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Pediatric granulomatosis with polyangiitis presenting with acute kidney injury: A case report and management challenges

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Abstract. *Granulomatosis with polyangiitis (GPA) is a rare ANCA-associated vasculitis in children, often characterized by severe multisystem involvement and diagnostic challenges. We report a case of a 17-year-old female evaluated at the Department of Pediatric Rheumatology and Autoinflammatory Diseases of the SI "Academician Lukyanova Institute of Pediatrics, Obstetrics and Gynecology of the NAMS of Ukraine" (Kyiv, Ukraine). The disease initially manifested with febrile fever and sinusitis with bloody-purulent discharge, followed by arthralgia and joint swelling. After temporary regression with antibiotic therapy, relapse occurred four months later with fever, hemorrhagic papular rash with necrotic lesions, dyspnea, and hemoptysis. Imaging revealed bilateral polysegmental pneumonia with 65% lung involvement. Differential diagnosis included systemic lupus erythematosus and other systemic connective tissue diseases. A tenfold elevation of anti–proteinase 3 antibodies confirmed GPA. Despite pulse methylprednisolone, cyclophosphamide, and antibiotic therapy, the patient developed rapidly progressive acute kidney injury requiring urgent renal replacement therapy. Subsequent treatment with rituximab resulted in marked clinical improvement and disease regression.*

This case is notable for the delayed diagnosis and fulminant renal progression requiring dialysis in a pediatric patient, highlighting the importance of early ANCA testing and timely initiation of biological therapy in refractory GPA.

Keywords: *acute kidney injury, granulomatosis with polyangiitis, children, diagnostics, treatment.*

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Гранулематоз з поліангіїтом з розвитком гострого пошкодження нирок у дитини: клінічний випадок та труднощі ведення

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Резюме. *Гранулематоз з поліангіїтом (ГПА) – рідкісний ANCA-асоційований васкуліт у дітей, що часто характеризується тяжким мультисистемним ураженням і діагностичними труднощами. Представлено клінічний випадок 17-річної пацієнтки, яка проходила обстеження у відділенні дитячої ревматології та аутозапальних захворювань ДУ «Інститут педіатрії, акушерства і гінекології імені академіка О. М. Лук'янової НАМН України» (м. Київ, Україна). Захворювання дебютувало фебрильною гарячкою та синуситом із кров'янисто-гнійними виділеннями, з подальшим розвитком артралгій і припухлості суглобів. Після тимчасового регресу симптомів на тлі антибактеріальної терапії через чотири місяці відбувся рецидив із підвищенням температури тіла, геморагічним папульозним висипом з некротичними елементами, задишкою та кровохарканням. За даними інструментальних методів обстеження виявлено двобічну полісегментарну пневмонію з ураженням близько 65% легеневої тканини. У межах диференційної діагностики розглядали системний червоний вовчак та інші системні захворювання сполучної тканини. Десятикратне підвищення рівня антитіл до протеїнази 3 (anti-PR3) підтвердило діагноз ГПА. Незважаючи на проведення пульс-терапії метилпреднізолоном, циклофосфамідом та антибактеріальної терапії, у пацієнтки розвинулося швидкопрогресуюче гостре пошкодження нирок, що потребувало невідкладної ниркової замісної терапії. Подальше призначення ритуксимабу зумовило виражене клінічне покращення та регресію захворювання.*

Представлений випадок є показовим щодо пізньої верифікації діагнозу та блискавичного прогресування ниркового ураження з необхідністю проведення діалізу в дитячому віці, що підкреслює важливість раннього визначення ANCA та своєчасного призначення біологічної терапії при рефрактерному перебігу ГПА.

Ключові слова: *гостре ураження нирок, гранулематозний поліангіїт, діти, діагностика, лікування.*

Introduction. Since 2011, following the recommendations of leading international rheumatological societies (ACR, ASN, EULAR), a new nomenclature has been adopted for the systemic vasculitis previously known as Wegener's granulomatosis — granulomatosis with polyangiitis (GPA). This term reflects the hallmark characteristics of the disease: the formation of granulomas and systemic inflammation of predominantly small-to-medium-sized vessels.

GPA is classified as an antineutrophil cytoplasmic antibody (ANCA)-associated systemic vasculitis, along with eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss syndrome), microscopic polyangiitis (MPA), and renal-limited necrotizing crescentic glomerulonephritis. The overlapping clinical features of these entities often complicate the differential diagnosis [**1**].

