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CASE REPORT

Renal-limited vasculitis in an 8-year-old child: Rare cause of rapidly progressive glomerulonephritis progressing to end-stage chronic kidney disease.

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Glomerulonephritis, Antibodies, antineutrophil cytoplasmic, Kidney failure, chronic, Anti-neutrophil cytoplasmic antibody-associated vasculitis.

Abstract

Glomerulonephritis is one of the main renal involvements in the pediatric age group, usually secondary to infection with group A beta hemolytic streptococcus. However, although rare, ANCA-related vasculitis can also be a cause of glomerulonephritis. The aim of this report is to describe a case of glomerulonephritis secondary to ANCA-related vasculitis, given its low incidence in childhood and the rapid evolution to chronic nephropathy in this case. L.E.F, 8 years old, female, mixed race, sought care due to macroscopic hematuria, anasarca, headache and arthralgia. On admission, he presented a hypertensive crisis, and in laboratory tests, a significant increase in urea and creatinine; Positive P-ANCA and anti-MPO. Hemodialysis, antihypertensives and pulse were started with Methylprednisolone (30mg/kg/day), followed by prednisolone at a dose of 2mg/kg/day. In addition, renal biopsy showed glomerular sclerosis and negative immunofluorescence. Diagnosis of Restricted Kidney Vasculitis was performed. She evolved stable, but with no improvement in her kidney function, requiring her to remain on hemodialysis and being referred to a kidney transplant outpatient clinic. Related ANCA vasculitis are divided into Granulomatosis with Polyangiitis, Eosinophilic Granulomatosis with Polyangiitis, Microscopic Polyangiitis, and Restricted Kidney Vasculitis. They are rare in the pediatric age group, but it is important to know about them, both in relation to their involvement of the upper and lower airways, as well as their renal involvement, so that the diagnosis can be made earlier, making the treatment and prognosis favorable .

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INTRODUCTION:

Glomerulonephritis (GN) is defined as glomerular injury and inflammation. The condition, also known as nephrotic syndrome, manifests as hematuria, edema, oliguria, and hypertension in many cases [1]. The causes can be primary when the condition is restricted to the kidneys or secondary in cases of systemic involvement [2]. The condition generally affects children and adolescents in developing countries after group A beta-hemolytic streptococcal infection (PSGN) [3]. However, other diseases, such as ANCA-associated vasculitis, may also precede the onset of GN in the pediatric population. This article describes the case of a girl diagnosed with glomerulonephritis secondary to ANCA-associated vasculitis, an occurrence of low prevalence in the pediatric age group. Our patient had severe involvement that progressed to chronic nephropathy one month after the onset of symptoms.

CASE REPORT

A previously healthy brown 8-year-old girl from Fortaleza, in the Brazilian northeastern state of Ceará, was taken to a pediatric emergency unit after having macroscopic hematuria for a month. She had symmetrical arthralgia in the wrists, elbows, and knees. Joint pain appeared 15 days after the onset of hematuria. The child also had headaches and edema in the abdomen and legs. In the initial examination, she had a blood pressure of 140 x 100 mmHg (above the 95+12 percentile for age and height), anasarca, and laboratory tests showing increased urea (150 mg/dl) and creatinine (6 mg/dl) levels. She was referred to the nephrology ward, where she was started on hemodialysis.

