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CASE REPORT

CONGENITAL NEPHROTIC SYNDROME SECONDARY TO CONGENITAL INFECTION: A CASE REPORT

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Abstract

Congenital nephrotic syndrome (CNS) is a rare glomerular disease characterized by massive proteinuria, hypoproteinemia, and generalized edema that manifests in the first 3 months of life. This report describes the case of a patient with congenital nephrotic syndrome secondary to congenital infection in a pediatric patient. The article aims to sensitize pediatricians to the pathology and its etiologies, considering that clinical suspicion allows for better therapeutic management of affected patients and the prevention of potential sequelae.

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INTRODUCTION:

Congenital nephrotic syndrome (CNS) is a rare glomerular disease characterized by massive proteinuria (>50 mg/kg/day or >40 mg/m²/h in 24-hour urine), hypoproteinemia (albumin <2.5g/dL) and generalized edema, which manifests itself during the first 3 months of life[1]. It can be classified, according to its etiology, as primary, mostly of genetic origin; and secondary, originating from systemic diseases such as congenital infections, metabolic and autoimmune diseases, tumors, drugs and mercury poisoning[2]. These two large groups differ markedly in terms of their treatments and prognoses, considering that genetic causes have a high mortality rate and secondary causes have the possibility of curative treatment with total resolution of the condition[3]. There are few data in the Brazilian literature that indicate the general incidence of congenital nephrotic syndrome, and international data demonstrate 1-3 cases/100,000 children under 16 years of age[4]. The vast majority of cases are linked to genetic inheritance, the most common being the Finnish type, related to the NPHS1 gene mutation. There is no response to immunosuppressive therapy and supportive measures are maintained, with kidney transplantation being the only curative treatment in many types[1]. CNS secondary to congenital infections, of maternal origin, has the unique characteristic of its resolution with the treatment of the underlying disease. There is a description in the literature of an association between CNS and syphilis, toxoplasmosis, CMV and rubella, despite representing a rare complication[4].

CASE REPORT:

AVS, female, mixed race, born and living in Recife, 1 month and 22 days old, referred from the Emergency Care Unit (UPA) to the emergency room of a quaternary level hospital with a history of 01 fever spike associated with large amounts of vomiting, as well as another feverish episode 1 week before. The mother reported no other symptoms. Upon physical examination, the patient was pale and tachycardic. Her abdominal palpation showed hepatosplenomegaly and extremities with edema in the lower limbs and light scaling on the edges of her feet, suggestive of plantar pemphigus. Her mother had had a cesarean section due to non-progression of a normal birth. She was born at term, with a birth weight of 3.325 grams, with good vitality. Her prenatal care counted on 12 consultations and non-reactive tests for syphilis and HIV. Her toxoplasmosis serology had a positive IgG fraction, all in the first trimester. She had no other complications during pregnancy and birth. The patient was admitted to the hospital for investigation and was started on antibiotic therapy with Crystalline Penicillin and Gentamicin. Her blood count showed bicytopenia (Hb: 7.2, Platelets: 105,000), associated with leukocytosis with left shift. Her urinalysis revealed massive proteinuria and hemoglobinuria, without findings suggestive of urinary tract infection. Subsequently, the investigation was complemented with findings of hypoalbuminemia (1.85g/dL); and she had high protein/creatinine ratio in the urine (16; reference value for nephrotic levels: greater than 2), which defined the diagnosis of nephrotic syndrome, with additional findings of elevated cholesterol and triglycerides, in addition to normal C3. The method of measuring proteinuria through urinary ratio in an isolated sample was chosen due to greater technical ease because of the patient's young age. As the patient had severe hemolytic anemia with hemodynamic decompensation, transfusion of packed red blood cells was indicated, initially due to the presence of sequentially positive cross-tests. During the etiological investigation, VDRL 1/64 was found to be associated with neurological involvement with the presence of epileptic seizures (CSF evaluation with pleocytosis at the expense of lymphomononuclear cells and with negative VDRL), as well as positive IgM and IgG serologies for Toxoplasmosis, CMV, HSV 1 and 2 and Rubella. Furthermore, the infant also had a transfontanella ultrasound with an interventricular septum in the ventral horn of the lateral ventricle, which could be suggestive of congenital infection. Fundoscopy and BERA were unremarkable.

The patient developed further worsening of proteinuria and hypoalbuminemia after completing the complete regimen for congenital syphilis with post-neonatal treatment, and as evidence of positive urinary PCR for CMV (269 copies). We then decided to start treatment with Ganciclovir, carried out for 21 days, associated to enalapril due to its antiproteinuric effect. She showed progressive improvement in the edema and CMV copy number, as well as laboratory workup improvement, and was discharged from hospital for outpatient follow-up. During outpatient follow-up, she remained well, with no proteinuria, and serology for TORCHS was repeated - with evidence of negative VDRL, positive CMV IgG and negative IgM, and other non-reactive TORCHS (IgG and IgM).