The incidence of GPA ranges from 2 to 12 cases per million inhabitants, with an equal distribution between men and women. In the pediatric population, the disease is exceptionally rare, occurring predominantly in girls. While the estimated annual incidence of GPA in adults is 1:100,000 (with 90% of cases reported in Caucasians), the pediatric incidence is significantly lower, at approximately 0.1:100,000 [**2**]. Consequently, standardized and regulated treatment regimens for children remain limited.

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The etiopathogenesis of systemic vasculitis is complex and autoimmune in nature. It involves the production of ANCAs directed against proteinase 3 (PR3) in approximately 80% of GPA patients, or against myeloperoxidase (MPO) in about 10% of patients with MPA. Furthermore, antibodies to lysosomal membrane protein 2 (LAMP-2) may play a role in the pathogenesis through molecular mimicry [**3**].

GPA may present as a localized form, typically affecting the upper respiratory tract, or as a more severe and aggressive systemic form. Clinical manifestations depend on the specific vascular beds involved. Beyond the classic diagnostic triad – granulomatous inflammation of the upper and lower respiratory tracts and necrotizing pauci-immune glomerulonephritis associated with ANCA – the disease can also involve the central and peripheral nervous systems, skin, gastrointestinal tract, and musculoskeletal system [**4**].

Clinical presentation often varies depending on the disease stage and the extent of multi-organ involvement. While the clinical and laboratory features of GPA have been well-characterized in several large adult co-

horts, pediatric data remain scarce due to the rarity of the disease in childhood [5].

Renal involvement is observed in 38% to 100% of GPA cases. Renal manifestations, typically presenting as pauci-immune necrotizing glomerulonephritis, occur in 70–85% of patients at some stage of the disease. Initial laboratory and clinical signs of renal damage are present in approximately 25% of patients at disease onset. A rapidly progressive form of glomerulonephritis, characterized by a swift decline in renal function, occurs in about 28% of GPA patients. In other instances, renal involvement develops later, during the subsequent months or even years [4, 7]. Pathognomonic signs of renal damage in GPA include proteinuria, hematuria, and a decreased glomerular filtration rate (GFR).

Patients with renal insufficiency face a significantly increased risk of mortality, particularly those requiring renal replacement therapy, with mortality rates rising over time. The most critical complication of GPA is acute kidney injury (AKI). According to some reports, the incidence of AKI among hospitalized patients can reach 91.5%. Without targeted intervention, AKI rapidly progresses to end-stage renal disease (ESRD) and remains a primary cause of mortality.

The overall mortality rate for GPA is 43.5 per 1,000 person-years. During the first year following diagnosis, this rate peaks at 97.4 per 1,000 person-years before gradually declining. If left untreated, the one-year mortality rate for GPA is as high as 90% [6].

This report aims to describe and analyze a rare clinical case of GPA in a pediatric patient complicated by severe AKI.

Case presentation. In June 2023, a 17-year-old female patient was admitted to the Department of Pediatric Rheumatology and Autoinflammatory Diseases of the SI "Academician Lukyanova Institute of Pediatrics, Obstetrics and Gynecology of the NAMS of Ukraine." The primary objectives of hospitalization were diagnostic verification and the determination of a therapeutic strategy. Upon admission, the patient presented with edema of the ankle, wrist, and knee joints, as well as a polymorphic rash localized on the shins, hands, elbows, forehead, and ears. Additionally, she reported a sporadic cough and severe generalized weakness.

At the time of admission, a preliminary diagnosis was established: ANCA-associated systemic vasculitis (Granulomatosis with Polyangiitis, GPA), characterized by an acute progressive course in the active phase (Activity Stage III). The disease activity, assessed using the Birmingham Vasculitis Activity Score (BVAS), was 27 points at onset, indicating high clinical activity.

The patient's medical history revealed that six months before admission, she had developed right-sided sinusitis with bloody-purulent discharge. She was treated with amoxicillin/clavulanate (1000 mg for 5 days), which resulted in transient clinical improvement. However, one week later, she developed arthralgia in the knee joints and swelling of the ankle joints. Following a subsequent 6-day course of ciprofloxacin, the joint syndrome regressed.

