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CASE REPORT

Visual Recovery to 6/6 After Plasma Exchange Begun 29 Days Into a Corticosteroid-Refractory Aquaporin-4-IgG-Positive Optic Neuritis Attack: A Case Report

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ABSTRACT

Background: Optic neuritis in aquaporin-4 immunoglobulin G (AQP4-IgG)-positive neuromyelitis optica spectrum disorder (NMOSD) is severe and frequently corticosteroid-refractory. Plasma exchange is recommended within days of onset, and the evidence that later treatment still helps is thin. Whether an attack first treated a month after onset can still recover fully is unresolved.

Objective: To describe the visual and structural recovery that followed therapeutic plasma exchange begun 29 days after onset — far outside the recommended window — in a corticosteroid-refractory aquaporin-4-IgG-positive optic neuritis attack, and to audit the record against the quantified determinants of outcome.

Case presentation: A 34-year-old woman with systemic lupus erythematosus, antiphospholipid syndrome and AQP4-IgG seropositivity documented one month earlier presented 24 days after the onset of painful visual loss in the right eye. Best-corrected visual acuity was 3/60 and the Ishihara score 0 of 25. No relative afferent pupillary defect was demonstrable in the affected eye, because the fellow eye, atrophic since an attack 11 years earlier, showed the defect instead. A full Optic Neuritis Treatment Trial course of intravenous methylprednisolone, from day 24 to day 27, produced no measurable change. Plasma exchange was started on day 29; acuity reached 6/60 on day 33 and 6/6 on day 35, and the Ishihara score rose to 5 of 25 by day 40 without any procedure-related adverse event. At day 53 the peripapillary retinal nerve fibre layer measured 91 micrometres in the treated eye against 41 in the fellow eye.

Conclusion: Complete recovery of high-contrast acuity followed plasma exchange begun 29 days after onset, far outside the recommended window, while colour vision recovered only partially. A chronically damaged fellow eye can abolish the relative afferent pupillary defect in an acutely inflamed eye, and the attack occurred on azathioprine in a patient already known to be seropositive.

1. Introduction

Optic neuritis is among the commonest causes of acute or subacute visual loss in adults under fifty, and the single question that most changes management is whether the attack is typical or atypical. Typical demyelinating optic neuritis recovers well in most eyes; atypical optic neuritis, of which neuromyelitis optica spectrum disorder (NMOSD) is the most consequential cause, damages the nerve severely, recurs, and blinds. NMOSD is rare. A contemporary multi-ethnic cohort covering more than 39 million person-years identified only 153 cases and estimated an age- and sex-standardised incidence of 0.32 per 100,000 person-years in Asian or Pacific Islander people, against 0.90 in Black and 0.13 in White people.[1] A cross-sectional study of 25,743,039 patients in the United States found 1,772 with the diagnosis, a standardised prevalence of 6.88 per 100,000, with a female prevalence of 9.48 against 3.52 per 100,000 in males.[2] In a Taiwanese hospital cohort of 193 seropositive patients the recorded incidence rose more than tenfold between 2006 and 2021 as testing spread, and the median annualised relapse rate in adults was 0.49.[3] Rarity of this order means that most clinicians will see very few attacks and will have little personal calibration for the decisions the disease demands.

Those decisions turn on a single antibody. Immunoglobulin G directed against aquaporin-4 (AQP4-IgG), the dominant water channel of astrocytic end-feet, defines a disease in which complement-dependent astrocytic injury precedes demyelination, and the antibody burden itself tracks severity: among 546 patients stratified by titre, those at 1:100 or below had significantly fewer severe optic neuritis attacks, a lower incidence of visual disability and a lower annual recurrence rate than those at 1:320 or above.[4] Seropositivity also travels with systemic autoimmunity. In a national registry of 136 patients, 50

(36.8%) carried at least one further autoimmune disorder and seropositive patients had a 5.2-fold higher odds of such comorbidity (odds ratio 5.2, 95% confidence interval 1.4 to 18.5); across the whole 136-patient registry, systemic lupus erythematosus was present in 5.1% and primary antiphospholipid antibody syndrome in 2.9%.[5] Among 16,360 inpatient episodes carrying a diagnosis of neuromyelitis optica, 1,425 (8.71%) also carried lupus or Sjogren syndrome, and the odds of the diagnosis in lupus were 12.29.[6] In a Mexican cohort of 86 seropositive patients, 16 (18.6%) had a coexisting systemic autoimmune disease and optic neuritis was the presenting event in 68.8% of that overlap group.[7] When a patient carries both lupus and antiphospholipid syndrome, the optic neuropathy that follows has at least three credible explanations, and they do not share a treatment.

