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Pauci-immune crescentic glomerulonephritis with systemic thrombotic microangiopathy and fatal pulmonary hemorrhage mimicking IgA vasculitis in a child

Somayeh Talaeipour
Shahid Sadoughi University of Medical Sciences and Health Services
Yaser Mohammadi Dahaj
Shahid Sadoughi University of Medical Sciences and Health Services
Seyedeh Zalfa Modarresi
Shahid Sadoughi University of Medical Sciences and Health Services
Fariba Binesh
Shahid Sadoughi University of Medical Sciences and Health Services
Shekoofeh Savabieh
sh.savabieh@ssu.ac.ir

Shahid Sadoughi University of Medical Sciences and Health Services https://orcid.org/0009-0000-4973-1793

Research Article

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Abstract

Background

Childhood antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) complicated by systemic thrombotic microangiopathy (TMA) is rare, and its presentation can mimic IgA vasculitis.

Case-Diagnosis/Treatment

A 9-year-old girl presented 2 weeks after an upper respiratory infection with palpable purpura, ankle arthritis and cola-colored urine. Creatinine was 6.1 mg/dL, hemoglobin 7.4 g/dL and lactate dehydrogenase 1,875 U/L with schistocytes; platelets later fell to 41,000/μL. Perinuclear ANCA was positive. ADAMTS13 activity was normal without an inhibitor. Kidney biopsy showed diffuse sclerosing glomerulonephritis with residual cellular crescents, acute interstitial nephritis and negative immunofluorescence. Despite methylprednisolone, cyclophosphamide, hemodialysis, plasma exchange and intravenous immunoglobulin, recurrent diffuse alveolar hemorrhage developed and she died on day 18.

Conclusions

In a child with an IgA vasculitis-like presentation and severe kidney failure, early ANCA testing and kidney biopsy are essential. Normal ADAMTS13 activity favors AAV-associated secondary TMA over thrombotic thrombocytopenic purpura.

Summary – What is new

Childhood ANCA-associated vasculitis can mimic IgA vasculitis and present with systemic thrombotic microangiopathy despite normal ADAMTS13 activity, an overlap that may culminate in fatal pulmonary hemorrhage.

Introduction

ANCA-associated vasculitis (AAV) is rare in childhood; microscopic polyangiitis predominates, and kidney involvement is frequent and often severe [1]. Systemic thrombotic microangiopathy (TMA) is an uncommon complication of AAV, with only 15 cases identified in a recent literature review [2]. Recognizing this overlap matters because TMA in a child raises competing diagnoses—immune thrombotic thrombocytopenic purpura (TTP) and complement-mediated or infection-associated hemolytic uremic syndrome—that are treated differently [3, 4]. We describe a child whose presentation

resembled IgA vasculitis but who had p-ANCA-positive pauci-immune crescentic glomerulonephritis, systemic TMA features with normal ADAMTS13 activity, and fatal diffuse alveolar hemorrhage.

Case report

A 9-year-old girl was admitted with palpable purpura of the lower extremities, bilateral ankle arthritis, leg edema, recurrent vomiting, fatigue and pallor. About 2 weeks earlier she had an upper respiratory infection with coryza and myalgia, during which cola-colored urine was noted but not evaluated. Two outpatient courses of nonsteroidal anti-inflammatory drugs and antibiotics had not helped. Her mother had a history of anemia and pregnancy-associated thrombocytopenia.

On admission, serum creatinine was 6.1 mg/dL with non-oliguric kidney failure, hemoglobin 7.4 g/dL (mean corpuscular volume 78 fL) and lactate dehydrogenase (LDH) 1,875 U/L; the peripheral blood smear showed schistocytes (2+). Reticulocytes were 1.5% and total/direct bilirubin 1.8/0.5 mg/dL; the direct Coombs test and D-dimer were negative, and haptoglobin and fibrinogen were not measured. p-ANCA was positive on two occasions, whereas c-ANCA and anti-glomerular basement membrane antibodies were negative. Complement levels were normal (C3 128 mg/dL [reference 90–180], C4 36 mg/dL [10–40], CH50 43 U/mL [30–75]). ADAMTS13 activity was 0.7 IU/mL (approximately 70%; reference 0.4–1.3), the ADAMTS13 inhibitor screen was negative (11.4 U/mL; negative < 12.0), and ADAMTS13 antigen was 1.0 IU/mL (reference 0.41–1.41).

