



## POSTSTREPTOCOCCAL GLOMERULONEPHRITIS WITH ATYPICAL SKIN RASH – DIFFERENTIAL DIAGNOSIS

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**Abstract:** Poststreptococcal glomerulonephritis is a rare condition in developed countries. Skin rash is a common symptom associated with a variety of diseases. Due to non-specific features of poststreptococcal glomerulonephritis, the condition requires a broad differential diagnosis.

A case is presented involving a 19-year old woman who was admitted to the hospital after pharyngeal infection, with symptoms indicative of acute kidney injury. The patient exhibited lower limb oedema, dyspnoea, hypertension and an atypical skin rash. The patient was diagnosed with poststreptococcal glomerulonephritis. Therapeutic interventions, including antibiotic therapy and symptomatic treatment, resulted in complete recovery.

This case highlights the importance of accurately determining the etiology of symptoms, as skin rash is an uncommon manifestation in poststreptococcal glomerulonephritis. The patient's perspective and a thorough interview are of critical value. A broad differential diagnosis and multidisciplinary approach are crucial for establishing the correct diagnosis.

**Keywords:** postinfectious glomerulonephritis, poststreptococcal glomerulonephritis, skin rash, proteinuria, haematuria

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## INTRODUCTION

Postinfectious glomerulonephritis (PIGN) is a type of glomerular injury associated with a previous infection, most commonly streptococcal pharyngitis or impetigo, and is referred to as poststreptococcal glomerulonephritis (PSGN). PSGN is an immune complex-mediated disease caused by nephritogenic strains of streptococci. Its pathophysiology may involve glomerular deposition of immune complexes formed in circulation or in proximity to the glomerular basement membrane (GBM), causing in situ immune complex diseases. Additionally, autoimmune reactivity — possibly triggered by streptococcal neuraminidase secretion — may contribute to the pathogenesis of the condition [8].

The incidence of PSGN is very low in Central Europe due to advancements in medical care. It increasingly affects elderly patients, particularly those with debilitating comorbidities [7]. PSGN frequently presents as acute nephritic syndrome 1 to 4 weeks after the initial infection. Clinical features of this condition include haematuria, usually mild proteinuria, oedema, mild hypertension and renal insufficiency. These manifestations generally subside spontaneously; treatment involves antibiotic therapy and focuses on symptomatic management. However, in some patients, proteinuria or haematuria may persist for several years [4].

This case report presents an unusual manifestation of PSGN associated with an atypical skin rash in a young adult woman, highlighting the importance of differential diagnosis and multidisciplinary medical care for patients affected with this condition.

## CASE REPORT

A previously healthy 19-year-old female was admitted to the authors' department for diagnostic evaluation of proteinuria and haematuria. Upon admission, PSGN or an autoimmune disease was suspected.

At the beginning of September, the patient experienced an acute pharyngeal infection accompanied by fever, musculoskeletal pain and a one-day episode of wrist stiffness. Particular attention was drawn to a macular rash located on the medial aspects of both thighs. Ambulatory antibiotic therapy with azithromycin and symptomatic treatment was provided. Following temporary improvement, fever and right-sided lymphadenopathy developed. The patient was then admitted to the Infectious Diseases Department in a regional hospital with suspected mononucleosis. During hospitalisation, the patient experienced transient dyspnoea, oede-

ma of the lower limbs, foamy urine and purpura of the face, neck, thoracic cage and limbs. Neither atopy nor allergies were present. Physical examination revealed the presence of bilateral pleural fluid and elevated blood pressure.

Laboratory tests revealed elevated levels of inflammatory markers, D-dimers (2806 ng/ml) and anti-streptolysin O (ASO - see table 1). Serum creatinine was increased (1.3 mg/dl), followed by gradual normalization (to 0.6 mg/dl). Hypoalbuminemia was observed (min. 2.9 g/dl) and elevated 24-hour urinary protein excretion (Table 1), indicating acute kidney injury. Ultrasound examination showed multiple enlarged lymph nodes in the head and neck region. A thoracoabdominal CT scan revealed pleural fluid (up to 29 mm on the right and up to 17 mm on the left), a small amount of intraperitoneal fluid, pancreatic enlargement with obliteration of peripancreatic fat planes, thickening of the gallbladder wall and kidneys of normal size. Echocardiography was performed twice. Both examinations showed small mitral and tricuspid valve regurgitation with an ejection fraction of 65%–68%. Treatment with cefuroxime, low-molecular-weight heparin, albumin supplementation and oxygen therapy led to a significant improvement of the patient's condition.

