

Double filtration plasmapheresis in anti-amphiphysin antibody syndrome mimicking multiple system atrophy: A case report

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Case Report

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Abstract

We retrospectively analyzed a patient with a positive anti-amphiphysin antibody status to characterize the clinical manifestations, diagnostic workup, and treatment results of anti-amphiphysin antibody disease that mimics multiple system atrophy (MSA), and we reviewed the relevant literature. The patient primarily presented with Parkinsonism, cerebellar ataxia, and autonomic dysfunction. An 82-year-old male presented with a subacute onset of bradykinesia, ataxia, and severe orthostatic hypotension. Brain magnetic resonance imaging (MRI) revealed hippocampal and cerebellar atrophy. Serum autoimmune neurological antibody testing was positive for anti-amphiphysin IgG (titer 1:320). Based on the multisystem involvement and exclusionary diagnostic workup, the patient was diagnosed with anti-amphiphysin antibody-associated MSA-like autoimmune neurological syndrome. After three sessions of double filtration plasmapheresis (DFPP) and sequential therapy with mycophenolate mofetil, the patient's motor function and orthostatic hypotension improved significantly. At the 6-month follow-up, the antibody titer decreased to 1:32, and the clinical condition remained stable. Anti-amphiphysin antibody syndrome can mimic MSA. Prompt neuronal autoantibody and long-term tumor screening are required for rapidly progressive atypical MSA-spectrum patients with severe autonomic failure. DFPP combined with immunosuppression achieves a favorable neurological prognosis.

1 | Part I: Introduction

Multiple system atrophy (MSA) is a rare, rapidly progressive neurodegenerative disorder characterized pathologically by abnormal accumulation of α -synuclein within oligodendrocytes. Its clinical manifestations typically include autonomic dysfunction, Parkinsonism, cerebellar ataxia, and pyramidal signs ^[1]. To date, disease-modifying therapy is available for sporadic MSA, an irreversible α -synucleinopathy. Immune dysregulation has been implicated in atypical parkinsonian-ataxia syndromes, but anti-amphiphysin IgG as a reversible MSA mimic remains rarely characterized in aged cohorts. Distinguishing immune-mediated MSA mimics from degenerative MSA is critical, as immunotherapy can produce durable clinical recovery in the former group ^[2, 3].

Anti-amphiphysin antibodies are well-known markers for paraneoplastic neurological syndromes (PNS), most frequently accompanying breast cancer or small cell lung cancer ^[4, 5]. While the classic clinical phenotype is stiff-person syndrome (SPS), these antibodies can also present as encephalomyelitis, limbic encephalitis, and autonomic dysfunction ^[6]. Here, we describe an elderly patient with anti-amphiphysin IgG presenting with a full MSA clinical triad (parkinsonism, cerebellar ataxia, autonomic failure) without detectable baseline malignancy, who achieved sustained clinical remission after double filtration plasmapheresis (DFPP) followed by mycophenolate mofetil maintenance. This case expands the phenotypic spectrum of anti-amphiphysin autoimmunity and provides therapeutic evidence for blood purification in MSA mimic syndromes.

2 | Part II: Clinical History

An 82-year-old male was admitted in April 2025. He presented with a 1-year history of gait difficulty that had worsened over the preceding 2 months. One year before admission, the patient developed gait difficulty and bradykinesia without an obvious trigger. This was accompanied by postural dizziness, choking on liquids, and urinary frequency and urgency. Symptomatic treatments at a local hospital were ineffective. Two months before admission, his symptoms progressively worsened. He then developed nocturnal visual and auditory hallucinations, as well as fecal and urinary incontinence. Past medical history included 30 years of hypertension managed with oral metoprolol, and 20-year coronary artery disease treated with percutaneous coronary stent placement.

3 | Part III:Neurological Examination

The patient was conscious and articulate. He exhibited masked facies. Muscle strength was grade 5/5 in all four extremities. Muscle tone was increased with cogwheel rigidity. Bilateral finger-to-nose and heel-to-shin tests were dysmetric. He had difficulty initiating gait, with short steps and postural instability. Bilateral pathological reflexes were negative. Supine blood pressure measured 157/71 mmHg; after 3 minutes of standing, systolic blood pressure fell by 53 mmHg and diastolic blood pressure by 10 mmHg, consistent with severe orthostatic hypotension per American Autonomic Society criteria (≥ 30 mmHg systolic drop). The MDS-Unified Parkinson's Disease Rating Scale Part III motor score was 35 at baseline.

