinal hernia and testicular torsion, whereas epididymo-orchitis, idiopathic (intrapartum) scrotal hemorrhage and testicular tumors are less frequent etiologies [7,8]. Rare etiologies of intra-abdominal events such as neonatal adrenal hemorrhage, presenting primarily as scrotal swelling, are also occasionally reported [9]. We are reporting a rare case of CNS with primary presentation as scrotal cellulitis and

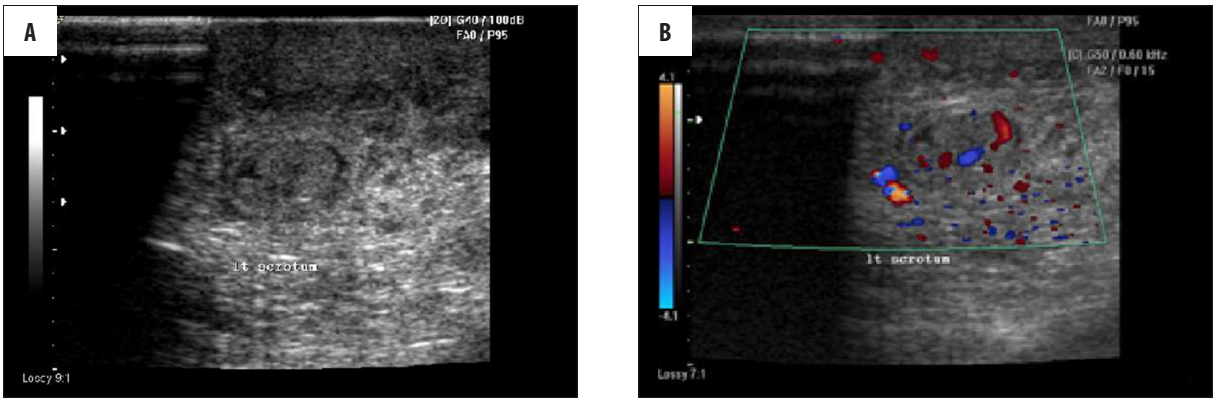

Figure 1. (**A**) Sonogram showing enlarged testes with increased echo texture, marked thickening of the scrotal skin and minimal fluid collection in the sac. Left epididymis is enlarged and shows increased echotexture. (**B**) Color Doppler of the left scrotum shows increased vascularity of the testis.

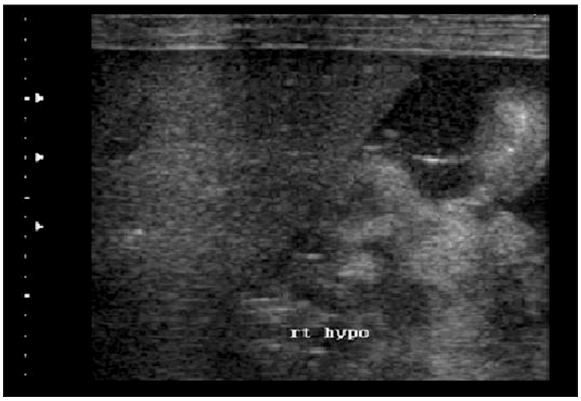

Figure 2. Sonogram of the abdomen shows free fluid with low-level internal echoes in the hepato-renal space.

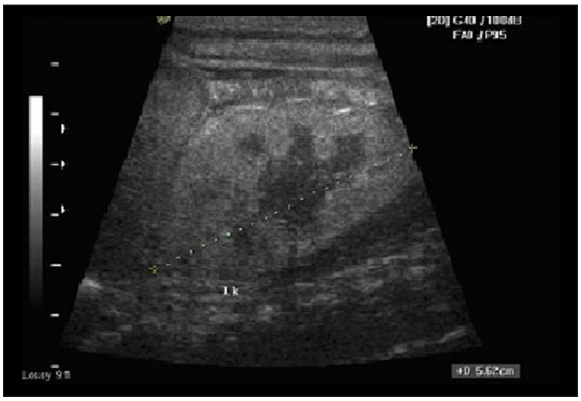

Figure 3. Sonogram shows enlarged left kidney, cortical hyperechogenicity and pleomorphic-appearing renal pyramids with loss of cortico-medullary differentiation.

epididymo-orchitis. In this neonate scrotal and abdominal ultrasound examination, together with laboratory data, lead to the accurate diagnosis of congenital nephrotic syndrome complicated by peritonitis tracking into the scrotal sacs.

