Case Report

Acute Post-Streptococcal Glomerulonephritis in a Known Nephrotic Syndrome Patient: A Case Report.

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ABSTRACT

Nephrotic syndrome (NS) is one of the most common childhood kidney diseases. Idiopathic NS (INS) can affect children of any age from infancy to adolescence and predominantly occurs in those aged 1–6 years.

Acute glomerulonephritis (AGN) is a disease characterized by edema, oliguria, hematuria, and hypertension. It characterized by inflammation of the glomerulus with proliferation of cellular elements secondary to an immunologic mechanism. Acute post-streptococcal glomerulonephritis (APSGN) results from an antecedent infection of the skin (impetigo) or throat (pharyngitis) caused by nephritogenic strains of group A beta-hemolytic streptococci.

Here we present a case of APSGN in a patient with known steroid dependent INS.

Key words: Nephrotic syndrome, Poststreptococcal glomerulonephritis, Minimal change disease

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INTRODUCTION

Nephrotic syndrome (NS) is one of the most common childhood kidney diseases. The prevalence of childhood NS worldwide is approximately 16 cases per 100,000 children, with an incidence of 2 to 7 cases per 100,000 children. Idiopathic NS (INS) can affect children of any age from infancy to adolescence and predominantly occurs in those aged 1– 6 years **[1-4].**

Acute glomerulonephritis (AGN) is a disease characterized by edema, oliguria, hematuria, and hypertension. It is characterized by inflammation of the glomerulus with proliferation of cellular elements secondary to an immunologic mechanism. **[5, 6].** Acute post-streptococcal glomerulonephritis (APSGN) results from an antecedent infection of the skin (impetigo) or throat (pharyngitis) caused by nephritogenic strains of group A beta-hemolytic streptococci **[7, 8]**. Nephritogenicity is mainly restricted to certain M protein serotypes (i.e., 1, 2, 4, 12, 18, 25, 49, 55, 57, and 60) that have shown nephritogenic potential **[9]**.

Here we present a case of APSGN in a patient with known steroid dependent INS.

CASE REPORT

A 14-year old male patient, is a known case of NS following-up in the Pediatric Nephrology Clinic in Alexandria University Children's Hospital. He presented at the age of 6 years with manifestations of NS. At presentation (May 2014), the boy was normotensive, had no hematuria, and had normal complement 3 (C3) and 4 (C4) levels. Although he was steroid-responsive, he was steroid-dependent with frequent relapses on high doses of steroids and developed steroid toxicity. The patient received 3 months of oral cyclophosphamide (cumulative dose=180 mg/kg) but he continued to suffer from frequent relapses on high doses of steroids. Kidney biopsy was done and revealed minimal change disease (MCD) by light microscopy **(Figure 1)**, and negative staining by immunofluorescence microscopy.

Cyclosporin A (CSA) was started together with gradual steroid withdrawal. The boy responded well with no further relapses and stopped all medications in August 2019. The boy was in complete remission during follow-up visits for 3 consecutive years.

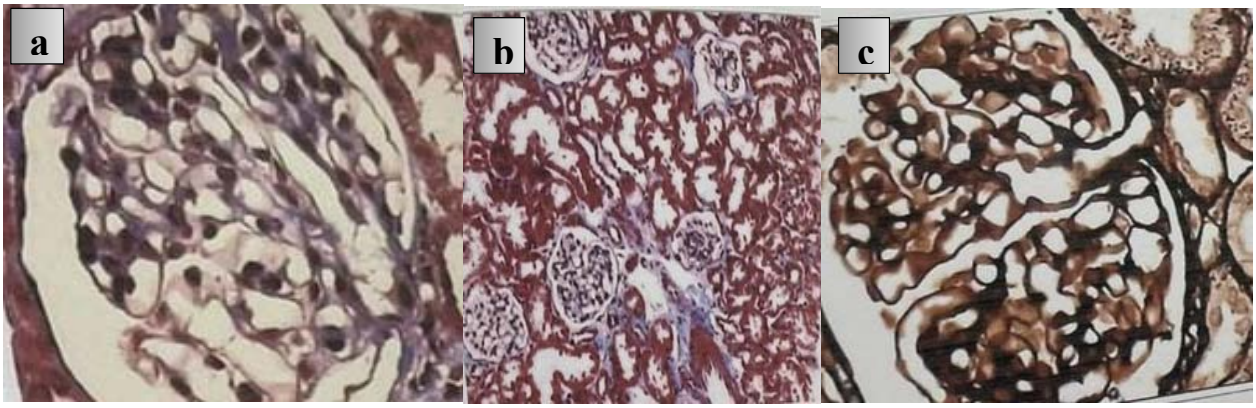

Figure 1: **(a)** glomerulus appear normal as regards basment membranes, celluarity and mesangium. **(b)** No tubular atrophy, no interstitial fibrosis or inflammatory infiltrate. **(c)** Silver stain does not show any basement membrane abnormalities.

