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Case Report

Challenges in Management of Renal Failure due to Glomerulonephritis associated with Serine Proteinase 3 and Myeloperoxidase Anti-Neutrophilic Cytoplasmic Antibodies and Anti-Glomerular Basement Membrane Antibody in a Jehovah's Witness

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ABSTRACT

Triple-seropositive disease (TPD), defined here as concurrent MPO-ANCA, PR3-ANCA, and anti-GBM antibodies, is rare and typically severe. We report a 71-year-old Jehovah's Witness who presented with advanced kidney failure and a large pericardial effusion. Serology confirmed triple positivity, but kidney biopsy tissue was markedly limited. Plasma exchange (PLEX) was declined on religious grounds. Induction was therefore undertaken with high-dose glucocorticoids and rituximab, coordinated with hemodialysis and bloodless-medicine strategies. Despite therapy, she remained dialysis dependent. This case highlights pragmatic, preference-concordant management in the setting of sparse tissue, triple seropositivity, and refusal of PLEX.

Keywords: Triple-seropositive disease; Plasma exchange; Pericardial effusion; High-dose glucocorticoids

Introduction

Rapidly progressive glomerulonephritis (RPGN) most commonly arises from ANCA-associated vasculitis (AAV) or anti–glomerular basement membrane (anti-GBM) disease. The better-described "double-positive" overlap (ANCA plus anti-GBM) has emerged as a true hybrid phenotype, characterized by severe initial kidney injury and pulmonary risk but an AAV-like propensity to relapse, prompting recommendations for both anti-GBM–intensity induction and AAV-style maintenance. In contrast, triple-positive disease (TPD) remains exceptionally rare, with only a small number of cases reported across renal-limited and pulmonary–renal presentations. No guideline addresses TPD explicitly, and current management is extrapolated from double-positive overlap, AAV, and anti-GBM disease. We present this case to illustrate the challenges of TPD, particularly in the setting of significant diagnostic and treatment limitations.

Case Report

A 71-year-old Jehovah's Witness woman with a history of hypertension presented with 10 days of malaise, anorexia, and intermittent nausea. In the few days preceding admission, she developed vomiting and noted "foamy" urine. Physical examination was largely unremarkable, notable only for mild lower-extremity pitting edema and muffled heart sounds. She had not followed her primary care physician for routine preventive medical care and was not taking any medications. The patient reported a 10-year history of weekend employment as a cleaning worker with exposure to cleaning chemicals; this employment ended two years prior to presentation. She denied any occupational or environmental exposure to silica dust and reported no participation in agricultural or farming activities. Her sister had died from complications of systemic lupus erythematosus in her 20s. Her last known laboratory studies (obtained during an emergency department visit) six years earlier showed a creatinine of 0.81 mg/dL and BUN of 13 mg/dL. **(Table 1)** shows the laboratory parameters at admission. **(Table 2)** shows the results of urinalysis at admission and **(Table 3)** shows the results of autoantibody profile.

Table 1: Lab Results with Reference Ranges.

Component	Result	Reference Range
WBC	3.43 ×10³/µL	3.6 – 11.2 ×10³/µL
Lymphocytes	16%	~20 – 40%
Eosinophils	0.3%	~0 – 5%
Hemoglobin	10.4 g/dL	12.0 – 16.5 g/dL
Platelets	291	150 - 400 K/CMM
BUN	96.3 mg/dL (6 yrs ago: 13)	8.0 – 23.0 mg/dL
Creatinine	6.96 mg/dL (6 yrs ago: 0.81)	0.44 – 1.03 mg/dL
eGFR	6 mL/min/1.73 m²	≥ 60 mL/min/1.73 m²
Calcium	8.3 mg/dL	8.9 – 10.3 mg/dL
Phosphorus	5.2 mg/dL	2.5 – 4.5 mg/dL
Albumin	3.0 g/dL	3.5 – 5.2 g/dL
ESR	87 mm/hr	<30 mm/hr
CRP	75 mg/L	<5 mg/L

Table 2: Urinalysis Results.