In late May 2023, the patient developed a sore throat, dry cough, and a febrile temperature of 38.1°C. Despite a 5-day course of cefixime, which provided transient relief, her condition deteriorated immediately following the cessation of antibiotic therapy. Her body temperature rose to 38.6°C, accompanied by the appearance of a papular rash on the shins, hands, elbows, face, and ears, with a marked tendency toward necrotic transformation.

Chest X-ray revealed signs of bilateral pneumonia. The patient's clinical status progressively worsened, characterized by dyspnea, cough with hemoptysis, severe myalgia, and arthralgia, leading to hospitalization at a regional pediatric hospital.

Upon admission, the patient was in critical condition with a body temperature of 38.6°C, oxygen saturation (SpO2) of 80% on room air, and a respiratory rate of 26–28 breaths per minute. Physical examination revealed a polymorphic rash with necrotic elements localized on the extremities, face, and auricles. Laboratory findings indicated a systemic inflammatory response: erythrocyte sedimentation rate (ESR) was 52 mm/h and C-reactive protein (CRP) was 48 mg/L. The D-dimer level was significantly elevated at 4.66 μg/mL (normal < 0.5). Screening for tuberculosis (TBC), HSV, EBV, and CMV was negative. While SARS-CoV-2 PCR was negative and IgM was 0.297 (negative), IgG to SARS-CoV-2 was 6.884 (positive). Serological testing for autoimmune markers showed positive anti-double-stranded DNA (anti-dsDNA) antibodies at 35.71 IU/mL (normal < 20.0), while antinuclear antibodies (ANA) were negative.

The patient was initially diagnosed with severe community-acquired bilateral polysegmental pneumonia and Grade II respiratory failure (Fig. 1).

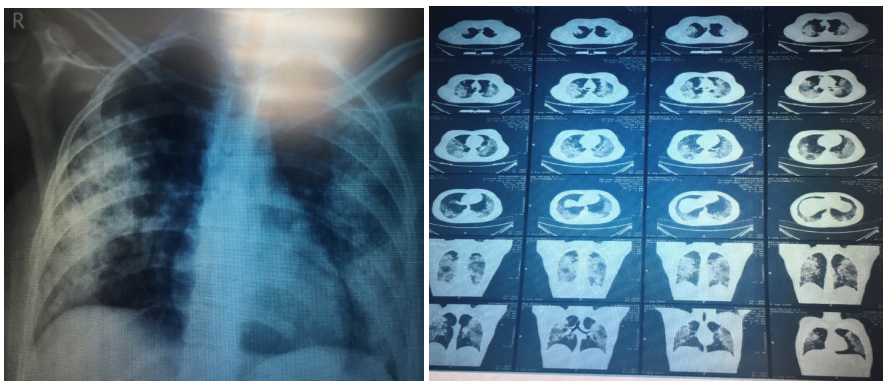

Fig. 1. Chest X-ray and CT scans of a patient with GPA. Findings demonstrate bilateral polysegmental pneumonia with an estimated total lung involvement of approximately 65%.

Radiographic findings showed homogenous opacities of medium intensity in the middle and lower lobes of both lungs, more pronounced on the right, with visible air bronchograms. The pulmonary markings were enhanced, and the hilar regions were structureless and infiltrated. High-resolution CT (HRCT) of the chest confirmed bilateral polysegmental pneumonia with approximately 65% total lung involvement. Hematological analysis revealed Grade III anemia (red blood cell count 2.6–3.0 × 10^{12}/L, hemoglobin 63.0–80.0 g/L). Urinalysis showed moderate erythrocyturia, mild proteinuria (0.264–0.297 g/L), and slight leukocyturia (up to 16 cells/hpf). Musculoskeletal ultrasound revealed signs of synovitis in the right ankle joint and free fluid (up to 4 mm) in the left ankle joint.

Oxygen therapy was initiated via a facial mask, maintaining oxygen saturation (SpO2) between 94% and 99%. On June 13, 2023, the patient received a transfusion of 250 mL of leukocyte-depleted packed red blood cells (Group A (II) Rh+). On June 22, 2023, multi-drug antibiotic therapy was administered, including linezolid (600 mg IV), meropenem (1000 mg), and moxifloxacin (400 mg). A bone marrow aspiration performed on June 14, 2023, revealed a cellular marrow with a normoblastic type of hematopoiesis.