Kidney biopsy yielded a 1.1 × 0.1 cm core containing 22 glomeruli. Nearly all glomeruli showed global or segmental sclerosis, and residual cellular crescents were present in some (Fig. 1a). The interstitium had a moderate mononuclear and polymorphonuclear infiltrate with tubulitis; red blood cell casts were present in tubular lumens, and vessels showed prominent endothelium. Trichrome staining showed no abnormal interstitial fibrosis (Fig. 1b). Immunofluorescence was negative. The diagnosis was diffuse sclerosing glomerulonephritis consistent with the chronic sequel of crescentic glomerulonephritis, with acute interstitial nephritis; pauci-immune crescentic glomerulonephritis was considered most likely.

Intravenous methylprednisolone and cyclophosphamide were started, and hemodialysis was required for progressive uremia. On hospital day 8, diffuse alveolar hemorrhage required mechanical ventilation, and plasma exchange was initiated; the effluent of the second session was dark and blood-stained. Creatinine subsequently rose to 7.1 mg/dL and LDH to 4,664 U/L, the platelet count fell to 41,000/μL, and hemoglobin was later 9 g/dL. Intravenous immunoglobulin, continued glucocorticoids and supportive care were given, but massive pulmonary hemorrhage recurred on day 18, followed by refractory hypoxemia, cardiac arrest and death.

Discussion

This case combined three features rarely reported together in a child: pauci-immune crescentic glomerulonephritis, systemic TMA features and fatal diffuse alveolar hemorrhage.

Purpura, ankle arthritis, a preceding respiratory infection and macroscopic hematuria in a school-age child strongly suggest IgA vasculitis with nephritis [5]. However, severe kidney failure at presentation, p-ANCA positivity and negative immunofluorescence pointed to AAV. ANCA testing and kidney biopsy should therefore not be deferred when apparent IgA vasculitis presents with a markedly elevated creatinine. The predominance of sclerosed glomeruli would place this biopsy in or near the sclerotic class of the Berden classification, which carries the poorest kidney prognosis [6], and suggests that glomerular injury evolved before admission, possibly during the unevaluated episode of cola-colored urine.

Anemia, thrombocytopenia, schistocytes and rising LDH with kidney failure indicated a TMA process. Immune TTP, defined by severe ADAMTS13 deficiency (activity < 10%) and previously reported with AAV in an adolescent [7], was not supported, because ADAMTS13 activity was about 70% with a negative inhibitor screen at the time of testing. The negative Coombs test argued against autoimmune hemolysis, and normal C3 and CH50 did not suggest complement consumption, although normal complement levels do not exclude complement-mediated TMA, which requires genetic and functional evaluation [4]. AAV-associated secondary TMA was therefore the most plausible explanation. In published AAV–TMA cases, myeloperoxidase-ANCA and crescentic glomerulonephritis predominate, and kidney recovery is poorer than hematologic recovery [2]. Endothelial and glycocalyx injury has been proposed as a common pathway of secondary TMA in children [3]; the prominent endothelium on biopsy is in keeping with endothelial injury, although fibrin thrombi were not described. Pulmonary hemorrhage, plasma exchange and dialysis may also have contributed to thrombocytopenia.

Diffuse alveolar hemorrhage in children frequently requires mechanical ventilation and carries substantial mortality [8]. Routine plasma exchange did not reduce death or kidney failure in severe AAV in the PEXIVAS trial [9], and current KDIGO guidance reserves it for selected patients, including those with diffuse alveolar hemorrhage and hypoxemia [10]. In our patient, it was used for life-threatening pulmonary hemorrhage but did not prevent recurrence.

This report has limitations. ANCA antigen specificity (myeloperoxidase or proteinase 3) was not determined; haptoglobin and fibrinogen were not measured, so the hemolytic and coagulation profile could not be fully characterized; complement genetic testing was not performed; and no autopsy was obtained.

