

Atypical Adult-Onset IgA Vasculitis With Extremely Rare Complications Including Diffuse Alveolar Hemorrhage, Heart Failure, and Stroke

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Abstract

IgA vasculitis (IgAV) generally occurs in young people and presents with a tetrad of symptoms: purpura, abdominal pain, arthralgia, and nephritis. However, it may have an atypical course without the typical tetrad. Diffuse alveolar hemorrhage (DAH), heart failure, and stroke are known complications of IgAV but are all very rare. We herein report a case of adult-onset IgAV that developed simultaneously with these rare complications without the typical tetrad. A 31-year-old man without any medical history presented with fever and blood-tinged sputum. Two months later, these symptoms worsened, and he was admitted to the hospital with DAH, nephritis, heart failure, and stroke. Initially, these symptoms were considered indicative of vasculitis syndrome, and he was finally diagnosed with IgAV based on the results of a renal biopsy. The treatment was successful with corticosteroids alone. IgAV should, therefore, be considered in the differential diagnosis when a patient presents with vasculitis syndrome, even with an atypical course.

Categories: Rheumatology, Allergy/Immunology, Pulmonology

Keywords: cardiac magnetic resonance, cmr, dah, diffuse alveolar hemorrhage, iga nephropathy, igav, iga vasculitis

Introduction

Vasculitis syndrome is suspected in the presence of pulmonary renal syndrome (PRS), complicated by both diffuse alveolar hemorrhage (DAH) and nephritis, or when vascular disorders such as heart failure or stroke are present in addition to PRS [1].

IgA vasculitis (IgAV) is a vasculitic disorder characterized by the deposition of IgA1-dominant immune complexes in small vessels, typically resulting in a tetrad of symptoms, including purpura, abdominal pain, arthralgia, and nephritis [2]. However, it is very rare for IgAV to present with symptoms in the respiratory, cardiovascular, and central nervous systems, although some cases have been reported [3-5]. This case report describes a young man with an atypical course of IgAV, complicated by DAH, heart failure, and stroke, which was diagnosed through various tests, including renal biopsy. When a young person presents with severe clinical symptoms suggestive of vasculitis syndrome, IgAV should be considered as a differential diagnosis, even in the absence of the typical tetrad.

Case Presentation

A 31-year-old man without any past medical history presented with a fever and blood-tinged sputum. He reported these symptoms for two months, with recent worsening.

On admission, he had a fever of 38.5°C, blood pressure of 152/72 mmHg, a heart rate of 94 beats per minute, a respiratory rate of 20 breaths per minute, and an O2 saturation of 93% in room air. Physical examination revealed purpura on the lower extremities, although the patient had not initially reported this symptom. No other signs suggestive of vasculitis, such as gastrointestinal symptoms or joint pain, were noted.

Initial laboratory findings were significant for elevated creatinine (1.80 mg/dL; ref. 0.61-1.04 mg/dL), elevated C-reactive protein (1.7 mg/dL; ref. 0.0-0.3 mg/dL), and elevated N-terminal pro-brain natriuretic peptide (5975 pg/mL; ref. 0-125 pg/mL). Urinalysis indicated proteinuria (4+), microscopic hematuria (2+), and red blood cells (5-9/high power field). Granular, epithelial cells, and fatty casts were observed with elevated urinary β2-microglobulin (3561 µg/L; ref. 0-250 µg/L) and elevated urinary N-acetyl-beta-glucosaminidase (21.8 IU/L; ref. 0.7-11.2 IU/L). The autoimmune markers, including antinuclear antibodies, anti-neutrophil cytoplasmic antibodies (ANCA), and anti-glomerular basement membrane (GBM) antibodies, were negative. Influenza and COVID-19 were ruled out based on negative rapid antigen tests, though comprehensive viral panels were not performed. Tuberculosis and other acid-fast bacterial infections were excluded through negative interferon-gamma release assay results and negative cultures

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(Table 1).