4 | Part IV:Ancillary Investigations

Blood tests revealed mild anemia, with hemoglobin at 103 g/L. Lymphocyte subset analysis showed a CD19 + cell count of 654.44 μ L (reference range: 70–620 μ L) and a CD20 + cell proportion of 16.64% (reference range: 7.44–13.66%). Interleukin-8 (IL-8) was 26.13 pg/mL (reference range: 0-20.6 pg/mL). Liver and kidney function tests, thyroid function, systemic autoimmune antibody profiles, tumor markers, and flow cytometry of peripheral plasma cells were all unremarkable. Cerebrospinal fluid (CSF) opening pressure was 140 mmH₂O; CSF cell count, glucose, and total protein were within normal limits, with no malignant cells identified. Serum anti-amphiphysin IgG was strongly positive at a titer of 1:320 via cell-based assay (CBA, Fig. 1). Brain MRI revealed mild atrophy of the cerebellum and bilateral hippocampi (Fig. 2). Ambulatory electroencephalogram (EEG) showed moderate, short-segment, paroxysmal 5–7 Hz theta activity over both hemispheres. Chest and abdominal computed tomography (CT) scans indicated scattered chronic inflammation in both lungs and a small nodule in the left lung. No definitive signs of malignant solid tumors were found.

5 | Part V:Diagnostic Assessment and Differential Diagnosis

The core symptoms of this patient included Parkinsonism, cerebellar ataxia, and severe autonomic dysfunction (orthostatic hypotension and urinary dysfunction), presenting a clinical phenotype highly suggestive of MSA. However, the disease course exhibited subacute deterioration, accompanied by a high titer of serum anti-amphiphysin antibodies. Degenerative MSA (α -synucleinopathy) is characterized

by insidious, year-long progression without serologic autoantibodies and no sustained response to immunomodulatory therapy. In contrast, our patient exhibited subacute deterioration over 2 months, high-titer anti-amphiphysin IgG, and dramatic clinical improvement after immunotherapy, ruling out primary neurodegeneration. Considering the exclusionary ancillary investigations and the subsequent remarkable therapeutic response to DFPP, a purely neurodegenerative process could not fully account for the clinical manifestations.

In terms of differential diagnosis, nutritional-metabolic, infectious, and vascular encephalopathies were ruled out, as the relevant biochemical and imaging findings did not support these conditions. Following a comprehensive evaluation, the diagnosis was established as anti-amphiphysin antibody-associated MSA-like autoimmune neurological syndrome. Given the high-risk paraneoplastic nature of this antibody, although the initial screening revealed no overt malignancies, a high index of suspicion for an underlying paraneoplastic neurological syndrome (PNS) must be maintained.

6 | Part VI: Treatment Course and Follow-up

After excluding contraindications, the patient underwent three sessions of double filtration plasmapheresis (DFPP) on May 29, May 31, and June 2, 2025, using the Spectra Optia system (Terumo BCT, Lakewood, CO, USA). This device separates plasma by centrifugation. The Spectra Optia Apheresis System Exchange Set (10226, Terumo BCT, Lakewood, CO, USA) was utilized as the plasma separator, and the Cascadeflo EC (Asahi Kasei Medical, Tokyo, Japan) served as the plasma component fractionator. The EC-30W filter was used for the first session, while the EC-20W filter was employed for the subsequent two sessions. The patient's height was 162 cm, and weight was 55 kg. Detailed parameters are presented in Table 1.

Table 1
Settings and treatment parameters of double filtration plasmapheresis (DFPP).

Parameters	1st (May 29)	2nd (May 31)	3rd (June 2)
Hematocrit (%)	32.6	32.0	30.3
Serum albumin (g/L)	38.98	37.22	37.49
Treatment duration (min)	128	127	128
Processed blood volume (mL)	5876	5938	5749
Treated plasma volume (mL)	2393	2556	2694
Anticoagulant dose (mL)	445	458	474

Following the treatment, without the administration of anti-Parkinsonian or vasopressor medications, the patient's gait difficulty improved significantly, allowing him to walk independently. Postural dizziness was alleviated, and the difference between supine and standing blood pressure was markedly reduced upon re-evaluation. The MDS-UPDRS Part III score decreased to 10. Upon discharge, mycophenolate mofetil

(MMF) was prescribed for maintenance immunosuppressive therapy, initiated at 0.25 g twice daily (bid), escalated to 0.5 g bid after one week, and ultimately maintained at 1 g bid. At 6-month clinical follow-up, the patient maintained complete neurological remission without relapse. Serologic testing demonstrated reduction of anti-amphiphysin IgG titer from 1:320 to 1:32. Consistent with suppressed humoral immunity, CD19 + B-cell count normalized to 8.31/μL, CD20 + lymphocyte fraction fell to 9.58%, and proinflammatory IL-8 decreased from 26.13 pg/mL to 15.92 pg/mL. The diagnostic and therapeutic workflow, along with the changes in immunological parameters, are illustrated in Figs. 3 and 4.