In November 2022, the patient presented to us with a 2-day complaint of eye puffiness, 2 days later the boy developed hematuria, headache and persistent vomiting. His urine output (UOP) was about 0.7 mL/kg/hr and his blood pressure was 160/120 mmHg. He was admitted to the pediatric intensive care unit (PICU) on intravenous nitroglycerin infusion as well as intravenous furosemide as he was oliguric with circulatory overload (Inferior vena cava diameter was 18 mm with poor collapsibility). There was no evidence of renal vein thrombosis by urgent doppler on renal blood vessels. Computed tomography of the brain was unremarkable and fundoscopy was free. There were multiple pigmented lesions on the chin of both lower limbs due to previous skin abscesses 1 month earlier **(Figure 2)**. Based on these clinical features, the diagnosis of acute glomerulonephritis was suggested, and specific laboratory testing was performed to establish the diagnosis.

LABORATORY FINDINGS

Table 1 summarizes the laboratory findings. Urine analysis revealed 2+ proteins, RBCs casts, as well as innumerable RBCs/ HPF (Dysmorphic RBCs were 45% and acanthocytes were 7%). Serum creatinine was 0.74 mg/dL and serum albumin was 3.4 g/dL.

Immunological markers showed low serum C3 (3.5 mg/dL) which was repeated for confirmation and was 5.2 mg/dL, normal C4, and negative antinuclear antibodies (ANA) and anti-double stranded DNA antibodies (anti-dsDNA). Anti-streptolysin O titer (ASOT) was elevated (679 U/ml). Hence a diagnosis of post-streptococcal glomerulonephritis was made.

CLINICAL COURSE

In the PICU, blood pressure was controlled, IV antihypertensive medication was gradually withdrawn and the patient was discharged to the ward. During follow-up in the ward, UOP gradually improved, gross hematuria disappeared, and blood pressure normalized. Kidney biopsy was not done due to absence of its indications and due to rapid clinical improvement after blood pressure control. Six weeks after the admission, renal functions were normal, glomerular filtration rate was 109 mL/1.73m^2/min, there was no proteinuria (protein/creatinine ratio was 0.12). Urine analysis showed only microscopic hematuria (RBCs 8-10/HPF). Follow-up C3 was normal (106 mg/dL).

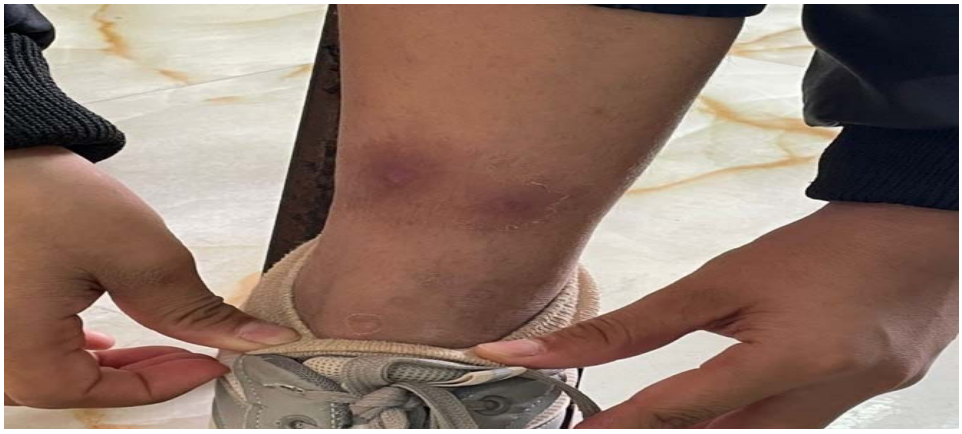

Figure 2: Evidence of healing skin abscesses on the lower limb.