In conclusion, in a child with an IgA vasculitis-like presentation and severe kidney failure, ANCA serology and kidney biopsy should be obtained early. When microangiopathic features coexist, ADAMTS13 testing helps to distinguish AAV-associated secondary TMA from TTP.

Declarations

Running title

Pediatric ANCA vasculitis with thrombotic microangiopathy

Article type

Clinical Insight

Declarations

Ethics approval

This case report was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (approval code: IR.SSU.REC.1405.148).

Consent for publication

Written informed consent for publication of this case report and the accompanying images was obtained from the patient's parents.

Competing interests

The authors declare no competing interests.

Use of artificial intelligence

A large language model was used to assist with language editing and condensing the manuscript. The authors reviewed and verified all content and take full responsibility for the final text.

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Author contributions

Somayeh Talaeipour conceived the report, drafted the manuscript and revised the final version. Yaser Mohammadi Dahaj collected and interpreted the clinical data. Seyedeh Zalfa Modarresi analyzed and interpreted the findings. Fariba Binesh reviewed the kidney biopsy, provided the pathology images and critically revised the manuscript. Shekoofeh Savabieh supervised the work and critically revised the manuscript. All authors read and approved the final manuscript.

Data availability

All data relevant to this case are included in the article. Further information is available from the corresponding author on reasonable request, subject to patient privacy.

References

1. Yeo L, Naheed A, Richards C, Ciurtin C (2024) Childhood-onset ANCA-associated vasculitis: from genetic studies to advances in pathogenesis, classification and novel therapeutic approaches. Int J Mol Sci 25:13704. https://doi.org/10.3390/ijms252413704
2. Shukla S, Sekar A, Naik S, Rathi M, Sharma A, Nada R, Kohli HS, Ramachandran R (2024) ANCA-associated vasculitis with systemic thrombotic microangiopathy: a review of literature. Indian J Nephrol 34:155–161. https://doi.org/10.4103/ijn.ijn_376_22
3. Ma AL, Alconcher L, Coccia P, Wong JW, Kusche-Vihrog K, Licht C (2026) Secondary thrombotic microangiopathy in children—a central role for the glycocalyx. Kidney Int 110:841–850. https://doi.org/10.1016/j.kint.2026.04.047
4. Stea ED, Pugliano M, Gualtierotti R, Mazzucato M, Santangelo L, Annicchiarico G et al (2025) Multidisciplinary consensus on the diagnosis and management of patients with atypical hemolytic uremic syndrome (complement-mediated TMA): recommendations from Italian scientific societies, patient associations and regulators. Pharmacol Res 216:107714. https://doi.org/10.1016/j.phrs.2025.107714
5. Ozen S, Marks SD, Brogan P, Groot N, de Graeff N, Avcin T et al (2019) European consensus-based recommendations for diagnosis and treatment of immunoglobulin A vasculitis—the SHARE initiative. Rheumatology (Oxford) 58:1607–1616. https://doi.org/10.1093/rheumatology/kez041
6. Berden AE, Ferrario F, Hagen EC, Jayne DR, Jennette JC, Joh K et al (2010) Histopathologic classification of ANCA-associated glomerulonephritis. J Am Soc Nephrol 21:1628–1636. https://doi.org/10.1681/ASN.2010050477
7. Agrawal V, Vaidya CK, Ye J, Freeman J, McKiernan C, Blier PR, Andrzejewski C, Germain M, Braden GL (2011) Concomitant thrombotic thrombocytopenic purpura and ANCA-associated vasculitis in an adolescent. Pediatr Nephrol 26:1317–1320. https://doi.org/10.1007/s00467-011-1862-5
8. Cohen SP, Eisner M, Fussner LA, Krivchenia K (2024) Diffuse alveolar hemorrhage in pediatrics: etiologies and outcomes. Pediatr Pulmonol 59:3364–3370. https://doi.org/10.1002/ppul.27207
9. Walsh M, Merkel PA, Peh CA, Szpirt WM, Puéchal X, Fujimoto S et al (2020) Plasma exchange and glucocorticoids in severe ANCA-associated vasculitis. N Engl J Med 382:622–631. https://doi.org/10.1056/NEJMoa1803537
10. Kidney Disease: Improving Global Outcomes (KDIGO) ANCA Vasculitis Work Group (2024) KDIGO 2024 clinical practice guideline for the management of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. Kidney Int 105:S71–S116. https://doi.org/10.1016/j.kint.2023.10.008

