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CASE REPORT

A progressive ANCA associated glomerulonephritis leading to chronic kidney disease and stroke in a child with congenital heart disease: a case report

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ABSTRACT

Nephrotic-nephritic syndrome in children is a rare but significant cause of chronic kidney disease (CKD). This case highlights a challenging diagnostic and therapeutic course involving persistent hematuria, ANCA positivity, refractory hypertension, and cerebrovascular complications. A 10-year-old female, post-patent ductus arteriosus (PDA) closure, presented with generalized swelling, hematuria, and proteinuria. Initial workup suggested post-infectious glomerulonephritis (PIGN) with persistently low complement levels (C3, C4), and she was managed with diuretics. However, recurrent episodes led to further evaluation, revealing PR3-ANCA positivity, nephrotic-range proteinuria, and progressive renal dysfunction. Despite treatment, she developed refractory hypertension and an intracranial hemorrhage. The absence of renal biopsy posed challenges in definitive diagnosis, and the patient is now on dialysis.

This case underscores the diagnostic challenges in differentiating between PIGN, ANCA-associated glomerulonephritis, and rapidly progressive glomerulonephritis (RPGN) in pediatric patients. The interplay between congenital heart disease and renal dysfunction highlights the need for interdisciplinary management. Early biopsy in recurrent nephrotic-nephritic cases is crucial to prevent irreversible renal damage. The case emphasizes the need for early renal biopsy and comprehensive management of pediatric nephrotic-nephritic syndrome with persistent proteinuria and hematuria.

INTRODUCTION

Nephrotic-nephritic syndrome is a rare but serious pediatric condition characterized by proteinuria, hematuria, and renal dysfunction. While post-infectious glomerulonephritis (PIGN) is more common, persistent hematuria and nephrotic-range proteinuria necessitate further investigation for alternative etiologies, including ANCA-associated glomerulonephritis (AAGN) and rapidly progressive glomerulonephritis (RPGN). AAGN is an uncommon but aggressive form of glomerulonephritis in children, with an increasing annual incidence in recent years.[1] Fortunately, mortality rates in pediatric AAV remain low (5–10%).[2] Despite advancements in immunosuppressive therapy, renal prognosis remains poor, with over half of pediatric AAGN patients progressing to chronic kidney disease (CKD) within a year.[1] Additionally, overlapping features between ANCA vasculitis, immune-complex GN, and cardiorenal dysfunction can further complicate diagnosis and treatment, often leading to delays in targeted intervention.

Here, we present a unique case of pediatric nephrotic-nephritic syndrome with PR3-ANCA positivity, initially misdiagnosed as post-infectious glomerulonephritis, later progressing to refractory hypertension, cerebrovascular complications, and end-stage kidney disease (ESKD). This case highlights diagnostic pitfalls, challenges in management, and the devastating consequences of missed early recognition in pediatric AAGN.

CASE REPORT

A 10-year-old female from Janakpur, with a past history of Patent Ductus Arteriosus (PDA) closure two years prior, presented with generalized swelling beginning from the face and later involved the legs, accompanied by red-colored urine for two days. Her blood pressure was normal, and laboratory investigations revealed hematuria, proteinuria (urine albumin

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2.2 g/day), persistently low C3 and C4 levels, and a positive ASO titer. Autoimmune markers, including ANA and anti-dsDNA, were negative. She was admitted with a provisional diagnosis of PIGN and managed symptomatically with furosemide. Her symptoms improved, and she was discharged.

One month later, she presented with similar complaints of anasarca and hematuria. Laboratory investigations showed persistent proteinuria and hypercholesterolemia (284 mg/dL). With a provisional diagnosis of nephrotic-nephritic syndrome, she was started on prednisolone. However, her swelling and hematuria persisted, despite normal blood pressure. The patient defaulted treatment, and at discharge, her serum creatinine was 0.6 mg/dL, and urine protein-creatinine ratio (PCR) was 70 mg/mmol.

Two months later, she was evaluated at a cardiac center for anasarca and was diagnosed with cardiac failure (elevated Troponin I). After stabilization, she was referred to a nephrology center, where persistent nephrotic-range proteinuria and hematuria were noted. Investigations revealed serum creatinine of 0.9 mg/dL, PR3-ANCA 7 IU/mL (Positive when > 2IU/mL), MPO-ANCA 1 IU/mL (normal when <3.4 IU/mL), and NT-proBNP >35,000 pg/mL. Renal ultrasound showed loss of corticomedullary differentiation, suggestive of CKD. Additional investigations revealed elevated iPTH (388.8 pg/mL) and low vitamin D levels (18.1 ng/mL).

