CASE REPORT

# Rapid Progression of ANCA-Positive IgA Nephropathy: A Fatal Case in a Young Woman

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## ABSTRACT

IgA nephropathy (IgAN) is the most prevalent primary glomerulonephritis, with a variety of clinical presentations, including asymptomatic microscopic haematuria and rapidly progressive glomerulonephritis (RPGN). The coexistence of anti-neutrophil cytoplasmic antibody (ANCA) positivity in IgAN is rare and associated with more severe clinical and histological manifestations. We present a case of a 20-year-old woman with ANCA-positive IgAN who initially presented with persistent microscopic haematuria and proteinuria. A renal biopsy confirmed IgA nephropathy with crescents formation, and ANCA testing revealed positive anti-myeloperoxidase antibodies. Despite initial follow-up challenges, her condition progressed to RPGN, requiring haemodialysis. Unfortunately, she later succumbed to severe pneumonia complicated by acute respiratory distress syndrome (ARDS). This case highlights the importance of recognising ANCA positivity in IgAN, as it may indicate a more aggressive disease course, requiring early and aggressive management. Further studies are needed to explore the pathogenic role of ANCA in IgAN and its implications for treatment.
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## INTRODUCTION

IgA nephropathy (IgAN) is the most typical form of primary glomerulonephritis, characterised by the presence of mesangial IgA deposits. Despite its typical presentation as isolated microscopic haematuria, it may occasionally present as rapidly progressive glomerulonephritis (RPGN). The coexistence of anti-neutrophil cytoplasmic antibody (ANCA) positivity in IgAN is rare, typically occurring in older patients, and is characterised by crescentic histological findings, more frequent systemic symptoms, and rapid progression of kidney failure, requiring aggressive immunosuppressive therapy compared to ANCA-negative IgAN. ANCA is a group of autoantibodies directed against neutrophil cytoplasmic antigens, primarily myeloperoxidase (MPO) and proteinase 3 (PR3). Their presence is commonly associated with systemic vasculitides. ANCA-associated vasculitis (AAV) is a group of autoimmune diseases that often cause inflammation of small blood vessels with little or no deposition of immune complexes in the vessel wall (pauci-immune). In contrast to IgAN, the renal lesions observed in AAV are pauci-immune, localised, and segmental necrotising crescentic glomerulonephritis. This case report highlights an uncommon presentation of ANCA-positive IgAN in a young lady with rapidly progressive renal decline, emphasising the need for timely diagnosis and management.

## CASE REPORT

A 20-year-old female with no prior medical illness was referred from a tertiary hospital to the Urology Clinic in our centre for evaluation of persistent microscopic haematuria, noted during a medical check-up six

months earlier. Patient was asymptomatic, denying episodes of gross haematuria, abdominal pain, dysuria, fever, skin rash, joint pain, cough, fatigue or the use of any supplements or traditional medications. Her urination was normal. The patient is the second of five siblings, with no significant family history of renal or other medical conditions. Initial urine analysis revealed blood 3+ and protein ±. Her serum urea and creatinine levels were 4.2 mmol/L and creatinine 62 µmol/L, respectively. An ultrasound scan showed no evidence of nephrolithiasis.

During follow-up visits to the Urology Clinic, persistent microscopic haematuria (blood 3+), proteinuria (protein 3+) (Erba Laura, semi-quantitative automated analyser), and negative nitrate and leukocytes were noted. The patient exhibited mild anaemia (Hb 9.0 g/dL) and worsening renal function, with serum urea increasing to 8 mmol/L and creatinine rising to 137 µmol/L. She was subsequently referred to the Nephrology Clinic for further evaluation and was counselled for a renal biopsy. Autoimmune testing showed negative antinuclear antibody (ANA) (enzyme-linked immunosorbent assay, ELISA) and anti-glomerular basement membrane antibodies (GBM) (ELISA). Further investigations revealed p-ANCA staining (indirect immunofluorescence assay, IFA) and a highly positive anti-MPO (>739.8 CU) (chemiluminescent immunoassay, CIA). Anti-streptolysin O titre (ASOT) was not sent for this patient, while her C-reactive protein and complement levels were normal.