DISCUSSION

Congenital syphilis still represents, especially in developing countries, an important cause of morbidity in the pediatric age group[5]. The diagnosis of congenital syphilis infection has been made in only 1-2% of women adequately treated during pregnancy, and observed in 70-100% of untreated pregnant women[6]. It is a preventable disease through the implementation of effective strategies for early diagnosis and treatment of syphilis in pregnant women and their sexual partners[5,6].

The signs and symptoms of congenital syphilis are nonspecific and frequently found in other congenital syndromes. They involve a variable clinical picture, which may involve gestational/perinatal changes, including miscarriages, prematurity and low birth weight; systemic involvement, such as fever, hepatosplenomegaly and generalized lymph node enlargement; hematological changes, including anemia, thrombocytopenia and variation in the number of leukocytes;

central, mucocutaneous and musculoskeletal involvement, in addition to other manifestations, such as pneumonitis and renal involvement[6]. Its relationship with kidney damage is already well established in the literature, and it can cause nephropathy with or without hematuria and proteinuria of different degrees. Nephrotic syndrome generally manifests itself from the 1st to the 4th month of life; and histological analysis can show deposits of immune complexes in the region of the glomerular basement membrane, mesangial proliferation and podocyte fusion and flattening[7,8]. Treatment with penicillin leads to the resolution of these changes, depending on the moment in which it is instituted – WIGGELINKHUIZEN et al., demonstrated that patients in whom treatment was started later presented glomerulosclerosis in more than half of the glomeruli on biopsy 6 months after the end of treatment[9].

The history of cytomegalovirus infection in the general population demonstrated by serology is also high, especially in developing countries; In Brazil, around 90-95% of women have already had primary CMV infection[6]. It has greater clinical importance in the context of immunosuppressed patients and in congenital infection - when there is viral detection within 3 weeks of life - and perinatal infection - with viral detection from the 4th to 12th week of life, considering that it can leave late consequences even in individuals who are initially asymptomatic. Although mostly asymptomatic in newborns, it can present as a variable condition with the presence or absence of hepatosplenomegaly, thrombocytopenia, central nervous system involvement, cholestasis, sensorineural hearing loss, among others[6]. CMV infection has been frequently reported in the literature in association with the CNS as its causative agent, always in line with other clinical manifestations of viral infections[10]. The mechanisms of kidney injury have not yet been well established, with direct injury by the virus or secondary to an immune response being suggested[4]. The most commonly described renal histological lesion is diffuse mesangial sclerosis, with or without the presence of viral inclusion bodies[10]. Diagnosis by isolation of viral DNA with polymerase chain reaction has good sensitivity and specificity; and treatment with ganciclovir can be efficacious[10]. It is currently suggested that patients with a genetic defect causing congenital nephrotic syndrome may be more susceptible to the occurrence of CNS secondary to CMV. Therefore, CMV infection does not exclude a genetic cause and, in particular, the lack of response to ganciclovir should lead to the need to investigate the underlying genetic cause[3].

In the reported case, the anemia presented by the patient showed characteristics of hemolysis, positive direct Coombs, in addition to positive cross-tests of the red blood cell concentrates ordered. There is an association between Treponema pallidum infection and autoimmune hemolytic anemia. Although the most common is hemolytic anemia with negative Coombs, which positivity is related to the Paroxysmal Cold Hemoglobinuria subtype (PCH). The peculiarity of this is hemolysis associated with high thermal amplitude[11]. We believe that the sequenced positivity of cross-matches may be related to the difficulty in handling and/or conserving these samples.

Regarding the therapeutic plan, treatment was initially carried out for congenital syphilis with subsequent need for treatment of CMV infection as well. The positive serological tests for the other TORCHS were attributed to cross-reaction, as already described in the literature, and there was also a record in prenatal care of positivity of the IgG fraction for Toxoplasmosis in the 1st trimester of pregnancy. In the case described, renal biopsy was not performed, since the patient had a clinical picture and positive serological tests for agents already recognized as causing CNS. The sustained clinical response during outpatient follow-up as well as the results of follow-up serology confirm the nosological etiology.

CONCLUSION

Congenital nephrotic syndrome, although rare, should always be considered in infants with edema. In populations such as the Brazilian, with a high prevalence of congenital infections, it is mandatory to investigate these as causes of this glomerulopathy, aiming for early diagnosis, with better treatment and prognosis for these patients.

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