Acute treatment is a two-step ladder. High-dose intravenous methylprednisolone is given first, and its timing matters: in 34 eyes of 22 seropositive patients followed for at least two years, treatment within three days was associated with better final acuity and better preserved ganglion cell-inner plexiform layer thickness.[8] Where health systems delay, the cost is measurable; among 100 patients with optic neuritis in a lower-resource setting, 58% were treated more than 14 days after onset, and recovery of at least three Snellen lines at three months fell from 66.7% to 31.0%.[9] When corticosteroids fail, the second step is therapeutic plasma exchange, classified by the American Society for Apheresis as a Category II indication with a Grade 1B recommendation.[10] Here too the published emphasis is on speed. The largest series of plasma exchange for optic neuritis, 395 attacks in 317 patients treated at a median of 2.6 weeks from onset, found on multivariate analysis that a longer delay independently predicted a worse result.[11] In a prospective cohort of 124 attacks in 122 patients, the time window to exchange entered both predictive models built in the AQP4-antibody-positive stratum.[12] Yet the picture is not uniform: a rescue study of 61 corticosteroid-unresponsive attacks concluded that the effective period for immunoadsorption may be longer than previously thought,[13] and an apheresis service reviewing 54 patients treated an average of 23 days after onset found no relationship at all between symptom duration and outcome.[14]

What is missing from this literature is a well-documented attack treated far outside the recommended window in which the ceiling of possible recovery is actually observed, together with an account of how much of that recovery routine bedside assessment would have captured. This report describes a seropositive attack in which plasma exchange was not begun until day 29 and high-contrast acuity nevertheless returned to 6/6, in which the relative afferent pupillary defect was absent from the acutely inflamed eye because the fellow eye had been destroyed 11 years earlier, in which colour vision recovered only to a fifth of the plates while acuity was already normal, and in which the attack itself occurred on azathioprine in a patient whose seropositivity had been documented a month before onset. The aim of this study was threefold: to describe the visual and structural outcome of late rescue plasma exchange in corticosteroid-refractory AQP4-IgG-positive optic neuritis; to set the three signs that were nearly missed, the absent pupillary defect, the acuity-colour dissociation and the uninterpretable structural reading, against what the primary literature says each of them measures; and to audit the record itself, item by item, against the determinants of outcome that recent primary research quantifies, and to convert what was missing into a minimum data set that any centre can adopt.

2. Case Presentation

History and referral pathway

Table 1 presents the demographic, systemic and ophthalmic characteristics recorded at the first neuro-ophthalmological assessment. A 34-year-old woman attended the neuro-ophthalmology clinic of Prof. Dr. I.G.N.G. Ngoerah General Hospital on 5 August 2025 with blurred vision in the right eye that had begun abruptly on 12 July 2025. The disturbance was accompanied by photophobia, black spots in the field of vision, and ocular pain provoked by eye movement in every direction. She denied redness, double vision, a curtain-like obscuration, discharge or epiphora. Systemically she reported myalgia of the legs and back but no arthralgia or bone pain.

The history that framed the episode is detailed in Table 1, in the block above the examination findings. She had suffered an equivalent event in the left eye in 2014, 11 years earlier, after which severe visual impairment had persisted without recovery. She was highly myopic in the right eye, corrected with -7.00 dioptres sphere and -1.00 dioptre cylinder, and had never undergone ocular surgery or sustained ocular trauma. Her systemic diagnoses were thyroid disease, systemic lupus erythematosus and antiphospholipid syndrome; she had neither hypertension nor diabetes and no drug allergy. Her regular medication comprised rivaroxaban once daily, azathioprine three times daily, vitamin D, a neurotropic supplement and low-dose oral methylprednisolone. Critically, a serum AQP4-IgG assay performed in June 2025, one month before this attack began, had already been reported positive.

The referral pathway is worth recording because it accounts for most of the treatment delay. She was assessed at a first hospital on 13 July 2025, the day after onset, and referred onward to a second institution for magnetic resonance imaging of the brain and orbits, which was performed on 30 July 2025. She was not seen at the present institution until 5 August 2025 and was admitted the same day. Twenty-four days therefore separated the onset of visual loss from the

first dose of intravenous corticosteroid, and 29 days separated it from the first plasma exchange.