Laboratory data	Laboratory value	Reference range
Blood tests		
WBC	9.8	3.9-9.7 K/mcL
Hgb	16.4	13.4-17.1 g/dL
Plt	217	153-346 K/mcL
Blood urea nitrogen	21	8-22 mg/dL
Creatinine	1.8	0.61-1.04 mg/dL
Total protein	6.1	6.7-8.3 g/dL
Albumin	3.5	3.9-4.9 g/dL
IgG	835	870-1700 mg/dl
IgA	173	110-410 mg/dl
IgM	98	35-220 mg/dl
NT-pro-BNP	5975	0-125 pg/mL
Anti-nuclear antibody	<1:40	<1:40
Complement C3	104	65-135 mg/dL
Complement C4	29	13-35 mg/dL
MPO-ANCA	<1.0	<4.0 IU/ml
PR3-ANCA	<1.0	<4.0
Anti-GBM antibodies	<2.0	<3.0
CRP	1.7 mg/dL	<1.0 mg/dL
Urinalysis		
Proteinuria	4+	Negative
Protein, urine	386	0-20 mg/dL
Creatinine, urine	196.8	Not available
Protein/creatinine ratio	1.96	≤0.15 gPR/gCR
Microscopic hematuria	2+	Negative
Erythrocytes urinalysis	5 to 9/hpf	Not seen
β2-microglobulin	3561	0-250 µg/L
N-acetyl-beta-glucosaminidase	21.8	0.7-11.2 IU/L

TABLE 1: Biochemical and biomarker test results on admission

WBC: white blood cells, Hgb: hemoglobin, Plt: platelets, IgG: immunoglobulin G, IgA: immunoglobulin A, IgM: immunoglobulin M, NT-pro BNP: N-terminal pro-brain natriuretic peptide, MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibody, PR3-ANCA: proteinase 3 anti-neutrophil cytoplasmic antibody, anti-GBM antibody: anti-glomerular basement membrane antibody, CRP: C-reactive protein, N. D.: not detected, RBC: red blood cells, hpf: high-power field

Chest X-ray showed bilateral pulmonary infiltrates, and a chest CT scan revealed diffuse ground-glass opacity with bilateral lower lobe predominance (Figure 1A-1D).

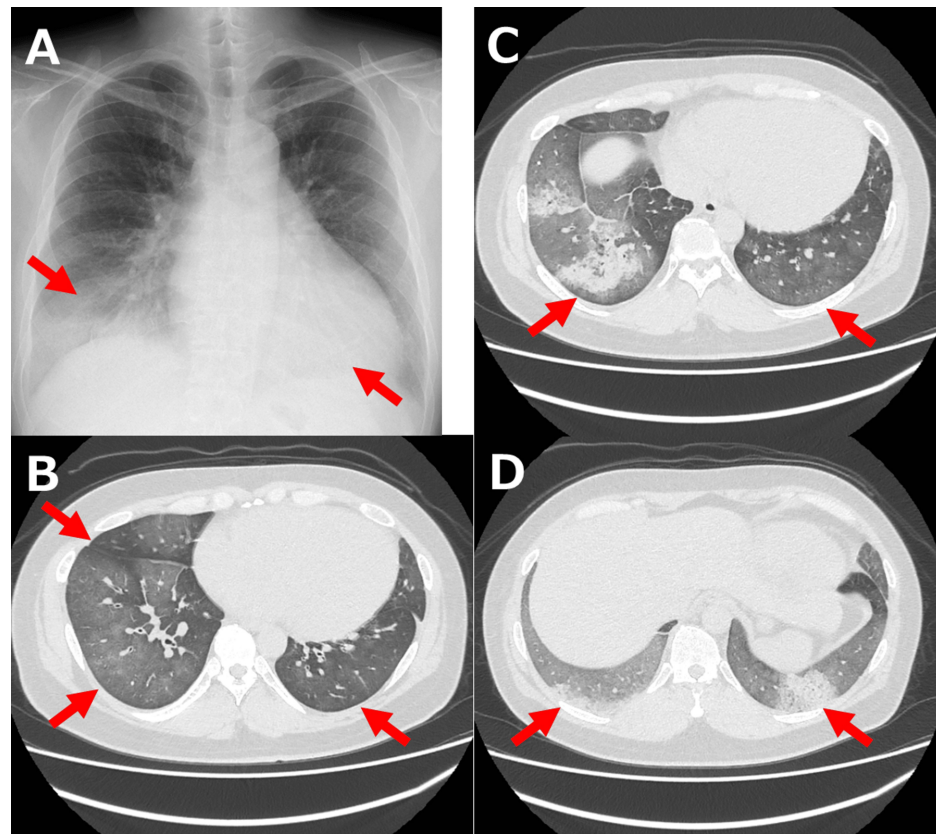


FIGURE 1: Chest imaging on admission

A: Chest X-ray showing bilateral pulmonary infiltrates. B-D: Chest CT scan revealing diffuse ground-glass opacity with bilateral lower lobe predominance.