7 | Part VII: Discussion

The clinical manifestations of anti-amphiphysin antibody-associated neurological syndromes are diverse. The amphiphysin protein is predominantly localized at the presynaptic membrane and is involved in clathrin-mediated synaptic vesicle endocytosis ^[7]. The antibodies disrupt GABAergic inhibitory neurotransmission, leading to abnormal nerve cell excitability ^[8, 9]. Although its classic phenotype is stiff-person syndrome, atypical cases with multisystem involvement have been frequently reported in recent years ^[6, 10]. The present case manifested as an MSA-like syndrome, suggesting that in the elderly population, the clinical presentation of autoimmune mechanisms can highly mimic neurodegenerative diseases, easily leading to clinical misdiagnosis.

Autonomic dysfunction was a prominent feature in this case. Anti-amphiphysin antibodies can extensively involve the central autonomic network and peripheral sympathetic/parasympathetic pathways. Degenerative MSA causes permanent neuronal loss within central autonomic nuclei, resulting in irreversible autonomic failure. By contrast, rapid resolution of orthostatic hypotension after DFPP in our case indicates that anti-amphiphysin IgG induces reversible synaptic dysfunction in autonomic circuits without permanent neuronal death, supporting early immunotherapeutic intervention before irreversible neuronal injury develops. This gives a theoretical basis for early clinical intervention.

As antibodies against intracellular antigens, anti-amphiphysin antibody-associated diseases are generally considered to be dominated by T-cell-mediated cellular immunity, with limited efficacy from humoral immunotherapy ^[5, 11]. However, the present patient responded favorably to DFPP. DFPP can efficiently eliminate circulating pathogenic autoantibodies, immune complexes, and inflammatory factors (such as elevated IL-8 in this case), thereby rapidly mitigating damage caused by peripheral immune responses at the blood-brain barrier and in the central nervous system. This suggests that in the early stages of the disease, before irreversible neuronal damage occurs, aggressive blood purification therapy combined with long-acting immunosuppressants can effectively halt disease progression ^[12, 13]. Specifically, the sequential use of mycophenolate mofetil (MMF) as a long-acting immunosuppressant provided effective maintenance therapy in this case. By selectively inhibiting inosine monophosphate dehydrogenase, MMF potently suppressed B-cell proliferation, which directly accounts for the marked reduction in CD19 + and CD20 + cell populations and the subsequent decline in antibody titers observed during the 6-month follow-up.

This report carries several limitations. First, single-case data cannot confirm a causal link between anti-amphiphysin IgG and MSA-mimetic clinical phenotype; larger cohort studies are required to validate this association. Second, due to the family's preference against self-funded testing, data on oligoclonal bands are missing, precluding further evaluation of the intrathecal immune synthesis status^[14]. Third, baseline whole-body PET-CT was not performed to rule out occult malignancy; serial thoracic imaging and delayed PET surveillance are required to characterize the indeterminate lung nodule given the high paraneoplastic risk of anti-amphiphysin antibodies. Finally, long-term (≥ 12 month) clinical and serologic follow-up data remain unavailable to assess sustained remission durability.

8 | Part VIII: Conclusion

Anti-amphiphysin IgG autoimmunity should be included in the differential diagnosis of rapidly progressive MSA-spectrum syndromes with severe autonomic failure, especially among elderly patients. We recommend tiered testing for neuronal autoantibodies in all patients with atypical parkinsonism-cerebellar ataxia inconsistent with classic α -synucleinopathy. Induction DFPP followed by maintenance mycophenolate mofetil represents an effective immunotherapeutic regimen to achieve durable neurological recovery in this reversible MSA mimic. Long-term oncologic surveillance is mandatory given the paraneoplastic risk of anti-amphiphysin antibodies.