The renal biopsy findings indicate a focal active proliferative pattern with 13.5% cellular crescent [Figure 1], moderate sclerosis (30% global sclerosis, 41% segmental sclerosis) [Figure 2] and chronic tubulointerstitial damage (30%). Immunofluorescence studies showed focal granular mesangial deposition of IgA (1+) [Figure 3], IgM (2+) and C1q (1+), while IgG and C3 were negative. Kappa and Lambda show no light chain restriction. The final diagnosis was consistent with IgA nephropathy.

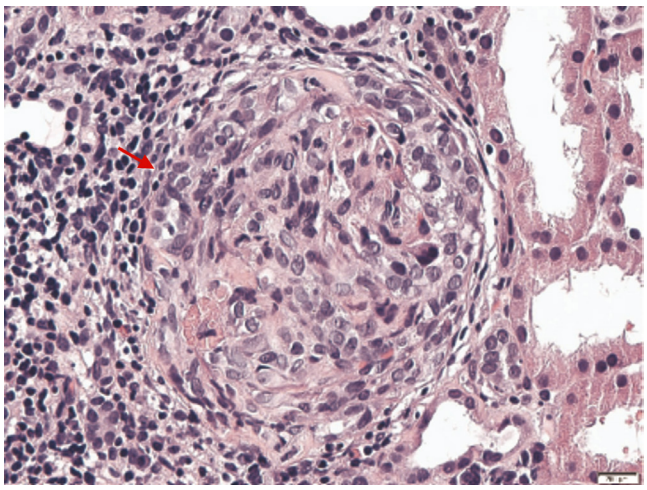

**Figure 1: Arrow showing a glomerulus with cellular crescent formation (Periodic acid Schiff, magnification x400)**

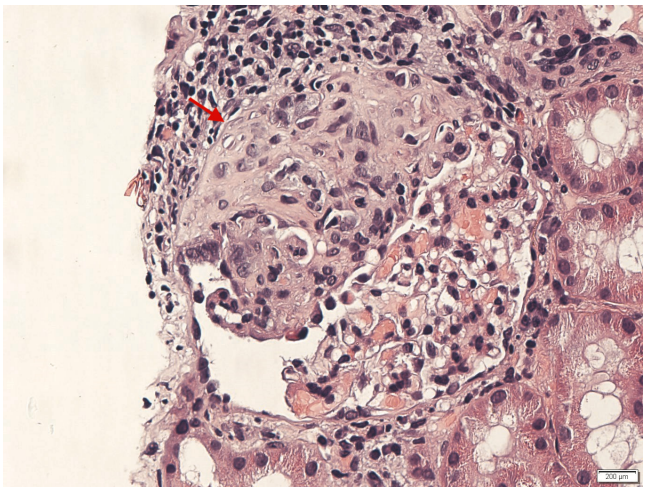

**Figure 2: Arrow showing a glomerulus with segmental sclerosis. (Periodic acid Schiff, magnification x400)**

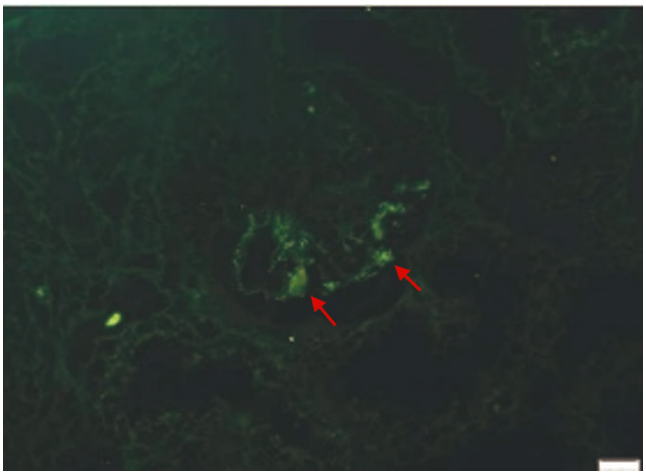

**Figure 3: Immunofluorescence study shows focal granular mesangial positivity for IgA (1+). Arrows showing IgA deposits (magnification x400)**