Ophthalmic examination

General examination showed stable vital signs. Figure 1 illustrates the anterior segment and fundus appearance of both eyes at this visit. In the right eye, uncorrected acuity was 1/60, improving to 2/60 with a pinhole and to 3/60 with optical correction, equivalent to 1.30 logMAR. As shown in Figure 1A, the eyelids and conjunctiva were unremarkable, the cornea clear and the anterior chamber deep, with a round and regular iris and a clear lens. Direct and consensual pupillary light responses were preserved and no relative afferent pupillary defect could be demonstrated. Fundus examination, illustrated in Figure 1C, revealed a clear vitreous, indistinct disc margins with temporal pallor and peripapillary atrophy, and a preserved macular reflex; the cup-to-disc ratio could not be assessed reliably. Intraocular pressure was 12 mmHg. Colour vision was profoundly impaired, with an Ishihara score of 0 of 25 plates, whereas confrontation visual field testing was within normal limits.

Colour vision was assessed with the 25-plate Ishihara pseudoisochromatic series, read under standard clinic illumination, and the score is reported throughout as the number of plates read correctly out of 25. A score of 0 of 25 in an eye that could still resolve 3/60 indicates a loss of chromatic discrimination out of proportion to the loss of high-contrast acuity, which is the pattern expected of an optic neuropathy rather than of a media or macular cause, and it is the baseline against which the later partial recovery to 5 of 25 should be read.

Table 1. Demographic, systemic and ophthalmic characteristics at the first neuro-ophthalmological assessment on 5 August 2025, 24 days after the onset of visual loss.

Characteristic	Right eye (OD)	Left eye (OS)
Patient and systemic profile		
Age, sex	34 years, female	34 years, female
Autoimmune diagnoses	Systemic lupus erythematosus; antiphospholipid syndrome; thyroid disease	Systemic lupus erythematosus; antiphospholipid syndrome; thyroid disease
Serum AQP4-IgG	Positive (June 2025, one month before onset)	Positive (June 2025, one month before onset)
Maintenance therapy at onset	Azathioprine 50 mg three times daily; low-dose oral methylprednisolone; rivaroxaban 20 mg once daily; vitamin D; neurotropic supplement	Same
Interval, onset to this assessment	24 days	Attack in 2014, 11 years earlier
Refractive error	-7.00 DS / -1.00 DC	Not recorded
Ocular surgery or trauma	None	None
Ophthalmic examination		
Uncorrected visual acuity	1/60	Light perception with good projection
Acuity with pinhole	2/60	Not assessable
Best-corrected visual acuity	3/60 (1.30 logMAR)	Light perception (>2.8 logMAR)
Ocular pain on eye movement	Present, in all directions	Absent
Ishihara colour plates	0 of 25	Not assessable
Relative afferent pupillary defect	Absent	Present
Direct and consensual light reflex	Preserved	Preserved
Anterior segment	Quiet; clear cornea; deep anterior chamber; clear lens	Quiet; clear cornea; deep anterior chamber; clear lens
Optic disc	Indistinct margins with temporal pallor and peripapillary atrophy	Well-defined but diffusely pale disc
Cup-to-disc ratio	Not reliably assessable	Not reliably assessable
Macular reflex	Preserved	Preserved
Intraocular pressure	12 mmHg	12 mmHg
Confrontation visual field	Within normal limits	Not assessable

*AQP4-IgG, aquaporin-4 immunoglobulin G; DC, dioptre cylinder; DS, dioptre sphere; logMAR, logarithm of the minimum angle of resolution; OD, oculus dexter; OS, oculus sinister. * Values in bold red are abnormal or of particular diagnostic weight.*

† The logMAR equivalent of light perception is not defined on a continuous scale; the value given is the conventional lower bound used for tabulation and was not used in any calculation.

In the left eye, acuity was limited to light perception with good projection. The anterior chamber was deep and the iris round and regular, direct and consensual responses were present, and a relative afferent pupillary defect was demonstrable on the left. The lens was clear. Posterior segment examination, in Figure 1D, showed a clear vitreous and a well-defined but diffusely pale disc with a preserved retina and macular reflex. Intraocular pressure was 12 mmHg. Colour vision and confrontation field testing could not be evaluated because of the depth of the visual loss. The juxtaposition set out in Table 1 is the clinically

important one: the acutely symptomatic eye had no afferent pupillary defect and the asymptomatic eye had one.