Component	Result	Reference Range
Color	Colorless	Yellow, Straw
Clarity	Cloudy	Clear
Specific Gravity	1.012	1.005 - 1.030
pH	5.0	5.0 - 8.0
Leukocytes	3+	Negative
Nitrite	Negative	Negative
Protein	1+	Negative, Trace
Blood	3+	Negative
WBC	51-100 /HPF	None Seen, 1-4 /HPF
RBC	51-100 /HPF	None Seen, 1-4 /HPF
Hyaline Casts	None Seen	None Seen, 0-2 /LPF
Granular Casts	Present	None Seen

She was given a bicarbonate infusion. Her urinary output in the first 24 hours was 350 mL. A chest x-ray showed pericardial effusion, and an echocardiogram revealed a moderate to large circumferential pericardial effusion which was approximately 3 cm in depth. It also showed early diastolic collapse of the right atrium, suggesting cardiac tamponade.

Table 3: Results of autoimmune antibody profile.

Test	Result	Value
ANA by ELISA	Positive	132
MPO-ANCA	Positive	>8 (Ref <0.4 negative)
PR3-ANCA	Positive	Qualitative only (no titer reported)
SS-A (RO) Antibody	Positive	132
GBM Antibody	Positive	3.6 Positive >=1.0

Plasma exchange was offered, but she declined it on religious grounds. Hence, she received IV methylprednisolone 250 mg daily for 3 days and then transitioned to Prednisone 60 mg/day with a taper over 3 months.

A tunnelled haemodialysis catheter was placed. Haemodialysis was initiated, and was performed daily for three sessions, then transitioned to a thrice-weekly schedule. A percutaneous kidney biopsy was performed, but the tissue was limited. On light microscopy, only 2 glomeruli are seen, 1 of which was globally sclerotic. The single open glomerulus showed no significant mesangial matrix expansion or hypercellularity. The glomerular basement membranes did not appear thickened, and no deposits or double contouring is seen. No crescents, fibrinoid necrosis, segmental sclerosis, or thrombi were observed. Mild arteriosclerosis and red blood cell casts within some distal tubules were seen. Tissue for immunofluorescence studies contained no glomeruli. Due to the limited nature of the specimen, electron microscopy was not performed. Repeat kidney biopsy was offered, but she declined.

After a negative TB screening and undetectable HBV DNA, she was given rituximab in a dose of 375 mg/m² weekly for 4 weeks. She also received Iron Sucrose infusions for 4 doses and subcutaneous darbepoetin for anemia, trimethoprim-sulfamethoxazole for Pneumocystis jirovecii prophylaxis, and a proton-pump inhibitor for gastrointestinal reflux. For the large pericardial effusion, no pericardiocentesis was required. A repeat Transthoracic echocardiogram showed a persistent large effusion without tamponade. Her kidney function did not improve with Rituximab and prednisone, and she remained dialysis dependent.

Discussion

Triple-positive disease (MPO-ANCA, PR3-ANCA, and anti-GBM) sits at the extreme end of the pathogenic spectrum, where profound loss of immune tolerance culminates in severe systemic injury, predominantly renal and pulmonary. Yet we still do not fully understand which mechanisms are truly driving the process. Most of our knowledge comes from larger double-positive cohorts and only a handful of triple-positive cases. Across the literature, double-positive patients (DPP) ANCA + anti-GBM disease emerge as a distinct hybrid phenotype rather than a simple variant of either condition alone[1-3]. The retrospective analysis of large multi-centre European cohort showed that these patients behave like anti-GBM early, with rapid kidney injury and pulmonary risk, yet relapse later like AAV, meaning that optimal care requires anti-GBM-style urgent induction and long-term AAV-type maintenance.1 Another cohort reinforces this picture: in the Chinese retrospective study, double-positive patients were typically older, had worse renal function at diagnosis than single positive MPO-AAV, and demonstrated

broader multiorgan involvement especially cardiac with clearly poorer renal and patient survival compared with MPO-AAV. Prognosis was tightly linked to kidney function. 2 A systematic review of DPP found that most patients present with acute kidney failure (~92%), about half with alveolar haemorrhage, and nearly one-third with ENT or joint disease, with MPO-ANCA overwhelmingly dominating over PR3-ANCA and true triple-positivity remaining rare at 2.9%. 3 When all three sources are considered together, they paint a consistent narrative: double-positive disease is severe at presentation, systemically active, recovery-capable yet relapse-prone, and biologically aligned to both AAV and anti-GBM, demanding treatment that is both aggressive up front and vigilant long-term.