The diagnostic laboratory tests ordered showed she had normocytic normochromic anemia (Hb:7.9 g/dl, MCV:78 fl, MCH: 28pg), a WBC count of 7481/mm³ (neutrophils = 64% - 4787/mm³, lymphocytes = 24% - 1881/mm³, eosinophils = 6% - 448/mm³), a platelet count of 257,700/mm³; urinalysis was as follows: 2+ hemoglobin and 3+ protein, density 1015, pH 7.5, negative for nitrite, cloudy urine, discrete bacterial flora, granular (rare) and hyaline casts, 3 pyocytes per field, and numerous well-preserved red blood cells; total protein = 6g/dl and albumin = 3.1g/dl, ANA 1/80 with a dense fine speckled pattern (negative for Anti-Ro, Anti-La, Anti-Sm and Anti-DNA), Rheumatoid Factor < 9.69UI /ml (reference value: up to 15UI/ml), ASO = 238UI/ml (reference value: < 200UI/ml), negative for Anti-Cardiolipin, Beta-2-glycoprotein 1, and Lupus Anticoagulant, P-ANCA = 1/ 80, negative for C-ANCA and atypical ANCA, anti-myeloperoxidase (anti-MPO) = 55 U/ml (reference value: up to 3.5U/ml), CH50 = 49.5 U CAE (normal between 60-145 U CAE), C3 = 107mg/dl (reference value: 90-180mg/dl) and C4 = 28.5mg/dl (reference value: 10-40mg/dl). Serologies for parvovirus, EBV and cytomegalovirus showing reactive IgG and non-reactive IgM, for toxoplasmosis with non-reactive IgG and IgM, and for Herpes type 2 IgM was indeterminate. Rapid test and RT-PCR for COVID were negative. Ultrasound examination of the urinary tract revealed enlarged kidneys with a diffuse increase in echogenicity and preserved corticomedullary differentiation. A kidney biopsy was requested, and treatment with pulse steroid therapy with methylprednisolone (30mg/kg/day for three days) was started.

The kidney biopsy results showed 12 glomeruli, all with advanced sclerosis (Figure 1), some with indications of segmental disease and multiple Bowman's capsule adhesions (Figure 2), in addition to tubules with irregular areas of atrophy surrounded by moderate interstitial fibrosis and sparse lymphocytic infiltrate. Immunofluorescence revealed the absence of deposits of immunoglobulins, complement fractions, or fibrinogen.

The patient had nephritic syndrome for a month, which developed into severe dialysis-dependent kidney injury and chronic nephropathy, confirmed by a kidney biopsy. She

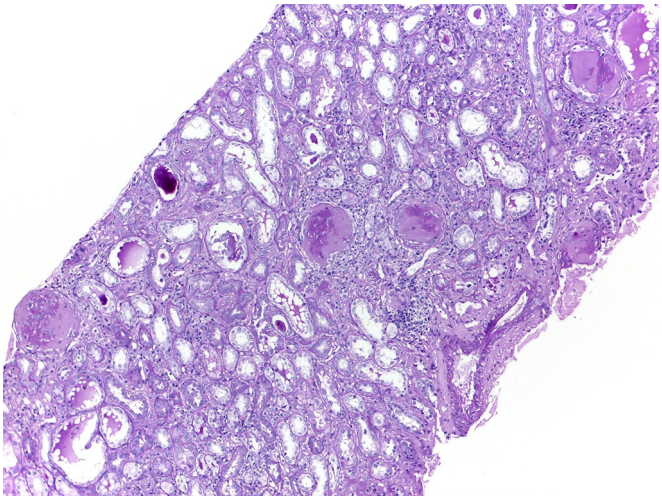

Figure 1. Globally sclerosed glomeruli, tubular atrophy and interstitial fibrosis (PAS - 100x)

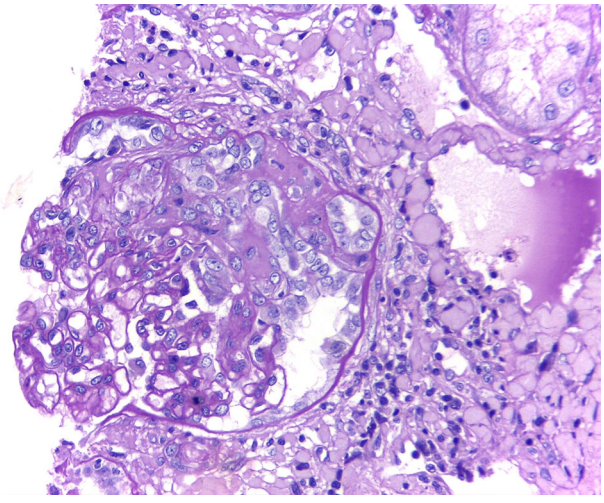

Figure 2. Segmental loss of glomerular architecture with fibrocellular crescent and rupture of Bowman's capsule (arrow) (PAS - 400x)

tested positive for P-ANCA and anti-MPO and negative for viral infection, consistent with ANCA-associated vasculitis. High-resolution computed tomography (CT) of the chest, CT of the facial sinuses, and CT angiography of the abdomen and chest were ordered, but none showed alterations. Therefore, the patient was diagnosed with ANCA-associated renal vasculitis.