Unfortunately, the patient missed subsequent clinic appointments and returned three months later with significantly worsened renal function, evidenced by elevated urea (18 mmol/L) and creatinine (437 µmol/L) levels. Despite remaining asymptomatic with no gross haematuria and adequate urine output, she was admitted with a diagnosis of IgA nephropathy with RPGN and underlying chronic kidney disease. She received a three-day course of intravenous methylprednisolone, followed by oral prednisolone, and was started on mycophenolate mofetil for two months. She underwent haemodialysis and was counselled regarding long-term renal replacement therapy. After a nine-day hospital stay, she was discharged on a biweekly haemodialysis schedule.

Over the course of one year, she had multiple episodes of admission due to pneumonia and fluid overload.

Prior to her demise, she developed haemoptysis and was intubated due to respiratory distress, with fresh blood noted in the endotracheal and Ryle's tube. She subsequently suffered cardiac arrest and cardiopulmonary resuscitation was performed, but it was unsuccessful. The cause of death was severe pneumonia with acute respiratory distress syndrome (ARDS).

## DISCUSSION

This is a case of a 20-year-old lady with ANCA-positive IgAN presenting with RPGN. IgAN is the most common cause of primary (idiopathic) glomerulonephritis. Although IgAN patients can present at any age, the condition is most common in the second and third decades of life. Based on The Malaysian Registry of Renal Biopsy 2022, a total of 2281 cases of IgAN were documented between 2005 to 2022. The leading primary glomerulonephritis were focal segmental glomerulosclerosis (30%), followed by minimal change nephropathy (28.9%) and IgAN (23.8%). A slight female predominance was observed (60.3% vs 39.7%), with the majority of cases (82%) occurring in individuals aged 15 to 45 years [1].

IgAN presents with diverse clinical manifestations, ranging from asymptomatic microscopic haematuria to RPGN. Its hallmark is mesangial IgA deposits, identified through immunofluorescence microscopy. These deposits show dominant or codominant IgA deposits, either alone or alongside IgG and/or IgM [2].

ANCAs are frequently associated with pauci-immune crescentic glomerulonephritis and vasculitis, which are conditions that are associated with a significant increase in mortality and morbidity. The coexistence of IgAN and ANCA seropositivity, as seen in this patient, is rare and not fully understood. Xie et al. (2018) reported ANCA positivity in 1.4% of 2,390 individuals with biopsy-proven IgAN [3], while other study reported prevalence of 2% [4].

In Malaysia, there is limited data on ANCA-positive IgAN. This is likely due to the rarity of the condition, with only a small proportion of IgAN cases globally showing ANCA positivity. In addition, ANCA testing is not routinely performed in all IgAN patients unless vasculitis is suspected, and access to specific assays may be limited to tertiary centers. Furthermore, national glomerulonephritis registries report overall IgAN prevalence but do not stratify patients by ANCA status. These factors contribute to under-detection and under-reporting rather than a true absence of disease.

According to Bantis et al. (2010), ANCA-positive individuals with crescentic IgAN had higher peak serum creatinine levels over the first three months and were more likely to develop rapidly progressive kidney failure than their ANCA-negative counterparts [4]. Although our patient did not meet the histological criteria for crescentic IgAN, the presence of crescents alongside MPO-ANCA positivity is notable. At just 20 years of age, she experienced a rapid decline in renal function, resulting in end-stage kidney disease requiring haemodialysis. This aggressive course is more characteristic of AAV, particularly in cases with MPO-ANCA positivity.

Xie et al. (2018) performed a retrospective case-control study reporting that 40% of ANCA-positive patients with IgAN experienced systemic symptoms, such as fever, anaemia, haemoptysis, arthralgia, and presented with rapidly deteriorating kidney function compared to ANCA-positive IgAN patients without systemic symptoms [3]. Natalia Chebotareva et al. (2020) described two patients with MPO-ANCA IgAN who presented with extra-renal manifestations but ultimately survived with immunosuppressive treatment [5]. In contrast, our patient, despite lacking systemic features, experienced a rapid decline in renal function, highlighting that severe renal outcomes may still occur in ANCA-positive IgAN, even in the absence of extra-renal manifestations.