Under the administered treatment, significant clinical improvement was observed, characterized by a reduction in systemic inflammatory activity, normalization of body temperature, stable SpO2 (95–97%), and regression of the necrotic skin rash. Follow-up chest X-rays demonstrated positive dynamics, showing a decrease in edematous and infiltrative changes. Oral glucocorticoid (GC) therapy was initiated with methylprednisolone (48 mg/day), which initially contributed to the positive clinical trend. However, the patient subsequently developed refractory vomiting (up to 10 episodes per day) with streaks of mucus and blood. Due to the clinical complexity and the need for specialized care, she was transferred to the Institute of Pediatrics, Obstetrics, and Gynecology (IPAG).

Patient history. The patient was born full-term following an unremarkable first pregnancy and uncomplicated delivery, with a birth weight of 2,400 g and a length of 52 cm. She was breastfed until two months of age, followed by formula feeding. Childhood vaccinations were administered according to the national schedule without complications. Her past medical history includes varicella and seasonal acute respiratory viral infections (2–3 times per year). In 2021, she contracted COVID-19, which was complicated by a persistent subfebrile temperature for one month. In December 2022, she was diagnosed with right-sided sinusitis, followed by bilateral pneumonia in early 2023. Menarche occurred at age 12 with regular cycles. No prior surgical interventions or significant traumas were reported. Family history was notable for type 2 diabetes mellitus in the maternal grandmother.

Physical examination (Admission to the ICU). Upon admission to the Intensive Care Unit (ICU), the patient's vital signs were as follows: body temperature 36.2°C, heart rate 95 beats per minute, and blood pressure 110/70 mmHg. Anthropometric measurements included a weight of 55 kg and a height of 165 cm (Body Mass Index [BMI] 20.2 kg/m^2; body surface area [BSA] 1.60 m^2).

The patient's general condition was assessed as moderately severe. She presented with an asthenic physique and adequate nutritional status. Physical examination revealed pallor of the skin and a widespread maculopapular rash with necrotic elements localized on the shins, elbows, hands, forehead, and auricles (Fig. 2).

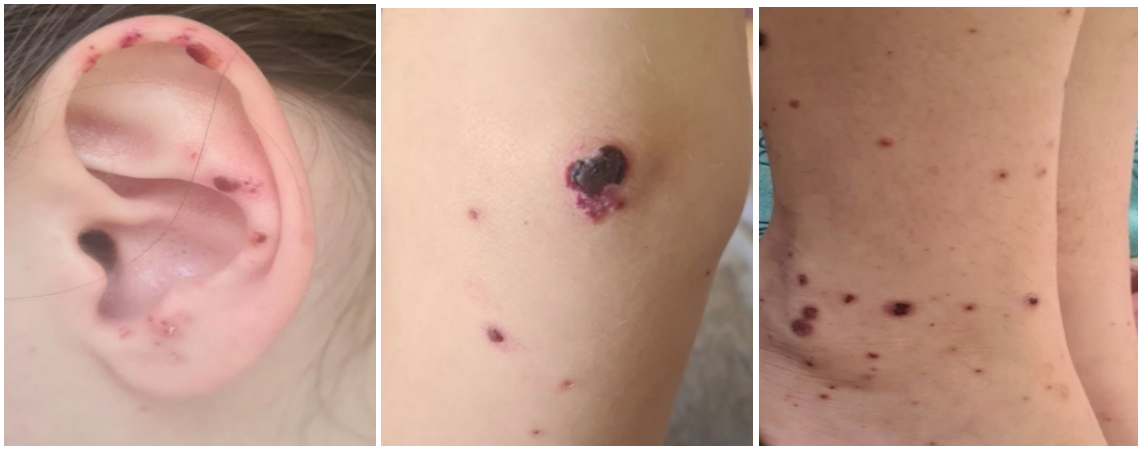

Fig. 2. Clinical appearance of a patient with GPA, demonstrating maculopapular rash with necrotic elements localized on the shins, elbow region, and auricle.

The visible mucous membranes were pink and moist; however, a solitary ulcer was noted on the buccal mucosa near the premolar teeth. The tongue was pink with a white coating. Peripheral cervical lymph nodes were enlarged to 0.5 cm, remained painless, and were not fixed to the surrounding tissues. Muscle tone was symmetric and satisfactory.