She was discharged after 21 days of hospitalization after macroscopic hematuria subsided and blood pressure was controlled with antihypertensive medication. However, kidney function did not improve, and she remained on hemodialysis every other day. The patient was stable at discharge and was placed on a pre-kidney transplant monitoring program under the nephrology and pediatric rheumatology outpatient clinic

DISCUSSION

Glomerulonephritis linked to ANCA-associated vasculitis tends to be more prevalent in adults over 50 and males. It is a rather uncommon condition in individuals of pediatric age. Its incidence is yet to be determined since most of the data about this age group comes from cohort studies. However, French and Canadian studies have described an increase in the condition's incidence over the last 15-25 years [4, 5]. In the pediatric age range, girls are preferentially affected, and most cases occur between the ages of 12 and 14 years [6, 7]. Our patient developed the disease when she was only eight years old.

Individuals with ANCA-associated vasculitis present involvement of small vessels and a positive test for ANCA (anti-neutrophil cytoplasmic antibody), which can be ascertained using immunofluorescence showing a C-ANCA (predominantly cytoplasmic), P-ANCA (predominantly perinuclear) or atypical ANCA pattern. ELISA kits can be used to assess the presence of specific antigens such as anti-myeloperoxidase (anti-MPO), which generally correlates with P-ANCA, and anti-proteinase 3 (anti-PR3), which usually correlates with C-ANCA [8, 9].

This group of conditions includes granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with Polyangiitis (EGPA), microscopic polyangiitis (MPA), and renal vasculitis [8, 10]. The first two usually affect the upper airways [11, 12] (recurrent epistaxis, purulent secretion), while GPA also involves the lungs [11] (lung nodules, pulmonary cavities, persistent infiltrates). MPA can also affect the lung parenchyma and cause alveolar hemorrhage. EGPA usually presents with asthma, eosinophilia, and a history of atopy, in addition to chronic sinus disease and peripheral neuropathy [12], unlike renal vasculitis, which solely affects the kidneys.

The rapid development of the disease seen in our patient, along with the need to start dialysis due to extremely high initial urea and creatinine levels, pushed our early diagnostic suspicions toward rapidly progressive glomerulonephritis. As she tested positive for P-ANCA and anti-MPO and had a kidney biopsy without immune complex deposition, the possibility of rapidly progressive glomerulonephritis secondary to ANCA-associated vasculitis was considered. High-resolution chest and sinus CT scans were ordered to evaluate the respiratory tract and GPA or EGPA diagnostic signs. Since the patient did not present signs of either condition, the diagnosis of renal vasculitis was confirmed.

Our patient tested positive for P-ANCA (1/80) and anti-MPO (55 U/ml vs. a reference value > 5 U/ml), and the literature describes a strong correlation between the two and MPA and renal vasculitis. Kidney involvement is present in most cases where anti-MPO is positive, and sclerosis is generally seen in biopsy [8, 13, 14]. As many as 81% of patients with renal vasculitis test positive for anti-MPO [8]. Our patient's kidney biopsy showed signs of chronic involvement, as described in the literature. Individuals with GPA often test positive for C-ANCA and anti-PR3 and present with necrosis and granulomas on kidney biopsy [8, 13, 14].

More evidence is needed about treating pediatric ANCA-associated vasculitis, and prescriptions are often based on therapies delivered to adults. Patients with acute kidney injury are generally treated with steroid pulse therapy, including methylprednisolone (30mg/kg for three days, followed by prednisone or prednisolone 1-2mg/kg/day) and cyclophosphamide (500-1000 mg/m² every 3-4 weeks, usually for 3-6 months). Plasmapheresis may be chosen in specific cases associated with corticosteroid therapy and cyclophosphamide. Maintenance therapy includes mycophenolate mofetil or azathioprine for at least 12 to 36 months [10, 15]. However, if the patient's biopsy specimen contains signs of chronic kidney disease without signs of active inflammation or systemic involvement, immunosuppression is usually not needed. Kidney transplantation is the treatment of choice in these cases.