The patient subsequently developed refractory hypertension requiring multiple antihypertensives, including furosemide, hydrochlorothiazide, spironolactone, enalapril, and labetalol infusion. She later developed right-sided hemiparesis, and a CT scan of the head revealed acute-on-chronic intracranial hemorrhage. She is currently undergoing dialysis but has since been lost to follow-up. Renal biopsy could not be performed because of financial constraints and patient non-compliance.

DISCUSSION

This case highlights a rare and complex interplay between nephrotic-nephritic syndrome, PR3-ANCA positivity, refractory hypertension, cardiorenal syndrome, and cerebrovascular complications in a pediatric patient. The progression from recurrent glomerulonephritis to CKD, hypertensive crisis, and stroke highlights critical challenges in early diagnosis and optimal management strategies.

ANCA-associated glomerulonephritis (AAGN) is a rare but significant cause of rapidly progressive glomerulonephritis (RPGN) and CKD. While its incidence is well-characterized in adults, pediatric cases remain exceedingly uncommon.[1] Unlike in adults, where AAV is more common in males, pediatric AAV exhibits a female predominance and typically presents in the early second decade of life, with a median age at diagnosis of 11–14 years, approximating the age of case presented.[2]The annual incidence of PR3-AAGN in adults is estimated at 0.5 per 100,000 population, with MPO-AAGN being more common at 1.5 per 100,000.[3] The low prevalence in children emphasizes diagnostic challenges and the need for early renal biopsy in persistent or atypical glomerulonephritis presentations.

The persistently low C3/C4 levels in this case argue against classical ANCA-associated vasculitis, which typically has normal complement levels, and instead suggest an immune complex-mediated process, but overlap syndromes and immune-complex mediated ANCA vasculitis are recognized enemies. Unfortunately, renal biopsy which could distinguish between ANCA-associated vasculitis, immune-complex glomerulonephritis, and other RPGN mimics, could not be performed in this case.

The interaction between congenital heart disease (CHD), cardiac failure, and CKD in this patient highlights the phenomenon of cardiorenal syndrome (CRS), where dysfunction in one organ exacerbates pathology in the other. Approximately 25-63% of heart failure patients exhibit some form of CRS,[4] making it a critical consideration in pediatric patients with CHD and renal dysfunction. The markedly elevated NT-proBNP (>35,000 pg/mL) likely reflects both volume overload and impaired renal clearance, as CKD is known to elevate NT-proBNP levels beyond that seen in heart failure alone.[5]

Additionally, secondary hyperparathyroidism (iPTH 388.8 pg/mL) and vitamin D deficiency may have further exacerbated vascular dysfunction, hypertension, and CKD progression. Early recognition of CRS in pediatric patients with both cardiac and renal disease is crucial, as delayed intervention may accelerate CKD progression and increase cardiovascular morbidity.

The child developed severe hypertension requiring multiple antihypertensive agents, including labetalol infusion, yet remained uncontrolled, suggesting refractory hypertension (RfH). This severe subtype of resistant hypertension, defined as uncontrolled BP despite ≥5 antihypertensives, including spironolactone and a thiazide diuretic, is associated with a high risk of target organ damage, including stroke.[6]

The acute-on-chronic intracranial hemorrhage in this child is particularly concerning, as hypertensive crisis in CKD patients predisposes them to cerebrovascular events. The combination of CKD, secondary hyperparathyroidism, and refractory hypertension likely created a high-risk environment for stroke, highlighting the importance of aggressive blood pressure control and early intervention in such patients.

CONCLUSION

This case highlights the importance of early renal biopsy in children with recurrent or persistent nephrotic-nephritic syndrome. PR3-ANCA positivity in pediatric patients should prompt consideration of AAGN and early immunosuppressive therapy. Additionally, aggressive management of hypertension is crucial in CKD to prevent severe end-organ damage. Recognition and treatment of secondary hyperparathyroidism in CKD are also essential. A multidisciplinary approach involving nephrology, cardiology, and neurology is vital for optimizing outcomes in such complex cases.

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