CT: computed tomography

Bronchoscopic examination revealed no evident active bleeding, but capillary dilation and airway edema were observed throughout the respiratory tract. Bronchoalveolar lavage (BAL) was subsequently performed via the right B4 and, on three consecutive occasions, demonstrated a gradual increase in blood components and revealed 65% phagocytic macrophages, strongly supporting the diagnosis of DAH (Figure 2A-2B).

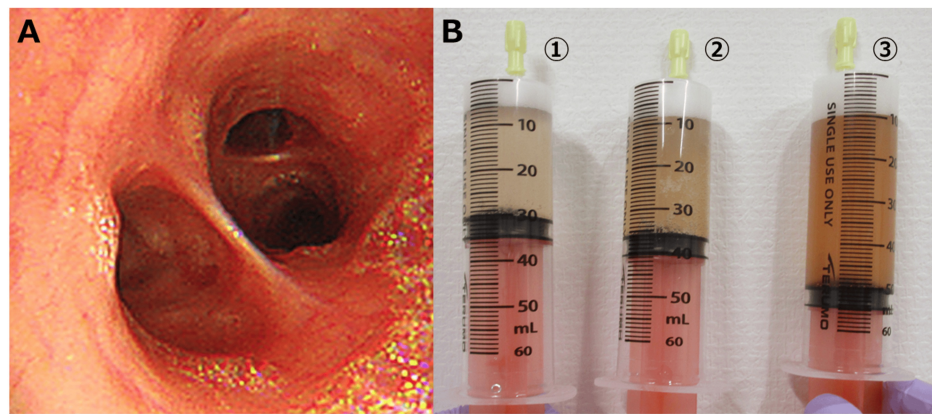


FIGURE 2: Bronchoscopic findings and BAL results

A: Bronchoscopic examination revealed capillary engorgement and mucosal edema throughout the visible range from the trachea to the subsegmental bronchi without evidence of active bleeding. B: BAL was subsequently performed via the right B4. Sequential BAL samples from three consecutive procedures demonstrated a gradual increase in blood components and revealed 65% phagocytic macrophages, strongly indicating DAH.

BAL: bronchoalveolar lavage, DAH: diffuse alveolar hemorrhage

A transthoracic echocardiogram (TTE) showed a decreased left ventricular ejection fraction (LVEF) of 20%. Due to concerns that these findings in the kidneys, lungs, and heart were secondary to vasculitis, the patient received 1000 mg methylprednisolone IV for three days, followed by oral prednisolone (PSL) of 70 mg/day (1 mg/kg/day). With this treatment, blood-tinged sputum and chest X-ray rapidly improved, but renal dysfunction persisted.

A skin biopsy was performed, which revealed inflammatory cell infiltration, including lymphocytes, although specific findings of leukocytoclastic vasculitis or IgA deposition were not observed (Figure 3A-3B). Notably, the absence of typical vasculitic changes or IgA deposition does not rule out IgAV, as these findings can be variable depending on the timing and location of the biopsy. The presence of inflammatory changes in the biopsy, combined with the clinical presentation of the rash, supports the possibility of a vasculitic process.