Material and Methods

A male neonate at 15 days of life was brought to hospital by the parents, with a history of bilateral scrotal swelling and discoloration, accompanied by abdominal distension of four days' duration. The rest of the general and systemic physical examination was normal. The antenatal and birth records were available and revealed no antenatal or perinatal contributory factors and were within normal range. The pediatric department immediately sampled blood and urine for a routine laboratory analysis including evaluation of TORCH infections. The neonate was referred for scrotal ultrasound with a working clinical diagnosis of orchitis with scrotal cellulitis. However, in view of abdominal distension, we performed both abdominal and scrotal ultrasound, which revealed features of CNS with peritonitis involving both scrotal sacs. In view of the ultrasound findings, additional laboratory investigations for a renal disease, including serum and urine immunoglobulin levels, were done. An ultrasound-guided peritoneal tap was obtained and the sample was sent for microbiological analysis.

Results

Sonographic examination of the scrotum revealed bilaterally enlarged testes (right testis: 3.2×2.0 cm, left testis: 3.2×2.2 cm) with increased echotexture, minimal fluid collection in the sac, and thickening and edema of the scrotal skin and subcutaneous tissue (Figure 1A). Bilateral epididymides were enlarged (right: 11 mm, left 12 mm at head region) and showed increased echotexture. Color Doppler showed increased vascularity in both testes and overlying skin (Figure 1B). Sonographic examination of the abdomen revealed moderate free fluid in the peritoneal cavity which was seen tracking into both scrotal sacs. The peritoneal fluid showed low-level internal echoes (Figure 2). Both kidneys were moderately enlarged (length-left kidney: 5.6 cm, right kidney: 5.5 cm). There was increased echogenecity of the cortices and loss of cortico-medullary differentiation along with a pleomorphic appearance of the renal pyramids in both kidneys (Figure 3). Sonographic diagnosis of congenital medical renal disease with peritonitis and epididymo-orchitis was considered by us.

The laboratory parameters supported our diagnosis since leukocytosis, hypoproteinemia, hypercholesterolemia, elevated serum creatinine and severe proteinuria were documented (Table 1). There was loss of immunoglobulins in the urine (Urine IgG – 16 mg/dL) and serum IgG was severely

Table 1. Laboratory parameters of the patient.

	Value	Lab reference range
Blood/serum		
Leukocytes	TLC-21,000/mm^3	4000–11,000/mm^3
Total serum protiens	5 gm/l	6.3–7.8 gm/l
Serum albumin	3.2 gm/l	3.5–5.5 gm/l
Total cholesterol	328 mg/dl	120–200 mg/dl
Serum creatinine	1.7 mg/dl	0.6–1.2 mg/dl
Serum Ig G	20 mg/dl	231–1411 mg/dl
Urine analysis		
Proteins	3+ and casts	Absent
RBC	2–3/hpf	Absent
Urine IgG	16 mg/dl	<0.5mg/dl
Ascitic fluid		
Pus cells	8–10/hpf	Absent
E. coli in culture	(10,000000 CFU)	<10,0000 CFU)

depleted (20 mg/dL). Moreover, the peritoneal fluid showed pus cells and gram-negative organisms (Table 1). Renal biopsy confirmed the diagnosis of congenital nephrotic syndrome (Figure 4). A final diagnosis of congenital nephrotic syndrome complicated by peritonitis, epididymo-orchitis and scrotal cellulitis was arrived at.

Appropriate antibiotic, anti-inflammatory and replacement therapy were immediately instituted but the infant succumbed on the 7th day of hospital admission. The parents (non-consanguineous couple) at that stage volunteered a history for a similar disorder in two elder male siblings who had died at the age of 3 and 5 months respectively and the death summary records from another hospital of national repute, bore a diagnosis of CNS for each infant. The medical history of both parents was insignificant. Although further investigations in the form genetic testing was refused by the parents, due to the persistent manifestation of the disease in all three consecutive offspring, the diagnosis of genetic variety of CNS was made.