Figures

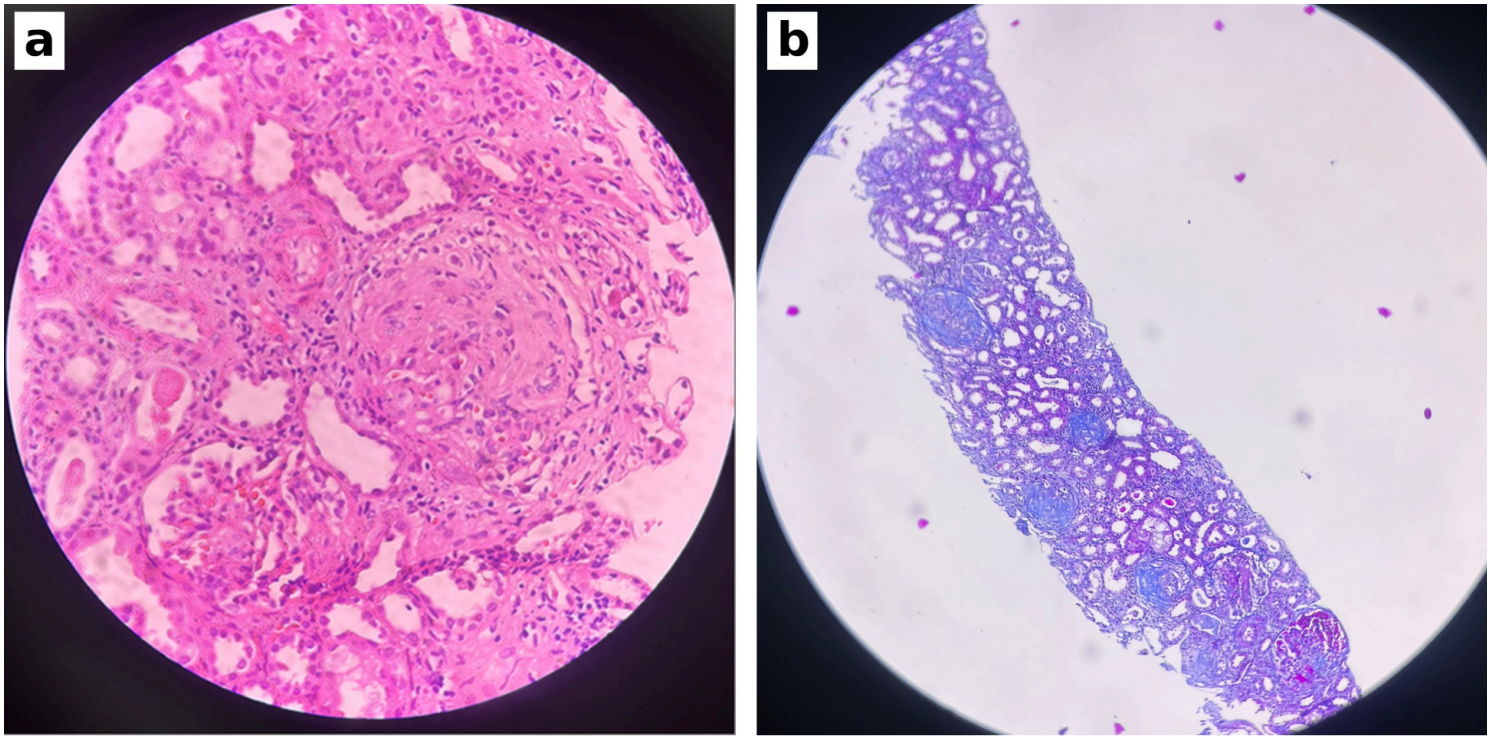


Figure 1

Kidney biopsy. **a**Hematoxylin and eosin (×40 objective): glomerulus with a crescent, surrounded by an interstitial inflammatory infiltrate and tubules. **b** Trichrome stain (×10 objective): biopsy core with multiple sclerosed glomeruli and no significant interstitial fibrosis

Supplementary Files

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