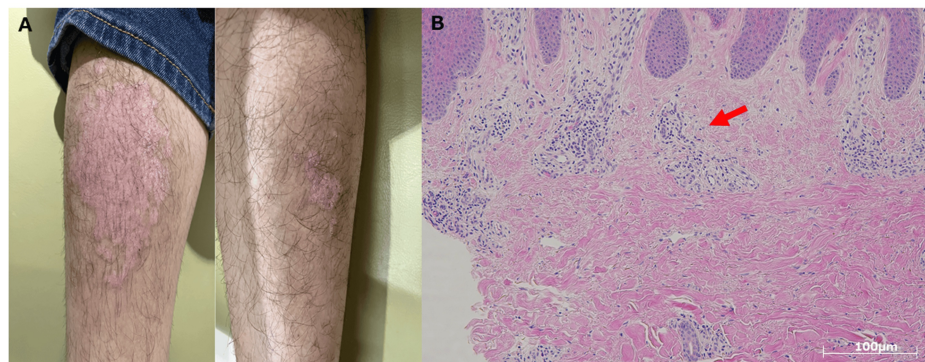


FIGURE 3: Clinical and histopathological findings of skin lesions

A: Palpable purpura on the lower extremities. B: Histopathological examination of skin biopsy showing mild papillomatosis with hyperkeratosis and perivascular inflammatory cell infiltration predominantly composed of lymphocytes (H&E staining, scale bar = 100 μ m). The red arrow indicates perivascular infiltration of inflammatory cells.

H&E: hematoxylin and eosin

On day 6, a renal biopsy was performed, demonstrating mesangial proliferative glomerulonephritis (Figure 4A). The immunofluorescence analysis showed mesangial deposition of IgA and C3c (Figure 4B). Electron microscopy indicated electron-dense deposits in mesangium (Figure 4C). Furthermore, we confirmed colocalization of aberrantly glycosylated IgA1 (Gd-IgA1) with IgA in the mesangial region using an anti-Gd-IgA1 monoclonal antibody (Figure 4D).

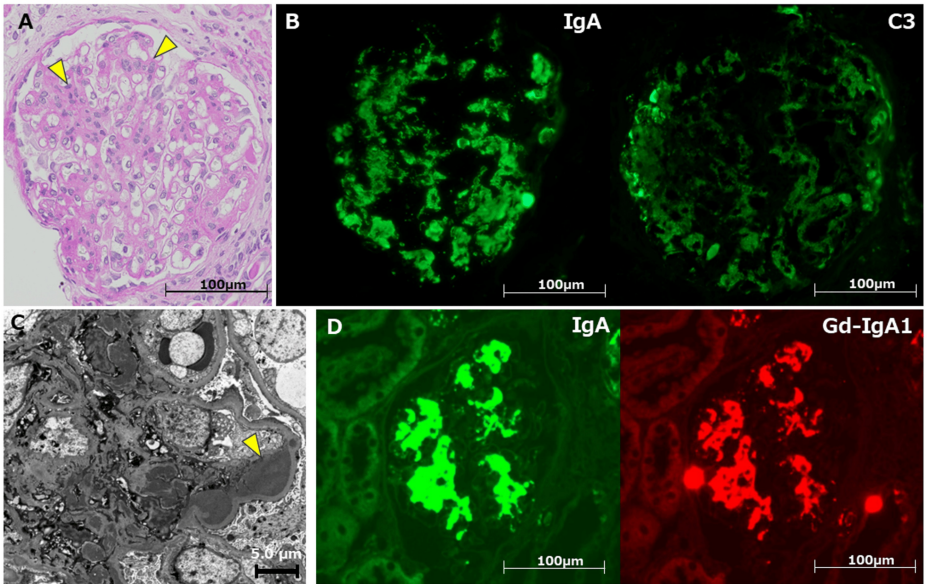


FIGURE 4: Renal biopsy confirmed the diagnosis of IgAV

A: Light microscopy showed diffuse mesangial proliferative glomerulonephritis without any crescent formation. Arrowheads indicate mesangial proliferation (H&E staining). B: The immunofluorescence analysis indicated mesangial deposition of IgA and C3c. C: Electron microscopic findings confirmed electron-dense deposits in the mesangial area. D: Gd-IgA1 colocalized with IgA in the mesangial region using an anti-Gd-IgA1 monoclonal antibody.

IgAV: IgA vasculitis, H&E: hematoxylin and eosin, IgA: immunoglobulin A

Contrast-enhanced cardiac magnetic resonance (CMR) revealed increased left ventricular myocardial weight (75.9 g/m²), diffusely reduced left ventricular wall motion, and highly decreased LVEF (18.3%). Late gadolinium enhancement showed patchy and linear abnormal enhancement at the right ventricular junction of the ventricular septum and in the left ventricular mid-myocardium, a pattern seen in hypertensive heart disease (Figure 5A-5B).