Discussion

The common etiologies to be considered by a sonologist in a neonate with a scrotal mass include hydrocoele, testicular torsion and orchitis [7]. Testicular torsion presents on ultrasound as echogenic parenchyma interspersed with hypoechoic radially-oriented fibrous septae. Orchitis reveals heterogeneously increased echogenicity and increased vascularity in the epididymis and testis. Scrotal cellulitis is known to have features of increased scrotal wall thickness and vascularity [8]. Our patient had sonographic findings consistent with epididymo-orchitis and scrotal cellulitis. In addition, ultrasound of the abdomen revealed peritoneal fluid with septae. Both kidneys were enlarged with increased echogenicity and pleomorphic appearance of the

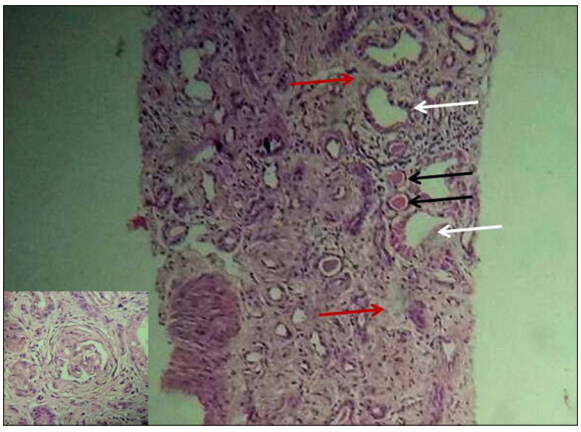

Figure 4. Light microscopy section of the renal cortices shows dilated tubules (white arrows), microcysts with hyaline cast (black arrows) with patchy interstitial edema (red arrows). Glomeruli (inset at left bottom corner) appear unremarkable.

renal pyramids. It was the abdominal ultrasound observations which lead us to the primary etiology being chronic medical renal disease, complicated by secondary peritonitis tracking into the scrotal sac and testis. The laboratory parameters and renal biopsy confirmed the diagnosis of congenital nephrotic syndrome with secondary peritonitis tracking into the scrotal sacs.

Nephrotic syndrome (NS) in childhood can be a rare congenital variety (CNS) or more common infantile and childhood varieties [1,3,4]. CNS presents at birth or within the first three months of life. Infantile nephrotic syndrome is diagnosed between the fourth and the twelfth month of life and childhood nephrotic syndrome develops after the first year of life [1,3–5]. Incidence of CNS is the highest in Finland with a reported rate of 1.2 per 10,000 live births [2,3]. Although scattered reports from other countries are found in the literature, we did not encounter any report from India. Etiology of congenital nephrotic syndrome is believed to be both due to genetic mutations and antenatal infections [1,4,5].

Our patient presented in the neonatal period with abdomino-scrotal swelling and the complication of peritonitis and epididymo-orchitis confirmed both by ultrasound and laboratory data. Ultrasound features were characteristic of CNS [10,11]. Additionally, echogenic peritoneal fluid was seen tracking into the scrotal sacs causing secondary epididymo-orchitis and cellulitis. The laboratory data further clinched the diagnosis since severely raised urine IgG and markedly depleted serum IgG levels were documented [12].

A review of the literature revealed sporadic reports of primary abdominal events such as neonatal adrenal hemorrhage presenting with acute scrotum [9]. However, the primary presentation of CNS with complication of epididymo-orchitis as documented in our patient has not been reported so far.

The significant contribution of sonography as an investigative modality in the diagnosis of CNS is supported not only by the findings documented in our index case but also by reports from other investigators [10]. The Finnish type

of CNS presents with hyperechoeic enlarged kidneys, with variable size and shape of the renal pyramids, which is related to the microcystic tubular dilatation. Similar ultrasound and pathology observations were documented in our case as well. On the contrary, patients with diffuse mesangial sclerosis present with parenchymal hyper-echogenicity involving areas of the renal cortex and medulla in a normal-sized kidney [10].

Echogenic kidneys with normal architecture and size are a normal finding in neonates. The differential diagnosis to be considered for hyperechoeic kidneys in neonates and infants is based on the renal size and the site of the increased echogenicity and status of renal architecture. The etiology for a small echogenic kidney with increased echotexture of the cortex and medulla is cortical and medullary necrosis due to chronic obstruction. Small kidneys with only medullary hyper-echogenicity are seen in nephrocalcinosis [11]. When the renal size and echogenecity are both increased with maintained renal architecture, the likely etiology is CNS. In CNS, the echogenecity is increased due to cortical microcysts. Sonographic appearance in CNS is similar in antenatal and postnatal life. In our patient the sonographic appearance was of bilaterally enlarged kidneys, with increased echogenicity of the cortex, which is the known appearance of CNS. When renal size and echogenecity are both increased with distorted renal architecture, one of the etiologies is polycystic kidney disease [11].