Pulmonary percussion revealed dullness bilaterally. Upon auscultation, diminished breath sounds were noted, with crepitus present in the right lung fields. Heart sounds were clear and rhythmic. Significant swelling and deformity of the knee, ankle, wrist (radiocarpal), and interphalangeal joints were observed. The affected joints were not warm to the touch and were painless on palpation; both active and passive ranges of motion were full, with preserved joint function. The abdomen was soft and non-tender upon superficial palpation. The liver was palpable 1.5 cm below the costal margin; the spleen was not palpable. Bowel movements were regular, and no voiding dysfunction was observed.

Preliminary diagnosis. A preliminary diagnosis was established: ANCA-associated systemic vasculitis (Granulomatosis with Polyangiitis, GPA). Clinical manifestations included: Skin – Maculopapular rash with necrotic elements; Upper respiratory tract – History of right-sided sinusitis; Lower respiratory tract – Bilateral community-acquired pneumonia with Grade II respiratory failure; Renal involvement – Persistent erythrocyturia and proteinuria; Musculoskeletal system – Polyarthritis involving the knee, ankle, wrist, and interphalangeal joints; Hematological – Chronic Grade III anemia.

Differential diagnosis and laboratory evaluation. The diagnostic priority was the differential diagnosis between systemic lupus erythematosus (SLE) and other systemic connective tissue diseases (SCTDs). The comprehensive diagnostic plan included: complete blood count (CBC), biochemical profile, quantitative C-reactive protein (CRP), antistreptolysin O (ASLO), rheumatoid factor (RF), antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA) panel, lactate dehydrogenase (LDH), serum electrolytes, throat culture, coagulogram, D-dimer, and ferritin. Additionally, antiphospholipid antibodies (APA), anti-double-stranded DNA (anti-dsDNA), serum immunoglobulins (IgG, IgM, IgA), urinalysis, the Nechiporenko test, 24-hour proteinuria and glucosuria, and a coprogram were performed.

Instrumental diagnostics included electrocardiography (ECG), echocardiography (Echo-KG), and ultrasound of the paranasal sinuses (ENT), kidneys, thyroid gland, and joints. Multidisciplinary consultations were conducted with an ophthalmologist, otolaryngologist (ENT), nephrologist, and dermatologist.

Laboratory investigations revealed the following significant abnormalities:

- Inflammatory markers: Persistent elevation of ESR (10–20 mm/h) and CRP (6–46 mg/L).
- Hematological profile: Grade I-II anemia with hemoglobin levels ranging from 88 to 100 g/L; ferritin elevation to 194 ng/mL.
- Hemostasis: A critical increase in D-dimer levels (exceeding 15,000 ng/mL).
- Specific biomarkers: A 10-fold increase in anti-proteinase 3 (anti-PR3) antibodies, with titers exceeding 200 U/mL (more than 10 times the upper limit of normal).
- Urinalysis: Hematuria (erythrocyturia up to 70 cells/hpf) and proteinuria (up to 0.99 g/L).

Therapeutic intervention and clinical course. The treatment regimen was initiated with intravenous (IV) pulse therapy consisting of methylprednisolone (1000 mg daily for three consecutive days), followed by a transition to oral methylprednisolone (60 mg/day). Induction immunosuppressive therapy included IV cyclophosphamide (750 mg). Supportive and adjunctive therapy comprised broad-spectrum antibiotics (meropenem and vancomycin), antithrombotic agents (rivaroxaban 10 mg/day, subsequently increased to 15 mg/day, and enoxaparin 0.4 mL), furosemide, and IV pentoxifylline (100 mg). Additional medications included detoxification therapy, enalapril (5 mg), Lespedeza extract, mesna (for uroprotection), and omeprazole. This comprehensive approach initially led to a reduction in systemic inflammatory activity and a decline in D-dimer levels.

However, the patient's clinical status was complicated by a rapid deterioration of renal function. Laboratory monitoring revealed a significant increase in serum creatinine (up to 248 μmol/L) and urea (up to 26.5 mmol/L), alongside rising potassium levels. The estimated glomerular filtration rate (eGFR) acutely declined to 27 mL/min/1.73 m^2. Due to the development of AKI, the patient was transferred to the Department of Intensive and Efferent Therapy for Acute Intoxications at the National Children's Specialized Hospital "OKHMATDYT" for urgent renal replacement therapy (RRT). Following a course of extracorporeal treatment, the patient's renal function parameters stabilized (creatinine 138 μmol/L, urea 13.2 mmol/L), allowing for her transfer back to the SI "IPAG named after O.M. Lukyanova NAMS" for continued management of the underlying disease.