Triple-positive disease case reports including our Jehovah witness case frame it as an extreme, rare variant on the same spectrum. Across these cases, a recognizable therapeutic pattern emerges early induction with high-dose corticosteroids, cyclophosphamide, and plasma exchange appears to be the central strategy, yet outcomes diverge widely depending on age, comorbid burden, and biopsy phenotype **(Table 4)**. Overall, better prognosis correlates with younger age, lower chronicity on biopsy, and timely therapy, whereas delayed presentation, comorbid disease, and complete glomerular destruction predict irreversible renal failure or death[4-10].

Table 4: Shows the details of TPD patients reported in the literature.

Ref#	Year	Age	Race	Clinical Phenotype	Histology	Treatment	Outcome
[4]	2025	29	Unknown	Pulmonary–renal	Extra capillary proliferation with fibro cellular and cellular crescents.	Methylprednisolone, Cyclophosphamide, Plasma exchange Maintenance treatment: Azathioprine	Renal and pulmonary improvement
[5]	2022	62	Caucasian	Renal Limited	Immunofluorescent staining showed linear deposition of IgG anti-GBM antibody	Steroid, Cyclophosphamide, Plasma exchange	Dialysis dependent.
[6]	2017	68	Unknown	Renal Limited	Pauci-immune type crescentic glomerulonephritis Global and segmental sclerosis, cellular and fibrocellular crescents. Prominent interstitial fibrosis, tubular atrophy, and infiltration of inflammatory cells.	IV Prednisolone, Cyclophosphamide, Plasma exchange	Renal function improved.
[7]	2021	54	Unknown	Renal Limited	Pauci-immune crescentic glomerulonephritis. Global sclerosis with crescents	Methylprednisolone, Cyclophosphamide, Plasma exchange	Renal function improved.
[8]	2023	79	Unknown	Renal Limited	Autopsy kidney biopsy Pauci-immune glomerulonephritis, fibrocellular crescents endocapillary hypercellularity, mesangial cell proliferation, tubular atrophy.	Methylprednisolone, Cyclophosphamide, Plasma exchange.	Fatal
[9]	2021	80	Caucasian	Pulmonary–renal	Linear deposition of IgG along the GBM Cellular crescents in 57% glomeruli with focal fibrinoid necrosis and mildly interstitial fibrosis, inflammatory infiltrate.	Methylprednisolone, Cyclophosphamide, Plasma exchange.	Respiratory symptoms improved. Renal function did not improve. Dialysis dependent.
[10]	2020	51	Caucasian	Renal Limited	Mesangial positivity for IgA, C3, lambda, and IgG4 positive plasma cell. Cellular crescents, segmental necrosis, lymphoplasmacytic infiltrate.	Methylprednisolone, Cyclophosphamide, Plasma exchange.	Renal function improved.

The biopsy spectrum across triple and double positive, linear IgG crescents, pauci-immune patterns without deposition, and IgG4- or IgA-rich infiltrates reinforces that the same serologic triad can sit atop different histologic and cellular pathways.1-10 More broadly, work in crescentic GN shows that crescents themselves represent a common structural response to diverse injuries, involving not only immune complexes but also intrinsic parietal epithelial cell proliferation and fibrogenic signaling[11].

Pathophysiologically, these cases together support the idea that triple-positive disease is not three separate illnesses layered by chance, but a manifestation of profound immune tolerance breakdown. ANCA-associated vasculitis reflects loss of B- and T-cell tolerance to MPO and PR3, with neutrophil activation, NET formation, complement engagement, and endothelial injury driving capillarity's and necrotizing glomerulitis. Anti-GBM disease adds antibodies directed against cryptic GBM epitopes in the glomerular and alveolar basement membranes. Intermolecular epitope spreading offers a plausible bridge ANCA-mediated injury could expose GBM antigens and trigger anti-GBM antibodies, or primary anti-GBM damage could unmask neutrophil antigens and provoke MPO/PR3 ANCA but in any given triple-positive patient we have no reliable way to know which process came first or which is dominant[12,13].