We opted to treat our patient with steroid pulse therapy with methylprednisolone. Her biopsy showed signs of chronic kidney disease, and she did not have active inflammation or systemic involvement. Therefore, she was not prescribed cyclophosphamide. The patient remained on prednisolone, with weaning planned during outpatient follow-up.

CONCLUSION

Glomerulonephritis secondary to ANCA-associated vasculitis is rare in pediatric patients. Knowledge of the condition is crucial to identifying symptoms early, initiating effective treatment, and improving the patient's prognosis. Late diagnosis often correlates with kidney biopsies with signs of chronic involvement and the need for kidney transplantation.

REFERENCES:

1. Mariani LH, Pendergraft WF 3rd, Kretzler M. Defining glomerular disease in mechanistic terms: Implementing an integrative biology approach in nephrology. Clin J Am Soc Nephrol. 2016;11(11):2054–60.
2. Kazi AM, Hashmi MF. Glomerulonephritis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2020.

3. Balasubramanian R, Marks SD. Post-infectious glomerulonephritis. Paediatr Int Child Health. 2017;37(4):240–7.
4. Jariwala MP, Laxer RM. Primary vasculitis in childhood: GPA and MPA in childhood. Front Pediatr. 2018;6:226.
5. Grisaru S, Yuen GWH, Miettunen PM, Hamiwka LA. Incidence of Wegener's granulomatosis in children. J Rheumatol. 2010;37(2):440–2.
6. Sacri A-S, Chambaraud T, Ranchin B, Florkin B, Sée H, Decramer S, et al. Clinical characteristics and outcomes of childhood-onset ANCA-associated vasculitis: a French nationwide study. Nephrol Dial Transplant. 2015;30 Suppl 1:i104-12.
7. Calatroni M, Oliva E, Gianfreda D, Gregorini G, Allinovi M, Ramirez GA, et al. ANCA-associated vasculitis in childhood: recent advances. Italian journal of pediatrics. 2017;43:1–9.
8. Jennette JC, Nachman PH. ANCA glomerulonephritis and vasculitis. Clin J Am Soc Nephrol. 2017;12(10):1680–91.
9. Csernok E, Moosig F. Current and emerging techniques for ANCA detection in vasculitis. Nat Rev Rheumatol. 2014;10(8):494–501.
10. de Graeff N, Groot N, Brogan P, Ozen S, Avcin T, Bader-Meunier B, et al. European consensus-based recommendations for the diagnosis and treatment of rare paediatric vasculitides–the SHARE initiative. Rheumatology. 2019;58(4):656–71.
11. Greco A, Marinelli C, Fusconi M, Macri GF, Gallo A, De Virgilio A, et al. Clinic manifestations in granulomatosis with polyangiitis. Int J Immunopathol Pharmacol. 2016;29(2):151–9.
12. Furuta S, Iwamoto T, Nakajima H. Update on eosinophilic granulomatosis with polyangiitis. Allergol Int. 2019;68(4):430–6.
13. Lionaki S, Blyth ER, Hogan SL, Hu Y, Senior BA, Jennette CE, et al. Classification of antineutrophil cytoplasmic autoantibody vasculitides: the role of antineutrophil cytoplasmic autoantibody specificity for myeloperoxidase or proteinase 3 in disease recognition and prognosis. Arthritis Rheum. 2012;64(10):3452–62.
14. Zonozi R, Niles JL, Cortazar FB. Renal involvement in antineutrophil cytoplasmic antibody-associated vasculitis. Rheum Dis Clin North Am. 2018;44(4):525–43.
15. Plumb LA, Oni L, Marks SD, Tullus K. Paediatric anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis: an update on renal management. Pediatr Nephrol. 2018;33(1):25–39.