Final diagnosis and revised therapeutic strategy. At this clinical stage, the definitive diagnosis was formulated as follows: ANCA-associated systemic vasculitis – Granulomatosis with Polyangiitis (GPA). The disease was characterized by an acute, multisystem course involving:

- Systemic symptoms: Persistent fever.
- Renal involvement: Pauci-immune necrotizing glomerulonephritis.
- Dermatological: Necrotic skin rash.
- Respiratory: Upper and lower respiratory tract involvement.
- Musculoskeletal: Polyarthritis.
- Ocular: Peripheral retinal vasculitis in both eyes.

The clinical activity was assessed at 27 points on the BVAS scale (Birmingham Vasculitis Activity Score). The current status was further complicated by a history of AKI in the recovery stage.

The therapeutic regimen was intensified and included:

- Glucocorticoids: Oral methylprednisolone (40 mg/day, administered in a split dose: 24 mg at 08:00, 8 mg at 13:00, and 8 mg at 18:00).
- Biological therapy: Induction with rituximab (500 mg IV, two doses).
- Supportive care: Intravenous immunoglobulin (IVIG), antiplatelet therapy (dipyridamole 50 mg twice daily, pentoxifylline 50 mg twice daily), enalapril (5 mg), and a β-blocker (2.5 mg).
- Prophylaxis and supplementation: Trimethoprim/sulfamethoxazole (240 mg daily) for Pneumocystis prophylaxis, folic acid (1 mg), vitamin D3 (2000 IU/day), calcium (1000 mg/day), omeprazole (20 mg/day), omega-3 fatty acids, and B-complex vitamins.
- Ophthalmological: Topical anti-inflammatory eye drops.

The initiated treatment resulted in significant positive clinical and laboratory trends, particularly regarding renal function (Table 1).

Table 1

Trends in selected laboratory parameters and kidney function in a 17-year-old patient with GPA during the recovery phase following AKI

Date	Total Cholesterol, mmol/L	Urea, mmol/L	Total Protein, g/L	CRP, mg/L	Creatinine, μmol/L	eGFR*, mL/min/1.73 m²
July 14	6.48	14.34	60.6	3	141	42
July 18	6.47	12.19	54.1	9	125	48
July 24	7.50	12.32	65.4	4	118	51
July 31	7.76	8.82	62.0	8	121	49
August 03	7.73	8.25	62.9	5	103	58

Note: *eGFR (estimated Glomerular Filtration Rate) calculated using the bedside Schwartz formula for pediatric patients; CRP – C-reactive protein.

However, some metabolic instability persisted, including fluctuations toward metabolic acidosis, transient episodes of hyperkalemia, and persistent hypocalcemia (Table 2).

Table 2

Trends in blood gas and electrolyte parameters in a patient with GPA during the recovery phase following AKI

Date	pH	pCO_2, mmHg	pO_2, mmHg	Hct, %	Sodium, mmol/L	Potassium, mmol/L	iCa^{2+}, mmol/L
July 14	7.448	40.6	25	29	137.7	4.32	1.03
July 17	7.420	47.1	21	25	139.8	3.83	0.91
July 25	7.252	55.9	22	30	143.2	5.03	0.71
July 31	7.397	42.8	29	34	142.1	5.26	0.98

Note: pCO_2 — partial pressure of carbon dioxide; pO_2 — partial pressure of oxygen; Hct — hematocrit; iCa^{2+} — ionized calcium.

The patient with GPA complicated by AKI received an intensive induction regimen consisting of the following pathogenetic therapies:

- Intravenous Pulse Cyclophosphamide: Administered at a dose of 750 mg every two weeks (3 doses), followed by a fourth dose of 750 mg after a three-week interval.
- High-Dose Glucocorticoids: Intravenous pulse therapy with methylprednisolone (1000 mg daily for three consecutive days).
- Biological Therapy: Induction with rituximab (500 mg IV, 2 doses).
- Adjuvant Immunotherapy: Intravenous immunoglobulin (IVIG) was administered to stabilize the immune response and mitigate infection risks during aggressive immunosuppression.

Discussion. The diagnosis of systemic vasculitis, including Granulomatosis with Polyangiitis (GPA), is primarily based on characteristic clinical manifestations. The "gold standard" remains histological exami-

nation, which typically reveals necrotizing small-vessel vasculitis and granulomatous inflammation characterized by the presence of multinucleated giant cells.