Declarations

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Author contributions

Lianshuang Wu, Bin Liu, and Qiuju Li contributed equally to this work and share first authorship. Lianshuang Wu drafted the manuscript. Bin Liu and Kan Wang revised the manuscript. Qiuju Li, Fang Yan, and Mingdan Shi collected the data. Yangtai Guan supervised the study. All authors read and approved the final manuscript.

Data availability statement

The patient provided written consent for publication, and his personal details were de-identified for privacy. Data are available from the corresponding author upon reasonable request.

Consent for publication

All enrolled patients provided written informed consent, granting permission for their personal clinical information and all identifiable imaging materials to be published in this research article.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Ethics statement

Not applicable.

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Table

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Figures

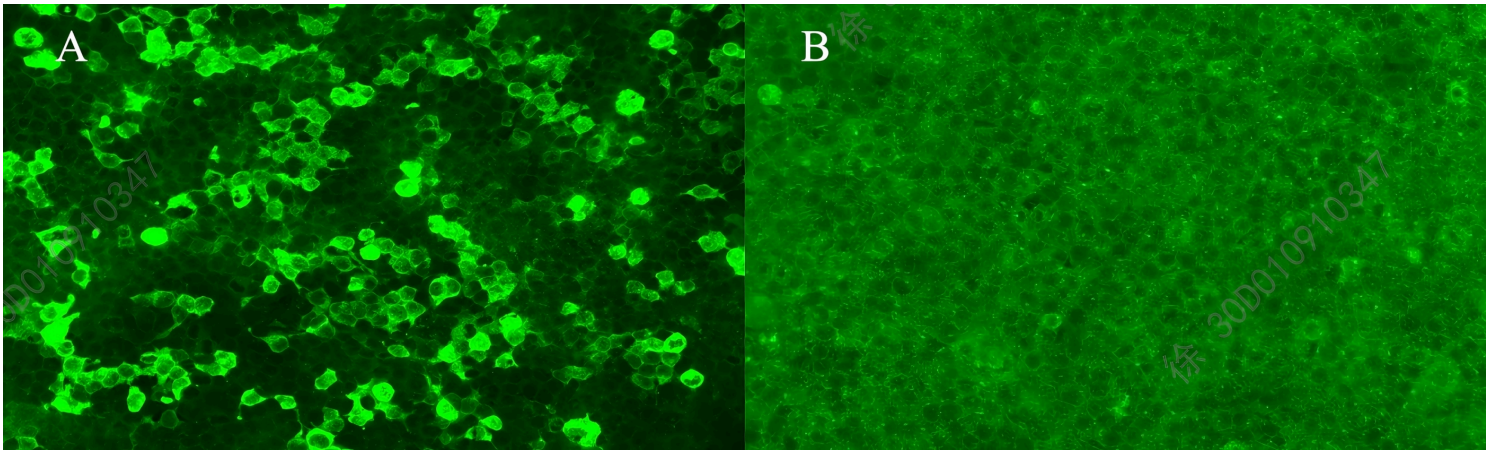


Figure 1

Detection of anti-amphiphysin antibodies in the patient's serum using a cell-based assay (CBA). Image A :Positive immunofluorescence staining. The patient's serum (titer 1:320) shows strong reactivity with HEK293 cells transfected with the amphiphysin antigen, displaying typical green fluorescence.

Image B:Negative control serum, demonstrating no specific fluorescent signal.