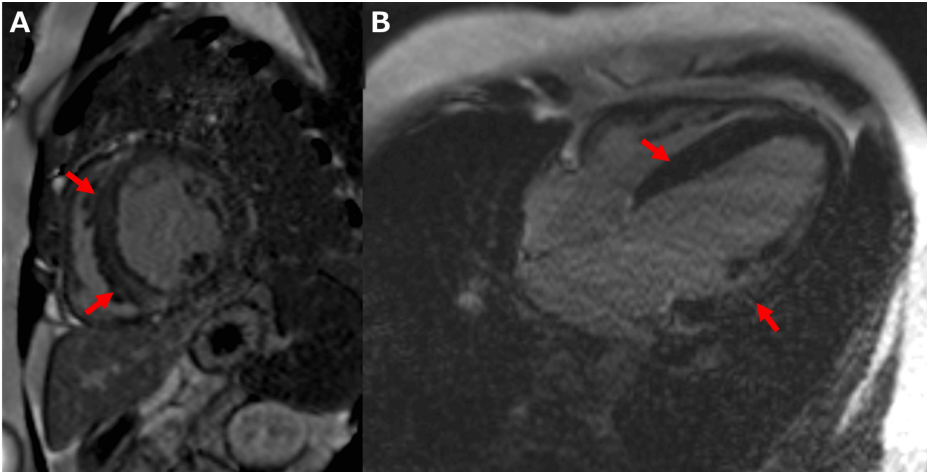


FIGURE 5: CMR imaging with late gadolinium enhancement

Short-axis view (A) and four-chamber view (B) show patchy and linear abnormal enhancement (arrows) at the right ventricular junction of the ventricular septum and in the left ventricular mid-myocardium.

CMR: cardiac magnetic resonance

Although asymptomatic, brain MRI showed multiple increased signal intensities on diffusion-weighted images, indicating multiple cerebral infarctions (Figure 6A-6B). It also showed multiple decreased signal intensities in the basal ganglia on T2 star-weighted images, indicating multiple micro-bleeds (Figure

6C-6D).