However, histopathological confirmation is frequently unattainable in the early stages of GPA. In patients presenting with suggestive clinical symptoms for whom a biopsy is either unfeasible or non-diagnostic, positive ANCA (antineutrophil cytoplasmic antibody) testing is pivotal for establishing the diagnosis. ANCAs are directed against two major neutrophil enzymes: serine proteinase 3 (PR3) and myeloperoxidase (MPO). Antibodies against PR3 (anti-PR3) are virtually pathognomonic for GPA, whereas antibodies against MPO (anti-MPO) are more characteristic of other primary necrotizing vasculitides, most notably microscopic polyangiitis (MPA) [6].

Two primary methodologies are utilized for the detection of ANCA: indirect immunofluorescence (IIF) and enzyme-linked immunosorbent assay (ELISA). IIF distinguishes between anti-PR3 and anti-MPO antibodies based on their characteristic staining patterns: the former is typically associated with cytoplasmic ANCA (c-ANCA), while the latter corresponds to perinuclear ANCA (p-ANCA). The identification of serum ANCA titers using IIF techniques provides strong diagnostic support, frequently enabling a clinical diagnosis in cases where a biopsy is either inconclusive or contraindicated.

The sensitivity of c-ANCA titers is closely correlated with disease activity. Notably, approximately 20% of patients with active systemic GPA may present with a negative ANCA result. This percentage increases to 30% in localized forms of the disease [3, 5].

Induction therapy typically consists of a combination of corticosteroids and cyclophosphamide; more recently, rituximab has been established as a standard for remission induction. This is followed by a maintenance phase involving low-dose corticosteroids in combination with azathioprine or other disease-modifying antirheumatic drugs (DMARDs) for several years.

Immunosuppressive regimens are integrated with comprehensive supportive care, which includes:

- Management of organ dysfunction (e.g., treatment of hypertension or renal replacement therapy);
- Prevention and treatment of treatment-related comorbidities (e.g., opportunistic infections, osteoporosis, or cataracts);
- Monitoring for the exacerbation of pre-existing conditions or the development of new pathologies.

Despite this multimodal approach to GPA management, relapses remain frequent, and therapy-related complications continue to be a major clinical concern. While the erythrocyte sedimentation rate (ESR) and c-ANCA titers are traditionally used to monitor disease activity and identify early signs of relapse, their clinical utility remains a subject of ongoing debate.

Consequently, the therapeutic strategy for each patient must be individualized, incorporating an assessment of disease severity and the specific clinical context. A review of the current literature provides relevant data on the clinical presentation of ANCA-associated glomerulonephritis in the pediatric population (Table 3).

Table 3

Clinical variants of ANCA-associated glomerulonephritis in children

Patient	Age (years)/ Gender	Type	AGN, %	CGN, %	CTIN, %	Treatment	Outcome
1	6 / F	MPA	-	-	-	S, C	RT
2	12 / F	MPA	100	0	0	S, C	RT
3	6 / M	MPA	10–21	80–90	20–30	S, C	PD
4	12 / F	MPA	0	60	20	S, C	RT
5	18 / M	GPA	90–100	0	0	S, C, R, P	NKF
6	16 / M	GPA	26–32	0	0	S, C	NKF
7	12 / F	MPA	23–37	50–60	30–40	S, C, R, P	HD
8	16 / M	GPA	67–73	0	0	S, R, P	ESRD

Note: MPA – microscopic polyangiitis; GPA – granulomatosis with polyangiitis; AGN – acute glomerulonephritis (% of affected glomeruli); CGN – chronic glomerulonephritis (% of sclerotic glomeruli); CTIN – chronic tubulointerstitial nephritis (% of affected interstitial tissue); S – Solu-Medrol (methylprednisolone); C – cyclophosphamide; R – rituximab; P – plasmapheresis; RT – renal transplantation; PD – peritoneal dialysis; HD – hemodialysis; NKF – normal kidney function; ESRD – end-stage renal disease.

Up to 30% of patients presenting with moderate-to-severe renal involvement require renal replacement therapy (RRT) at the time of diagnosis. Notably, between 40% and 70% of these patients may experience recovery of renal function following successful induction therapy [7].

Current clinical practice guidelines for ANCA-associated vasculitis with renal impairment recommend a first-line induction regimen consisting of intravenous pulse methylprednisolone combined with cyclophosphamide to achieve clinical remission. However, the long-term risk of relapse; furthermore, rigorous monitoring of absolute leukocyte counts before and after each infusion is mandatory.