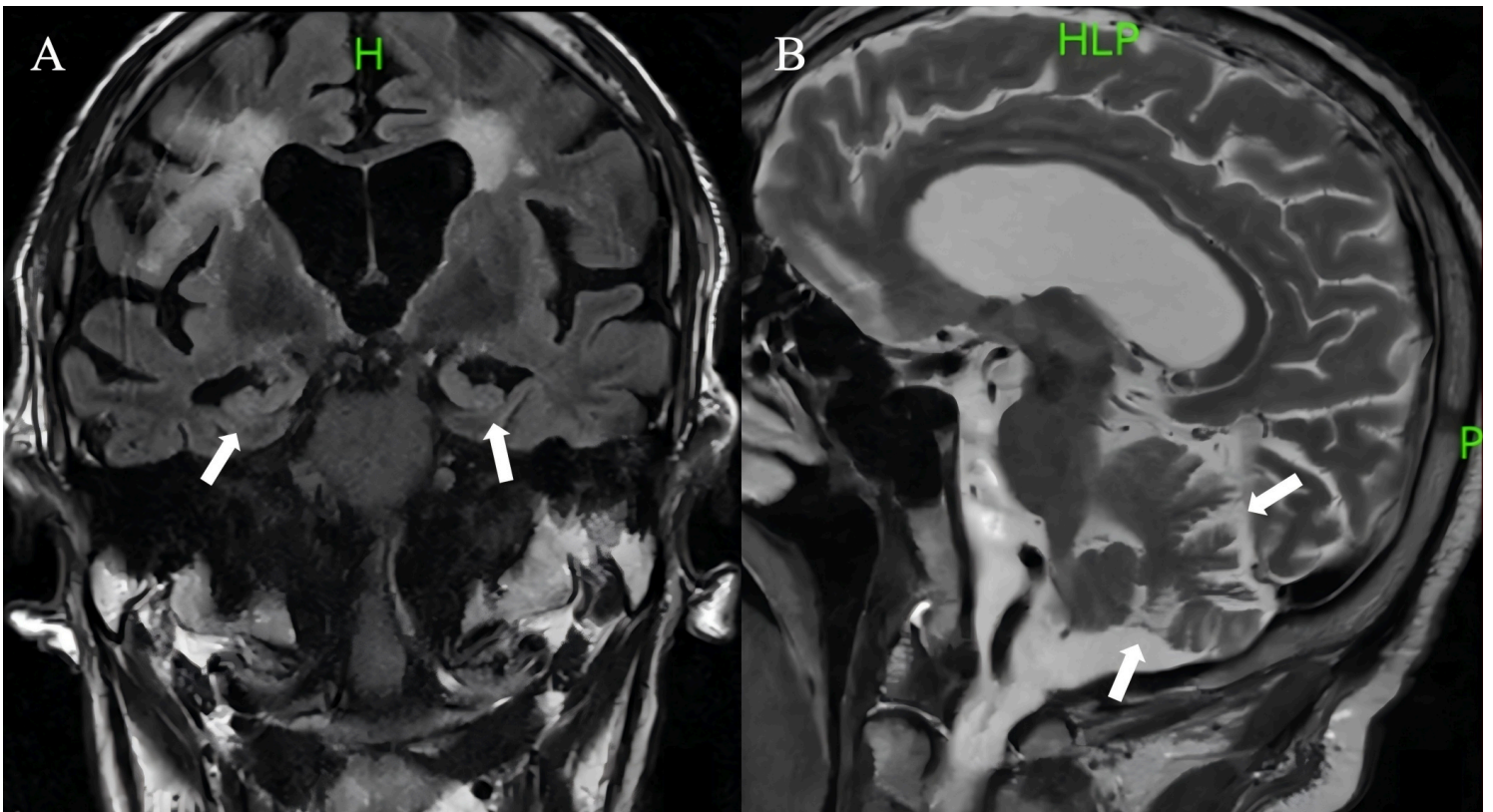


Figure 2

Brain 3.0T magnetic resonance imaging (MRI) findings of the patient. Image A : Coronal fluid-attenuated inversion recovery (FLAIR) sequence reveals mild atrophy of the bilateral hippocampi (white arrows).

Image B: Sagittal T2-weighted imaging (T2WI) sequence shows mild cerebellar atrophy (white arrows).