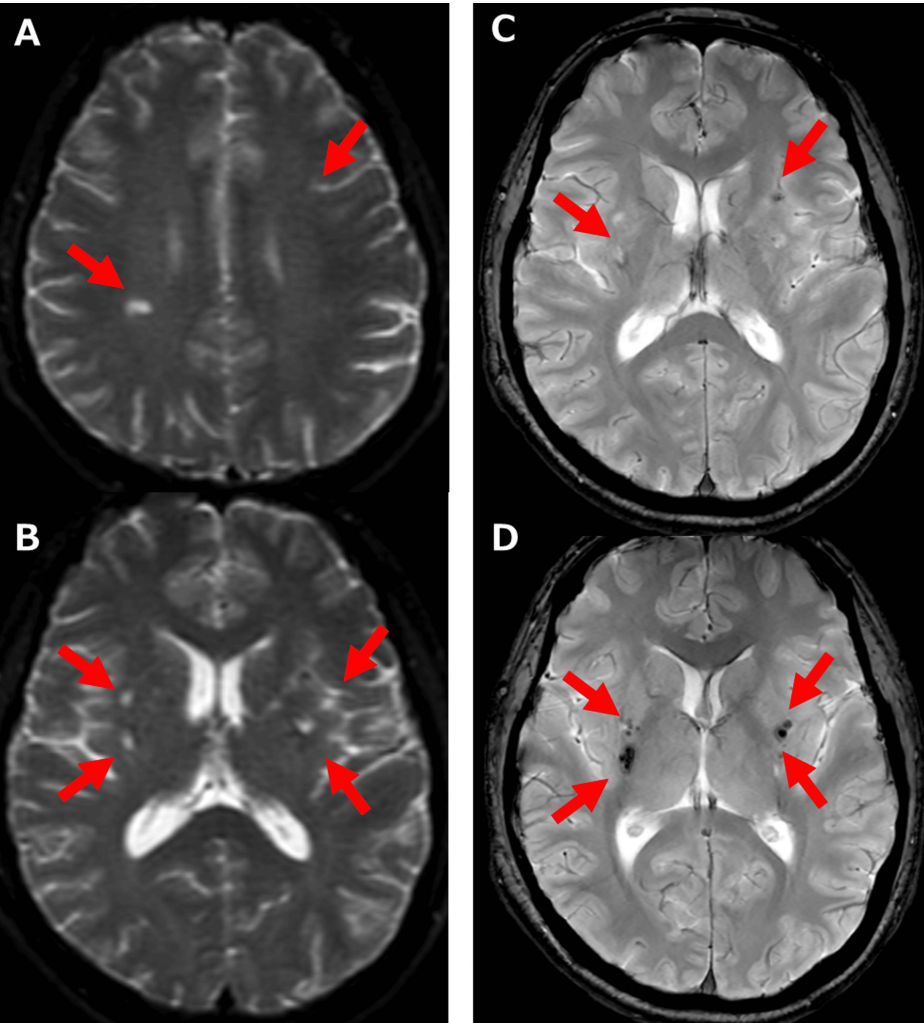


FIGURE 6: Brain MRI

A, B: Diffusion-weighted images showing multiple increased signal intensities (arrows), indicating multiple cerebral infarctions. C, D: T2 star-weighted images revealing multiple decreased-signal intensities in the basal ganglia (arrows), demonstrating multiple microbleeds.

MRI: magnetic resonance imaging

IgAV seemed to be the most likely explanation for these findings. As renal histological findings showed relatively mild renal injuries and the patient's airway symptoms improved, the PSL was reduced to 35 mg (0.5 mg/kg/day) on day 7 after consultation with the nephrologist. The patient was discharged on day 14 when his condition stabilized. The alveolar hemorrhage resolved, and the ejection fraction in the TTE improved to 53%. The patient is now primarily followed up in the nephrology outpatient clinic. His clinical course is illustrated in Figure 7.

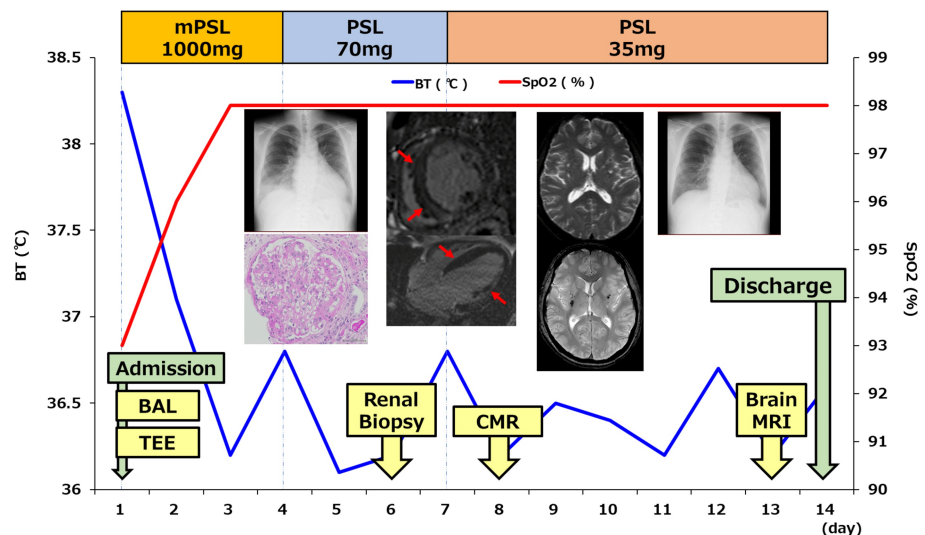


FIGURE 7: Summary of the patient's clinical course

mPSL: methylprednisolone, PSL: prednisolone, BT: body temperature, BAL: bronchoalveolar lavage, TEE: transthoracic echocardiogram, CMR: cardiac magnetic resonance, MRI: magnetic resonance imaging

