Carta al Director

Congenital nephrotic syndrome secondary to pertussis

Síndrome nefrótico congénito secundario a la tos ferina

Dear Editor,

Nephrotic syndrome shows itself as massive proteinuria, hypoalbuminemia, edema and hypercholesterolemia. In the first year of life, nephrotic syndrome is a rare but serious disease. The physio-pathology of congenital nephrotic syndrome (CNS), especially in the first 3 months of life, is different from other nephrotic syndromes of childhood. CNS may develop as a result of primary or secondary causes. NPHS1 or NPHS2 genes are detected in primary CNS, while secondary CNS often presents with intrauterine infections, drug reactions, and infantile systemic lupus erythematosus. The diagnosis of CNS should be based on various criteria such as clinical presentation, family history, laboratory findings, and genetic testing. Although primary CNS progresses to end-stage renal failure despite various treatments, the treatment of secondary CNS is more pleasing.[1]

Pertussis is an acute and contagious infectious disease characterized by overlapping and spasmodic coughing attacks. Pertussis can be seen in all age groups.[2] CNS secondary to pertussis is very rare in the literature.[3,4] In this study, we present a case with CNS that secondary to the pertussis in infant and improved with antibiotherapy.

A 45-day-old male applied to hospital with complaints of fever and recurrent coughing attacks. He was born at 3120 g with cesarean section after 39 weeks of pregnancy. It was learned from history that his mother had persistent cough attacks before one month ago. Physical examination revealed arterial tension was 92/51 mmHg, body weight 4.8 kg (25–50 percentile), height 53 cm (25th percentile), body temperature 36.2 °C, oxygen saturation 80%, pulse 160/min and respiration 66/min. There were intercostal retractions and rales, liver and spleen were palpable.

The patient's white blood cell was 56,000/mm^3 (64% polymorphonuclear leukocyte, 28% lymphocytes, 8% monocytes). Blood gases were normal. Chest X-ray examination revealed pneumonic infiltration. The patient was given 100 mg/kg ceftriaxone IV and 15 mg/kg clarithromycin IV. *Bordetella pertussis* PCR was detected as positive in nasopharynx swabs.

On the 5th day of follow-up, edema was detected on the eyelids. In laboratory tests, albumin was reported as 2.8 g/dl (*N*: 2.5–4.4), total protein 4.3 g/dl (*N*: 4.6–7.4) and triglyceride 150 mg/dl (0–150). In complete urinalysis pH was reported as 8, protein 2+. Protein/creatinine in spot urine was 3.6 ($N < 0.7$). Urine culture was negative. Renal ultrasonography revealed no pathology. Anti HCV(−), Anti HIV(−), HBsAg(−), Toxo IgM(−), CMV IgM(−), Rubella IgM(−), and VDRL(−) were detected. Genetic analysis revealed no mutation in NPHS1 and NPHS2 genes. Cough attacks significantly reduced, and edema and rales improved, and the antibiotics were discontinued on the 10th day. On discharge total protein was normal, protein/creatinine in spot urine was 1.6. At the age of 6 months development of the patient was normal and protein/creatinine was 0.5 in spot urine.

Massive proteinuria is caused from mutations in genes encoding structural or regulatory proteins of the renal filtration barrier in the glomerular capillary wall. Proteinuria is caused by the loss of size and load selectivity provided by this barrier.[5] CNS is often caused by primary causes, the most common cause being mutations in the NPHS1 and NPHS2 genes, respectively. Renal biopsy cannot explain the etiology of the disease, and patients should be examined for these two mutations especially for definite diagnosis.[6] In our study, no mutation was detected in NPHS1 and NPHS2 genes.

Secondary CNS is associated with many diseases such as cytomegalovirus infection, toxoplasmosis, congenital rubella, hepatitis B and human immunodeficiency virus infection. This type of CNS develops due to the triggering of nephropathy either directly or through immunomimetic mechanisms.[3] These diseases, which can be recycled and treatable, should be investigated in all cases thought.[7] One of the factors of secondary CNS is pertussis infection, which is rarely reported in the literature.[3,4]

Coughing adolescents and adults are the most important source of pertussis in childhood pertussis. In infants, the concentrations of transplacental pertussis antibodies decrease with a half-life of about 6 weeks and in 2–6 months of age the antibody against *B. pertussis* becomes undetectable.[8] Based on the anamnesis, the mother of our case was accepted as the source of pertussis.