Histologically, ANCA-positive IgAN correlates with more severe lesions. In contrast to ANCA-negative instances, ANCA-positive patients exhibited a greater proportion of crescentic glomeruli (54.3% versus 34.5%) and an increased extent of tubular atrophy (43% versus 28%) [5]. Interestingly, our patient's renal biopsy revealed only 13.5% crescents, yet she experienced severe clinical deterioration, suggesting that even limited histological activity may not reliably predict outcomes.

Immunosuppressive therapy, typically combining corticosteroids and cyclophosphamide, remains the standard approach for ANCA-positive IgAN and has led to remission or stabilisation of renal function in approximately 59.3% of cases [3]. Unfortunately, our patient missed early clinic appointments, resulting in delayed initiation of immunosuppression only after the diagnosis of RPGN. Early adherence to appointments and timely initiation of immunosuppressive treatment might have prevented her renal decline.

Her clinical deterioration prior to her death raised suspicion of pulmonary haemorrhage, though a CT pulmonary angiogram could not be performed due to her unstable condition. Given her MPO-ANCA positivity and renal involvement, an underlying vasculitis cannot be ruled out. While the presence of MPO-ANCA raises suspicion for AAV, the biopsy findings were not consistent with the classic pauci-immune necrotising vasculitis. Instead, mesangial IgA deposition was evident, supporting IgAN as the dominant pathology. Furthermore, her lack of systemic vasculitic features and relatively low crescentic burden further argues against AAV. Nevertheless, the co-existence of AAV and IgAN cannot be entirely excluded.

## CONCLUSION

This case illustrates several unique features compared to previously reported cases of ANCA-positive IgAN, including an extremely young age at presentation, the presence of MPO-ANCA without systemic involvement - an association typically linked to a milder disease course, severe clinical progression despite low crescent formation on biopsy, and the possibility of co-existence of AAV and IgAN. Early recognition, close patient follow-up, and prompt initiation of immunosuppressive therapy are essential to prevent irreversible renal damage. Further research is needed to better understand the role of ANCA in IgAN and to determine whether this represents a unique clinical condition or a coincidental occurrence.

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## REFERENCES

1. Thong KM, Yahya R and Wong I (Eds). 2025. 8th Report of the Malaysian Registry of Renal Biopsy 2022, Kuala Lumpur. 8th report of the Malaysian Registry of Renal Biopsy 2022, Kuala Lumpur
2. Wyatt R.J., Julian B.A. IgA Nephropathy. N Engl J Med 2013; 368:2402-14. DOI:10.1056/NEJMra1206793
3. Xie, L., He, J., Liu, X., Tang, S., Wang, W., Li, F., Zhang, Y., Zhang, J., Huang, Y., Zhao, J., Li, Y., & Zhang, J. (2018). Clinical value of systemic symptoms in IgA nephropathy with ANCA positivity. Clinical rheumatology, 37(7), 1953–1961. https://doi.org/10.1007/s10067-017-3931-z
4. Christos Bantis, Maria Stangou, Christoph Schlaugat, Efstathios Alexopoulos, Aphroditi Pantzaki, Dimitrios Memmos, Katrin Ivens, Peter J. Heering. Is Presence of ANCA in Crescentic IgA Nephropathy a Coincidence or Novel Clinical Entity? A Case Series. American Journal of Kidney Diseases, Volume 55, Issue 2, 2010. https://doi.org/10.1053/j.ajkd.2009.09.031
5. Natalia Chebotareva, Elena Kamyshova, Nikolay Bulanov, Lidia Lysenko, Sergey Moiseev. Antineutrophil cytoplasmic autoantibody (ANCA) positive immunoglobulin A (IgA) nephropathy: Case reports and review of literature. The Egyptian Rheumatologist. Volume 42, Issue 3, 2020 https://doi.org/10.1016/j.ejr.2020.06.002