Discussion

The patient initially presented with DAH, accompanied by renal dysfunction, heart failure, multiple cerebral infarctions, and multiple cerebral microbleeds. While these multiple complications might suggest concurrent pathologies, several features strongly support a unified diagnosis of IgAV. Although the typical tetrad was not fully observed initially, the patient exhibited two key diagnostic components: purpura and nephritis. Though initially overlooked by the patient, the purpura on the lower extremities is consistent with adult IgAV cases, where skin manifestations may be less prominent [6]. The diagnostic process was systematic and comprehensive. While ANCA-associated vasculitis was initially suspected, autoimmune markers were negative. Although the skin biopsy showed inflammatory changes without typical vasculitic findings or IgA deposition, this does not exclude IgAV, as these findings can vary depending on biopsy timing and location [7,8]. The renal involvement, evident through dysfunction and later confirmed by biopsy showing IgA nephropathy, provided crucial diagnostic evidence. The diagnosis of IgAV was further strengthened by several factors: first, the combination of purpura and nephritis, along with the absence of other explainable causes of vasculitis [9,10]. Second, the rapid improvement with corticosteroid therapy strongly suggested an immune-mediated process, particularly in both pulmonary hemorrhage and cardiac function. Third, the simultaneous occurrence of multiple organ involvement in a previously healthy young adult indicated underlying systemic vasculitis rather than isolated pathologies. Additional support came from advanced pathological analysis using an anti-Gd-IgA1 monoclonal antibody, which revealed Gd-IgA1 colocalizing with IgA in the mesangial region. This finding aligns with the IgAV diagnosis and suggests shared pathogenic features with primary IgA nephropathy [11]. This case exemplifies the importance of recognizing that IgAV can manifest without classic signs, particularly when complicated by pulmonary-renal syndrome [3,12-15]. The severity of complications in our case is noteworthy: alveolar hemorrhage, occurring in only 0.8% to 5.0% of cases, is associated with a 27.6% mortality rate and is more common in older male patients [3]. Cardiovascular complications are extremely rare and predominantly seen in adult patients [4], while stroke remains an exceptionally uncommon neurologic complication in severe IgAV [5,16]. Based on (1) the favorable response to corticosteroid therapy, (2) the pathological findings of Gd-IgA1, (3) the simultaneity of multiple organ involvement, and (4) the absence of findings suggesting other vasculitis, this case is most appropriately considered as IgAV presenting with an extremely rare combination of complications.

Conclusions

The dramatic response to corticosteroid therapy, along with the pathological evidence of Gd-IgA1 deposition and the pattern of multiple organ involvement in this young patient, strongly support systemic IgAV as the underlying pathological process rather than separate organ-specific pathologies. The simultaneous presentation of DAH (mortality rate 27.6%), heart failure, and stroke - three extremely rare complications in IgAV - makes this case particularly noteworthy.

To the best of our knowledge, there have been no reports of cases with these three overlapping serious complications, as seen in the present case. This case emphasizes that in adult-onset pulmonary-renal syndrome with additional complications such as heart failure or stroke. In contrast, various vasculitis syndromes are typically suspected, and IgAV should be considered a potential differential diagnosis, even in

the absence of the typical tetrad. Early recognition and prompt initiation of appropriate therapy may be crucial for favorable outcomes in such cases with multiple severe complications.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Supervision: Yuki Tanabe, Mai Motojima, Shinichi Sasaki, Kazuhisa Takahashi, Fumihiko Makino, Hitoshi Suzuki, Shigeki Tomita