Table 1: Summary of the laboratory findings

Laboratory investigation	Result
Hemoglobin	11.5 g/dL
White blood cell count	4.25 10^3/µL
Platelets	177 10^3/µL
Serum Albumin	3.4 g/dL
BUN	23 mg/dL
Serum Creatinine	0.74 mg/dL
Na	138 mmol/L
K	5.1 mmol/L
CRP	4.3 mg/L
C3	3.5 mg/dL, confirmation 5.2 mg/dL (N.90-180)
Follow-up C3 after 6 weeks	106 mg/dL (N. 90-180)
C4	20.9 mg/dL (N.10-40)
ANA	Negative
Anti-dsDNA antibodies	Negative
ASOT	Positive (679 U/mL)
Urine analysis	
Sp. Gravity	1030
Protein	+2
RBCs	Innumerable/HPF
WBCs	30-35/HPF (Urine culture: negative)
Casts	RBCs casts
Dysmorphic RBCs	Positive
Protein/ creatinine ratio	0.7

DISCUSSION

In children, the most common cause of NS is idiopathic nephrotic syndrome (INS) [3]. The most prevalent pathology of INS in children is minimal-change disease (MCD) [10]. Fortunately, the majority of children have steroid-sensitive nephrotic syndrome (SSNS). However, 60–80% of them do relapse [11]. Up to 50% of children with NS develop steroid-dependent NS (SDNS) and require steroid-sparing agents [12].

APSGN most frequently presents in children 1 to 2 weeks after a sore throat, or 6 weeks after a skin infection (impetigo) [13]. The annual incidence of new cases of PSGN in developing countries ranges from 8.5 to 28.5 per 100000 individuals [14]. Over the past three decades, PSGN incidence has significantly dropped in developed countries, while higher incidence is still present in developing countries [15]. The disease is more frequent in children aged 2-12 years, with a peak prevalence in individuals aged approximately 5-6 years [16].

Against the well-known medical rule that each patient should have one diagnosis, we report a case of APSGN in a known case of NS, with a steroid dependance pattern and MCD on kidney biopsy. On reviewing the literature, many cases of APSGN were reported to develop nephrotic syndrome during the illness or even present with nephrotic syndrome in different age groups [17-22] but this was not the situation in our case. Few cases with IgA nephropathy who complicate with APSGN were also reported [23-26]. While no reports describe the possibility of APSGN presentation in a patient with underlying MCD in remission. To support this unusual diagnosis, there are several points that we need to highlight.

Firstly, our patient did not have any nephritic manifestations throughout the

duration of his follow-up, which was more than 8 years. In each follow-up visit, patient's blood pressure was routinely check, urine dipstick for assessment of proteinuria, as well as for absence or presence of hematuria was done, laboratory investigations like serum creatinine, blood urea nitrogen and urinary protein/creatinine ratio were also done. His follow-up visits were as frequent as every 1-3 months. Therefore, we can confidently state that such nephritic manifestations were not present before.

Additionally, the patient had a latent period of 4 weeks between the appearance of his skin infection and the development of his nephritic manifestations, which is a typical latent period in case of post impetigo APSGN.

Presence of a possible thromboembolic complications precisely renal vein thrombosis was excluded, as the patient was in remission and doppler assessment of the renal vessels was free.

Lastly, these nephritic manifestations subsided completely. Hypertension subsided and antihypertensives were stopped, renal functions and GFR were normal. Urine analysis was normal except for microscopic hematuria (8-10 RBCs/HPF). Serum C3 normalized after 6 weeks, matching the clinical course of a self-limited case of APSGN.

CONCLUSION

We should have a high index of suspicion for APSGN in any patient presenting with hypertension, renal impairment, and oliguria even if the patient is being followed up in a Pediatric Nephrology specialized Clinic for another diagnosis.

ABBREVIATIONS

AGN	Acute Glomerulonephritis	CSA	Cyclosporin A
APSGN	Acute PostStreptococcal Glomerulonephritis	GFR	Glomerular Filtration Rate
		INS	Idiopathic Nephrotic Syndrome
ASOT	Anti Streptolysin O Titre	MCD	Minimal Change Disease
ANA	Anti Nuclear Antibody	NS	Nephrotic Syndrome
Anti-ds DNA	Anti-	UOP	Urine output
C_3	Complement 3	PICU	Pediatric Intensive care Unit
C_4	Complement 4		

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AUTHORS' CONTRIBUTIONS

The submitted manuscript is the work of the author & co-authors.

All authors have contributed to authorship, have read and approved the manuscript.

Acquisition of data: All authors

Analysis and/or interpretation of data: Last author

Drafting the manuscript: All authors.

Revising the manuscript critically for important intellectual content: Last author

Approval of the version of the manuscript to be published: All authors.

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This study protocol and the consents were approved and deemed sufficient by the Ethical Committee of Alexandria University Hospital and informed written consent was obtained from the legal guardian.

Consent for publication

"Not applicable"

Availability of data and material

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Conflict of interest

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