Methotrexate in combination with glucocorticoids may be considered as an alternative to cyclophosphamide for early systemic disease in patients with a preserved glomerular filtration rate (eGFR > 60 mL/min/1.73 m^2). Nevertheless, methotrexate has demonstrated lower efficacy in preventing relapses during the maintenance phase. It is strictly contraindicated in cases of renal or hepatic insufficiency. In such clinical scenarios, mycophenolate mofetil (MMF) combined with glucocorticoids serves as an appropriate alternative therapeutic option [**8**].

In 2014, the National Institute for Health and Care Excellence (NICE) recommended the use of rituximab in combination with glucocorticoids for the management of ANCA-associated vasculitis in the following scenarios:

When the cumulative dose of cyclophosphamide has reached its maximum threshold;

- When cyclophosphamide is contraindicated or poorly tolerated;
- In patients where the preservation of fertility is a priority;
- In cases of refractory or progressive disease despite 6 months of standard induction therapy;
- In patients with a history of or active urothelial neoplasia.

Plasmapheresis (therapeutic plasma exchange) as an adjuvant therapy may be indicated in severe cases of rapidly progressive glomerulonephritis (RPGN) to improve renal survival and reduce the dependence on long-term dialysis, as well as in patients presenting with diffuse alveolar hemorrhage.

Intravenous immunoglobulins (IVIG) have demonstrated significant therapeutic efficacy in ANCA-associated vasculitis and are considered a viable alternative for patients with refractory disease or those for whom conventional immunosuppressive therapy is contraindicated. Currently, there is no consensus on the optimal dose, frequency, or duration of IVIG administration. Some authors employ IVIG protocols based on small-scale clinical series, typically combining them with corticosteroids until conventional immunosuppressants can be safely reintroduced [**9**].

The optimal maintenance strategy for remission in GPA and other ANCA-associated vasculitides remains a subject of ongoing debate. Given the severity of the renal impairment in this case, we consider rituximab to be the optimal therapeutic strategy. According to the current literature, rituximab is associated with a lower risk of relapse and fewer secondary complications compared to traditional maintenance regimens. In the presented case, this approach enabled the prevention of early mortality and mitigated the direct impact of active vasculitis on renal function.

Despite these advancements, GPA remains a life-threatening condition until complete disease control or clinical cure is achieved. Consequently, further clinical observations and large-scale studies are essential to refine pharmacological interventions. Such efforts are necessary to increase patient survival rates, enable targeted treatment and prevention of associated complications, improve the quality of life, and minimize the cumulative toxicity of immunosuppressive therapy.

Conclusions:

1. The presented clinical case of GPA complicated by AKI in a pediatric patient is rare and carries a guarded prognosis. It demonstrates how pauci-immune glomerulonephritis due to systemic vasculitis can manifest initially as typical acute glomerulopathy, followed by rapid progression to a critical state of AKI.
2. Patients presenting with this clinical phenotype face a high risk of mortality and frequently require urgent renal replacement therapy (RRT) in specialized intensive care units.
3. A subset of patients can recover from this critical state with a return to normal renal function. Although the specific factors associated with renal recovery remain to be fully elucidated, they likely depend on the early initiation of intensive induction therapy and the use of high-dose immunomodulatory agents.
4. Rituximab has demonstrated superior efficacy and a more favorable safety profile compared to traditional immunosuppressive regimens. This makes it a highly viable therapeutic option for the management of GPA with renal involvement, including in the pediatric population.
5. Current treatment protocols for GPA, particularly in children, are based on clinical trials with limited sample sizes. Therefore, identifying the "ideal" treatment strategy — aimed at achieving lower recurrence rates, minimizing drug toxicity, reducing mortality, and optimizing functional recovery — requires further large-scale, prospective studies.

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Author contributions.

T. Budnik: Conceptualization, case management, writing – original draft;

O. Mukvich: Methodology, case management, scientific supervision;

N. Dyachenko: Case management, data curation, visualization (clinical images);

I. Knyazkova and ***L. Abramova:*** Writing – review & editing, literature search.

All authors have read and agreed to the published version of the manuscript.

Informed concept statement. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patient and her legal guardians for the diagnostic procedures, treatment, and publication of this case report and any accompanying images.

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