Renal biopsy is indicated mainly in infantile onset of nephrotic syndrome, gross hematuria and for exclusion of secondary causes amongst many others [13]. Renal biopsy in CNS shows tubular dilatation, interstitial fibrosis, inflammatory infiltrates and podocyte effacement which is common in all forms of CNS. Although renal biopsy confirms the sonographic diagnosis of CNS, genetic testing is required for precise differentiation between various genetic and non-genetic forms [3,10]. Renal biopsy in our patient revealed microcysts with patchy interstitial edema, and a positive family history in three consecutive male offspring indicated genetic etiology of CNS.

As most patients do not respond to standard corticosteroid or immuno-suppressive agents, the mainstay treatment of CNS is albumin infusion therapy along with diuretic agents using a central venous access. The ultimate goal of management is to overcome protein losses, prevent infections and renal failure till the child is old enough for a renal transplant, which is at around 1–2 years of age. Renal transplantation is the treatment which results in a good prognosis, i.e. over 90% five-year survival [1]. However, a recent report cites recurrence of CNS, occurring 8 months after renal transplantation [14].

Conclusions

Our report brings forth the occurrence of CNS in India and also documents its uncommon presentation with scrotal cellulitis and epididymo-orchitis. The sonographic renal appearances and biopsy correlation have been enumerated along with the relevant differential diagnosis, prognosis and treatment of this entity. In addition, the importance of comprehensive ultrasound examination to exclude the primary cause in the abdomen in a patient with a scrotal mass is highlighted.

Learning points

Although congenital nephrotic syndrome is characteristically a disease of the Finnish population, unusual cases may occur in other races, as seen in our patient from India.

Leading clinical presentation of congenital nephrotic syndrome is rapidly progressive renal failure but it may primarily present with infection at an atypical site such as scrotal cellulitis.

Sonography is the primary modality for diagnosis, differential diagnosis and detecting complications of congenital nephrotic syndrome.

Renal size and architecture along with the site of increased renal echogenecity helps in differentiating various aetiologies of hyperechoic kidneys in the newborn.

References:

1. Jalanko H: Congenital nephrotic syndrome. Pediatr Nephrol, 2009; 24(11): 2121–28
2. Badoe EV, Kumoji R: Congenital nephrotic syndrome of the finnish type. Ghana Med J, 2008; 42(1): 42–44
3. Niaudet P: Congenital Nephrotic Syndrome, Finnish Type.Orphanet encyclopedia, May 2004. *http://www.orphanet/data/patho/GB/uk-CongenitalnephroticSyndrome*
4. Machuca E, Benoit G, Nevo F et al: Genotype-phenotype correlation in non-finnish congenital nephrotic syndrome. J Am Soc Nephrol, 2010; 21(7): 1209–17
5. Fogo AB, Lusco MA, Najafian B, Alpers CE: AJKD atlas of renal pathology: Congenital nephrotic syndrome of finnish type. Am J Kidney Dis, 2015; 66(3): e11–e12
6. Guaragna MS, Cleto TL, Souza ML et al: NPHS1 gene mutations confirm congenital nephrotic syndrome in four Brazilian cases: A novel mutation is described. Nephrology (carlton), 2015 [Epub ahead of print]
7. Wilson-Storey D. Scrotal Swellings in the under 5s. Arch Dis Child, 1987; 62(1): 50–52
8. Celestino A, Goya E, Fite M et al: Gray-scale and color Doppler sonography of scrotal disorders in children: An update. Radiographics, 2005; 25: 1197–214
9. Adorisio O, Mattei R, Ciardini E et al: Neonatal adrenal hemorrhage mimicking an acute scrotum. J Perinatol, 2007; 27(2): 130–32
10. Avni EF, Vandenhoute K, Devriendt A et al: Update on congenital nephrotic syndrome and the contribution of US. Pediatr Radiol, 2011; 41: 76–81
11. Slovis TL, Bernstein J, Gruskin A: Hyperechoic kidneys in the newborn and young infant. Pediatr Nephrol, 1993; 7: 294–302
12. Harris HW Jr., Umetsu D, Geha R, Harmon WE: Altered immunoglobulin status in congenital nephrotic syndrome. Clin Nephrol, 1986; 25(6): 308–13
13. Bagga A: Revised guidelines for management of steroid-sensitive nephrotic syndrome. Indian J Nephrol, 2008; 18(1): 31–39
14. Derakhshan A, Derakhshan D, Fallahzadeh MH, Basiratnia M: Recurrence of nephrotic syndrome following kidney transplantation in a child with congenital nephrotic syndrome. Saudi J Kidney Dis Transpl, 2016; 27(1): 150–52