These mechanistic uncertainties flow directly into therapeutic uncertainty. Double-positive series tell us that overlap disease demands both anti-GBM intensity induction and AAV-style

maintenance, but they offer almost no triple-positive–specific guidance. The handful of published triple-positive cases and our Jehovah's Witness patient show that even with such aggressive regimens, many patients remain dialysis-dependent or die. Ultimately, triple-positive disease, and crescentic GN more broadly, expose the limits of our framework: we deploy powerful, largely non-specific immunosuppression and extracorporeal therapies against a process whose exact drivers, sequence, and points of reversibility remain only partly mapped, and we lack reliable tools to identify the dominant pathway in an individual patient. Until more cases are aggregated and mechanistic, work catches up with clinical observation; management will remain highly individualized and largely extrapolated from existing overlap data from DPP.

Conclusion

This case underscores that triple-seropositive disease (TPD) is not only biologically complex but also clinically challenging. Beyond the striking serology, our patient's care was shaped by late presentation, sparse tissue, dialysis-level kidney failure, and the patient's refusal of PLEX. Together with the small existing case series, our experience suggests that once chronic, structurally fixed injury is established, even well-constructed regimens may be unable to restore kidney function. For clinicians, this highlights the importance of early recognition of possible overlap disease, thoughtful use of limited biopsy material, and proactive involvement of bloodless-medicine and ethics teams when standard therapies conflict with religious beliefs. For the field, it emphasizes the need for collaborative registries and mechanistic studies focused specifically on triple-seropositive patients, so that future management can be guided by more than extrapolation and individual case reports.

References

1. McAdoo SP, Tanna A, Hruskova Z, et al. Patients double-seropositive for ANCA and anti-GBM antibodies have varied renal survival, frequency of relapse, and outcomes compared with single-seropositive patients. Kidney Int 2017;92(3):693-702.
2. Hu X, Shen C, Meng T, et al. Clinical features and prognosis of MPO-ANCA and anti-GBM double-seropositive patients. Front Immunol 2022;13:991469.
3. Philip R, Dumont A, Martin Silva N, et al. ANCA and anti-glomerular basement membrane double-positive patients: a systematic review of the literature. Autoimmune Rev 2021;20(9):102885.
4. Ghenam N, Dahmane R, Chebbi C, et al. Overlap syndrome: a rare triple-positive systemic vasculitis-ANCA (MPO, PR3) and anti-GBM. Kidney Int Rep 2025;10(2): S216.
5. Vedire A, Upadrasta G, Udongwo N, Rehman F, Hossain MA. Triple jeopardy: rapidly progressive glomerulonephritis induced by triple seropositive disease-a rare case. Case Rep Med 2022:2032525.
6. Sato N, Yokoi H, Imamaki H, et al. Renal-limited vasculitis with elevated levels of multiple antibodies. CEN Case Rep 2017;6(1):79-84.
7. Andhale A, Bhawane A, Acharya S, Shukla S, Annadatha A, Hulkoti V. Triple-positive renal-limited vasculitis presenting with rapidly progressive glomerulonephritis: a case report. J Acute Dis 2021;10(2):83-86.
8. Ishikawa H, Ota Y, Iwasaki K, Muta K, Nishino T. A fatal case of rapidly progressive glomerulonephritis with two anti-neutrophil cytoplasmic antibodies and anti-glomerular basement membrane antibody: autopsy findings. Cureus 2023;15(8):44160.
9. Palha V, Sá A, Pimentel T, et al. A rare case of pulmonary-renal syndrome triple seropositive for MPO-ANCA, PR3-ANCA, and anti-glomerular basement membrane antibodies. J Med Cases 2021;12(10):405-410.
10. Galante JR, Daruwalla CP, Roberts ISD, et al. An unusual presentation of propylthiouracil-induced anti-MPO and PR3-positive ANCA vasculitis associated with anti-GBM antibodies, IgA nephropathy, and an IgG4 interstitial infiltrate. BMC Nephrol 2020;21(1):295.
11. Wong MN, Tharaux PL, Grahammer F, Puelles VG. Parietal epithelial cell dysfunction in crescentic glomerulonephritis. Cell Tissue Res 2021;385(2):345-354.
12. Xiao H, Hu P, Falk RJ, Jennette JC. Overview of the pathogenesis of ANCA-associated vasculitis. Kidney Dis (Basel) 2015;1(4):205-215.
13. Nishibata Y, Nonokawa M, Tamura Y, et al. Possible implication of intermolecular epitope spreading in the production of anti-glomerular basement membrane antibody in anti-neutrophil cytoplasmic antibody-associated vasculitis. Clin Exp Rheumatol 2022;40(4):691-704.