On admission to the clinical department, the patient did not report any complaints and her body temperature was normal. Physical examination revealed no abnormalities; blood pressure was normal, and neither rash nor purpura were present. During hospitalisation, the patient reported transient, non-pruritic, painless purpuric skin lesions on the head, neck, thoracic cage and upper limbs, which subsided spontaneously after approximately after one hour. Laboratory tests revealed persistent leukopenia with neutropenia as well as anaemia, reticulocytopenia, and normal platelet count. Urinalysis demonstrated proteinuria, haematuria and an elevated albumin/creatinine ratio (ACR 295.4 mg/g normal <30 mg/g), while serum creatinine and blood urea nitrogen (BUN) and C-reactive protein (CRP) levels remained within normal ranges. Tests for EBV, CMV, HBV, HIV were negative. Serum immunoglobulins concentrations within normal limits, with the exception of an elevated immunoglobulin G (IgG) level. However, serological tests for antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), anti-dsDNA and anti-glomerular basement membrane (anti-GBM) antibodies were negative, excluding systemic autoimmune disease. Complement C3 level was decreased, while C4 remained within the normal

Tab. 1. Laboratory tests.

Hospitalisation		I		II		III		Normal and unit
Date		25.09	11.10	13.10	16.10	25.11	26.11	
Serum	HGB	10.7	10.7	10.1	11.3	12.8	11.3	12.0 - 15.1 g/dl
	WBC	-	3.37	3.41	4.22	4.94	4.97	4.30 - 9.64 x 10 <sup>9</sup> /l
	NEUT w.b	-	1.28	0.94	1.63	2.2	2.85	1.93 - 5.87 x 10 <sup>3</sup> /μL
	phosphorus	-	4.6	-	-	5.5	-	2.6 - 4.5 mg/dl
	ASO	1703	3410	-	-	-	-	<200 IU/ml
	C3	-	62	-	-	97	-	90 - 190 mg/dl
	IgG	-	-	1920	-	-	-	700 - 1600 mg/dl
	protein	100		15				0 mg/dl
	protein (24h urinalysis)	2.5 - 3		0.591		-		g/24h
	erythrocytes	-	495	-	-	344	-	<30.7/μL

HGB – haemoglobin; WBC – white blood cell; NEUT – neutrophils; ASO - Anti-streptolysin O antibodies; C3 – complement C3; IgG – immunoglobulin G



Fig. 1. Skin rash during hospitalisation (left) and after recovery (right).

range. Parameters of iron metabolism and thyroid function were within normal limits. At discharge, the patient was advised to take an angiotensin-converting enzyme (ACE) inhibitor and supplement vitamin D, iron and calcium. After a few weeks, the ACE inhibitor was discontinued due to hypotension and malaise. Subsequently, serological parameters returned to normal without further pharmacological intervention.

In November, a second hospitalisation took place in the department for a scheduled diagnostic biopsy of the left kidney. The patient reported good health and no infections and oedema. However, she noted the recurrence of medium-sized macular skin lesions, limited to the thoracic cage, which resolved spontaneously after a short period and appeared to have been associated with her emotional stress. She also reported experiencing a similar rash prior to the onset of the infection.

These features may suggest urticaria as the most probable diagnosis. No significant abnormalities were found during physical examination. Laboratory tests demonstrated normalisation of the blood count and complement levels, along with a reduction of proteinuria and haematuria. A diagnostic biopsy of the left kidney was performed after contraindications had been excluded. Subsequently, a follow-up blood test revealed mild anaemia. Ultrasound examination showed irregular, hypoechogenic lesions below the lower pole of the left kidney, consistent with a hematoma. No other abnormalities were detected.

The microscopic image of the biopsy was non-specific, suggesting glomerulonephritis in regression phase and revealed mesangial proliferation. Electron microscopy revealed a reduction in the number of podocytes, as along with flattening of their foot processes, which were detached from

the glomerular basement membrane (GBM) over short segments. Immunofluorescence staining for IgG,  $\lambda$  and  $\kappa$  free light chains showed enhancement of GBM and thin basement membrane (TBM) pattern; however, immune deposits were not observed.