Disclosures

Human subjects: Consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

- Jennette JC, Falk RJ, Bacon PA, et al.: 2012 revised international chapel hill consensus conference nomenclature of vasculitides. *Arthritis Rheum.* 2013, 65:1-11. [10.1002/art.37715](https://doi.org/10.1002/art.37715)
- Sunderkötter CH, Zelger B, Chen KR, et al.: Nomenclature of cutaneous vasculitis: dermatologic addendum to the 2012 revised International Chapel Hill consensus conference nomenclature of vasculitides. *Arthritis Rheumatol.* 2018, 70:171-84. [10.1002/art.40375](https://doi.org/10.1002/art.40375)
- Rajagopala S, Shobha V, Devaraj U, D'Souza G, Garg I: Pulmonary hemorrhage in Henoch-Schönlein purpura: case report and systematic review of the english literature. *Semin Arthritis Rheum.* 2013, 42:391-400. [10.1016/j.semarthrit.2012.07.004](https://doi.org/10.1016/j.semarthrit.2012.07.004)
- Yılmaz N, Yüksel S, Becerir T, et al.: Myocarditis and intracardiac thrombus due to Henoch-Schönlein purpura: case report and literature review. *Clin Rheumatol.* 2021, 40:1635-44. [10.1007/s10067-020-05317-8](https://doi.org/10.1007/s10067-020-05317-8)
- Pacheva IH, Ivanov IS, Stefanova K, et al.: Central nervous system involvement in Henoch-Schönlein purpura in children and adolescents. *Case Rep Pediatr.* 2017, 2017:5483543. [10.1155/2017/5483543](https://doi.org/10.1155/2017/5483543)
- Lapides R, Crespo-Quezada J, Thomas T, Carmona Pires F, Chera G: IgA vasculitis followed by IgA nephropathy without an identifiable trigger: the same disease or a spectrum of related conditions?. *Cureus.* 2023, 15:45639. [10.7759/cureus.45639](https://doi.org/10.7759/cureus.45639)
- Flood D, Barber B, Miletta NR: Diagnosing IgA vasculitis in the active duty population: the importance of early diagnosis and proper biopsy site selection. *Mil Med.* 2018, 183:663-6. [10.1093/milmed/usx234](https://doi.org/10.1093/milmed/usx234)
- Khor SY, Osman AF, Haddad I, AlAttal S, Khan N: Adult-onset immunoglobulin a vasculitis with renal involvement. *Cureus.* 2022, 14:23649. [10.7759/cureus.23649](https://doi.org/10.7759/cureus.23649)
- Fratice P, Benfaremo D, Gabrielli A: Diagnosis and management of leukocytoclastic vasculitis. *Intern Emerg Med.* 2021, 16:831-41. [10.1007/s11739-021-02688-x](https://doi.org/10.1007/s11739-021-02688-x)
- Darlington K, Googe P, Vedak P, Jain A, Long MD, Barnes EL, Herfarth HH: Lower extremity palpable purpura in a patient with quiescent inflammatory bowel disease. *Dig Dis Sci.* 2023, 68:2861-5. [10.1007/s10620-023-07934-0](https://doi.org/10.1007/s10620-023-07934-0)
- Suzuki H, Yasutake J, Makita Y, et al.: IgA nephropathy and IgA vasculitis with nephritis have a shared feature involving galactose-deficient IgA1-oriented pathogenesis. *Kidney Int.* 2018, 93:700-5. [10.1016/j.kint.2017.10.019](https://doi.org/10.1016/j.kint.2017.10.019)
- Ozen S, Pistorio A, Iusan SM, et al.: EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. *Ann Rheum Dis.* 2010, 69:798-806. [10.1136/ard.2009.116657](https://doi.org/10.1136/ard.2009.116657)
- Ito Y, Arita M, Kumagai S, et al.: Diffuse alveolar hemorrhage in IgA vasculitis with an atypical presentation. *Intern Med.* 2018, 57:81-4. [10.2169/internalmedicine.8984-17](https://doi.org/10.2169/internalmedicine.8984-17)
- Kolman M, Song S, Han T, Asado N, Ehrenpreis ED: A case report of diffuse alveolar hemorrhage coexisting

- with immunoglobulin A (IgA) nephropathy. *Cureus*. 2022, 14:31941. [10.7759/cureus.31941](https://doi.org/10.7759/cureus.31941)
15. Rajagopala S, Parameswaran S, Ajmera JS, Ganesh RN, Katrevula A: Diffuse alveolar hemorrhage in IgA nephropathy: case series and systematic review of the literature. *Int J Rheum Dis*. 2017, 20:109-21. [10.1111/1756-185X.12818](https://doi.org/10.1111/1756-185X.12818)
 16. Geraldes R, Santos M, Ponte C, et al.: Stroke frequency, associated factors, and clinical features in primary systemic vasculitis: a multicentric observational study. *J Neurol*. 2024, 271:3309-20. [10.1007/s00415-024-12251-1](https://doi.org/10.1007/s00415-024-12251-1)