Pertussis is diagnosed by culture or polymerase chain reaction (PCR). Culture is gold standard in diagnosis, but this method may give false negative results in the late period of infection, in vaccinated individuals and in antibiotic therapy areas. In recent years PCR has become more popular.[2]

The treatment of secondary CNS is directed at the underlying cause, and nephropathy is improved with the treatment directed against the agent. Macrolides are used in the treatment of pertussis. Macrolides have been shown to reduce the symptoms, especially when they are given in the early stages of the disease, to prevent contamination by increasing the elimination of nasopharynx[9] and to correct nephropathy.[4]

As a result, pertussis is a rare cause of secondary CNS, therefore edema or proteinuria, which can be detected in infants

who are followed due to pertussis, should be stimulating for CNS.

Funding

The authors have no financial or competing interests in relation to this work.

Conflict of interest

The authors declare that there is no conflict of interest.

BIBLIOGRAFÍA

1. Pais P, Avner E. Nephrotic syndrome. In: Kliegman RM, Stanton B, St Geme JW, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier Company; 2016. p. 2521–8.
2. Long S. Pertussis (*Bordetella pertussis* and *Bordetella parapertussis*). In: Kliegman RM, Stanton B, St Geme JW, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia: Elsevier Company; 2016. p. 1377–82.
3. Kim JJ, Clothier J, Sebire NJ, Milford DV, Moghal N, Trompeter RS. Nephrotic syndrome in infancy can spontaneously resolve. Pediatr Nephrol (Berlin, Germany). 2011;26:1897–901, http://dx.doi.org/10.1007/s00467-011-1911-0. PMID: 21611885 [Epub ahead of print].
4. Kaynak-Turkmen M, Cengiz-Erdem F, Sonmez F, Girisgen I, Telli M, Berdeli A. A newborn with pertussis accompanying nephrotic syndrome. Turk J Pediatr. 2014;56:665–8. PMID: 26388601 [Epub ahead of print].
5. Tryggvason K, Patrakka J, Wartiovaara J. Hereditary proteinuria syndromes and mechanisms of proteinuria. N Engl J Med. 2006;354:1387–401.
6. Koziell A, Grech V, Hussain S, Lee G, Lenkkeri U, Tryggvason K, et al. Genotype/phenotype correlations of NPHS1 and NPHS2 mutations in nephrotic syndrome advocate a functional inter-relationship in glomerular filtration. Hum Mol Genet. 2002;11:379–88.
7. Holmberg C, Jalanko H. Nephrotic syndrome in the first year of life. In: Kher KK, Greenbaum LA, Schnaper HW, editors. Clinical pediatric nephrology. 3rd ed. Florida: Taylor & Francis; 2017. p. 353–65.
8. Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. Pediatr Infect Dis J. 2005;24:S58–61.
9. Munoz FM, editor. Pertussis in infants, children, and adolescents: diagnosis, treatment, and prevention. Seminars in pediatric infectious diseases. Elsevier; 2006.

Mervan Bekdas[a,*], Recep Eroz[b], Busra Cihan[a]

[a] *Department of Pediatrics, Abant Izzet Baysal University Medical Faculty, Bolu, Turkey*
[b] *Department of Medical Genetics, Duzce University Medical Faculty, Duzce, Turkey*

[*] *Corresponding author.*
E-mail address: merbek14@yahoo.com (M. Bekdas).

https://doi.org/10.1016/j.nefro.2019.03.009

Carta al Director

Fracaso renal agudo asociado a inhibidores check-point

Renal damage secondary to check-point inhibitors

Sr. Director:

El tratamiento del carcinoma renal (CR) ha experimentado una revolución gracias al empleo de fármacos antiproliferativos e inmunomoduladores. Sunitinib (SUN) es un inhibidor de tirosina cinasa (TK) con efecto antiproliferativo y antiangiogénico[1]. Nivolumab (NIV) es un anticuerpo monoclonal humano, inhibidor check-point, que evita la evasión inmunológica propia del tumor, potenciando la respuesta inmune del paciente[2]. Ambos fármacos han demostrado aumentar la supervivencia del CR, pero también se han relacionado con toxicidad en distintos órganos. A continuación, describimos un caso de un paciente que presentó daño renal asociado al empleo de SUN y NIV.

Varón de 70 años, con marcapasos por bloqueo AV Mobitz, hipertensión arterial (HTA) y enfermedad renal crónica (creatinina basal 1,4-1,5 mg/dl) por pérdida de masa nefronal tras nefrectomía derecha secundaria a CR de células claras (pT3b Nx Mx), en 2014.

Recibió una primera línea con SUN por recidiva de la enfermedad tumoral, que se suspendió tras presentar toxicidad, entre ellas renal, quedando con una creatinina sérica (Crs) entre 1,4-1,8 mg/dl. Seis meses después, la enfermedad tumoral progresó, motivando una segunda línea con NIV.