Based on the biopsy results and clinical improvement, the patient was diagnosed with PSGN. Four months later, the patient reported complete resolution of symptoms, with the exception of the skin rash, which did not affect her well-being. Further treatment was deemed unnecessary; however, a follow-up appointment was scheduled.

## DISCUSSION

This case report presents an atypical presentation of PSGN. The diagnosis was supported by the temporal association with the preceding infection, decreased serum C3 levels, elevated anti-streptolysin O (ASO) and the presence of nephritic syndrome [4]. However, histopathological analysis of the renal biopsy did not reveal C3 deposits typically associated with PSGN. Instead, it indicated glomerulonephritis in the regression phase, suggesting that histopathological evaluation might have been performed too late to detect immune complexes. Moreover, earlier assessment of serum C3 might have facilitated a quicker diagnosis. Elevated ASO levels imply the presence of a streptococcal infection and poststreptococcal glomerulonephritis. Although this condition has been historically associated with the paediatric population, its epidemiological profile in developed countries now more commonly involves elderly patients with comorbid illnesses, including chronic ones [8]. Therefore, the case of this young adult patient is notable from an epidemiologic perspective. PSGN frequently develops as a complication of streptococcal pharyngitis. Upper respiratory tract infections are common among flight crew members, who often tend to disregard the need for medical consultation [5]. This increases the risk of post-infectious complications, which should be considered — alongside urinary tract infections — during the diagnostic work-up of proteinuria [10]. Accordingly, aviation physicians should pay particular attention to upper respiratory tract infections in this patient population.

Immunoglobulin A vasculitis (IgAV, also called Henoch-Schoenlein purpura) was a major consideration in the differential diagnosis due to the patient's age and the presence of macular rash on lower extremities. Moreover, IgAV may be as-

sociated with infection, as well as systemic disease, and often leads to glomerulonephritis and nephritic syndrome due through to the formation of immune complexes containing complement component C3, which was also observed in this case [3]. However, the rash observed in the patient was not typical for IgAV [1,6] and more closely resembled urticaria, as it appeared and resolved rapidly. Additionally, the association with stress suggested atypical cholinergic urticaria as the patient did not report itching and any relation to sweating or warming [2]. As a result, a dermatological appointment was recommended for further evaluation. Systemic lupus erythematosus (SLE) was also considered, as it may present with both skin lesions and glomerulonephritis. The patient's age and sex corresponded to the typical demographic for SLE onset and the rash appeared in areas exposed to ultraviolet radiation during sunny weather — another feature consistent with the disease. Moreover, the patient demonstrated leukopenia and anaemia which further supported this suspicion. Nevertheless, negative ANA tests excluded SLE according to current classification criteria [1]. C3 glomerulopathy was another diagnostic consideration based on the glomerulonephritis symptoms in our patient and the decrease in serum C3. However, normalisation of serum C3 in follow-up testing and the absence of immune deposits on the biopsy excluded this diagnosis which is clinically relevant, as both histopathological and clinical differentiation between PSGN and C3 glomerulopathy is often difficult and requires repetitive serum C3 evaluation of serum C3 level [9].

## CONCLUSIONS

In conclusion, this case highlights the critical importance of distinguishing the etiology of symptoms, whether they are attributable to a current diagnosis or previous conditions, as exemplified by the skin rash. The patient's perspective and through medical history play a significant role in this differentiation. Non-specific symptoms such as skin lesions and hypocomplementemia in the context of AKI require a broad differential diagnosis and multidisciplinary approach to patient care. Furthermore, up-to-date knowledge on the dynamically evolving epidemiology is essential in the diagnostic process, particularly in aviation medicine, where establishing a precise diagnosis is crucial not only for the well-being of pilots but also their future professional eligibility.

## AUTHORS' DECLARATION

**Study Design:** Paulina Jastrzębska, Marcel Kempieński, Elżbieta Głuch, Stanisław Niemczyk. **Data Collection:** Paulina Jastrzębska, Marcel Kempieński, Elżbieta Głuch, Stanisław Niemczyk. **Manuscript Preparation:** Paulina Jastrzębska, Marcel Kempieński, Elżbieta Głuch, Stanisław Niemczyk. The authors declare that there is no conflict of interest.

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