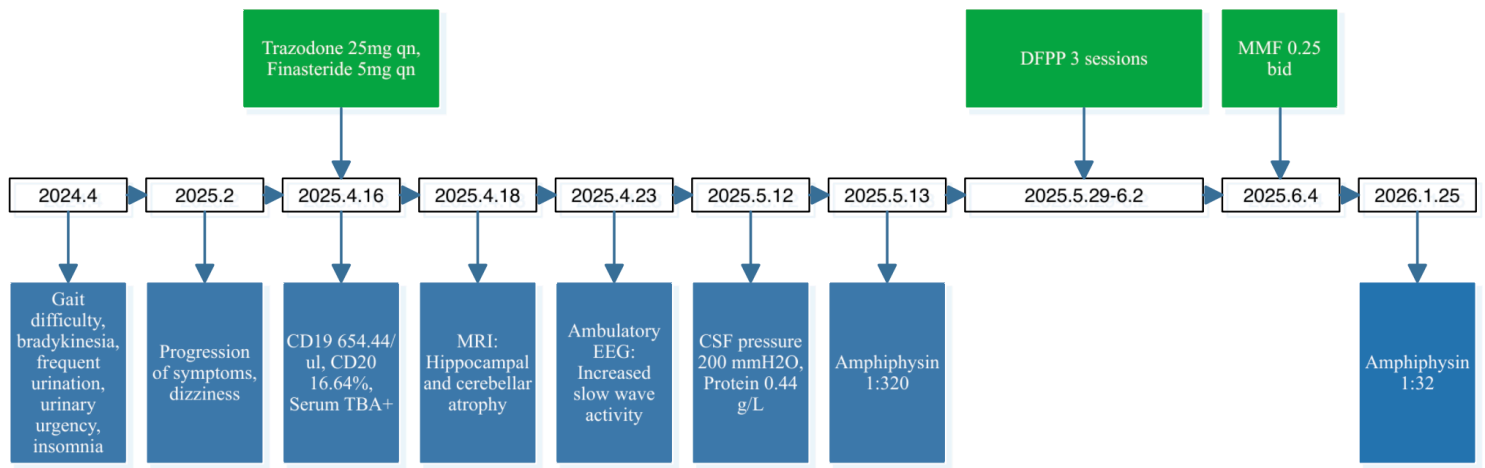


Figure 3

Clinical course and treatment timeline.

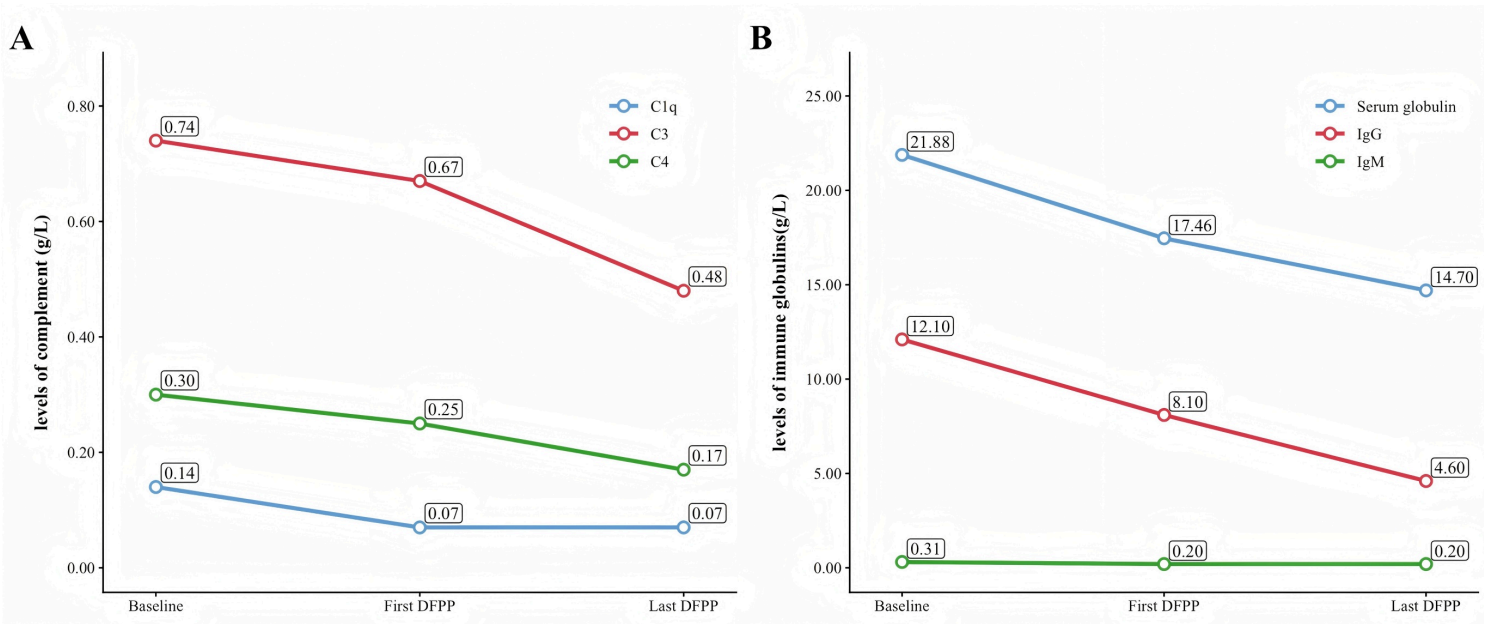


Figure 4

Dynamic changes in serum complement and immunoglobulin levels before and after double filtration plasmapheresis (DFPP). Image A: Changes in serum complement (C1q, C3, and C4) levels at baseline, and after the first and final DFPP sessions. Image B: Changes in serum immunoglobulin (serum globulin, IgG, and IgM) levels at baseline, and after the first and final DFPP sessions.