On these findings the working diagnosis was right optic neuritis, considered atypical and provisionally attributed to NMOSD, with established left optic atrophy. Admission was arranged for high-dose intravenous corticosteroid according to the Optic Neuritis Treatment Trial regimen and for review of the neuroimaging.

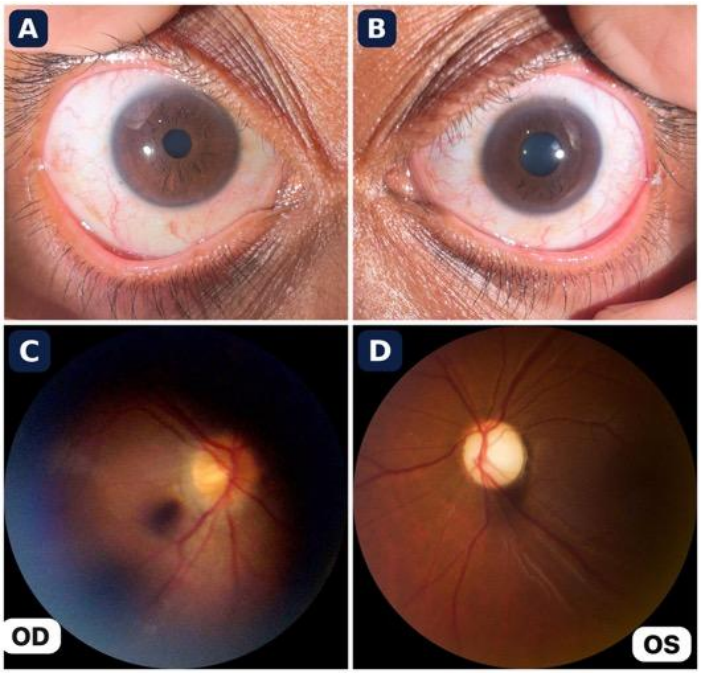

Figure 1. Ophthalmic findings at presentation on 5 August 2025, 24 days after the onset of visual loss. (A) Anterior segment of the right eye and (B) of the left eye, both quiet, with a clear cornea, a deep anterior chamber and a clear lens; laterality was assigned from the medial canthal landmarks and confirmed against the labelled fundus pair. (C) Right fundus, showing indistinct disc margins with temporal pallor and peripapillary atrophy against a preserved macular reflex. (D) Left fundus, showing a well-defined but diffusely pale disc, the residue of the attack of 2014. Intraocular pressure was 12 mmHg in each eye.

Laboratory and immunoserological investigation

Laboratory results obtained in July 2025 are summarised in Table 2 together with the reporting laboratory's reference intervals. The full blood count was unremarkable, with a haemoglobin of 12.3 g/dL, a haematocrit of 40.5%, an erythrocyte count of 5.15 × 10^6/µL, a platelet count of 333 × 10^3/µL and a leucocyte count of 9.6 × 10^3/µL. The erythrocyte sedimentation rate was mildly raised at 27 mm/hour. Liver and renal function were normal, with aspartate and alanine aminotransferases of 18 and 11 U/L, a urea of 27 mg/dL, a creatinine of 0.73 mg/dL and an estimated glomerular filtration rate of 108 mL/min/1.73 m^2. Fasting glucose was 79 mg/dL and serum urate 4.2 mg/dL. As shown in Table 2, the only metabolic abnormalities were a total cholesterol of 208 mg/dL and a low-density lipoprotein cholesterol of 129 mg/dL, with normal high-density lipoprotein cholesterol and triglycerides; the serum 25-hydroxyvitamin D of 32.3 ng/mL was sufficient but close to the lower limit.

The immunoserological panel, detailed in Table 2 below the metabolic block, is the part that decided management. Anticardiolipin IgG and IgM were within the reference range at 8 and less than 2. Anti-beta$_2$-glycoprotein I IgG was positive and the IgM negative. Lupus anticoagulant testing gave a dilute Russell viper venom time screening ratio of 1.06, a confirmatory ratio of 0.99 and a normalised ratio of 1.07, so no lupus anticoagulant was detected. Complement C3 and C4 were both within their reference intervals, at 130.2 and 30.4 mg/dL. Urinalysis showed a specific gravity of 1.034 with mild albuminuria at 25 mg/dL and a dipstick positive for blood at 25/µL, although microscopy found only 0 to 1 erythrocytes and 0 to 2 leucocytes per high-power field, with bacteria and amorphous urates but no pathological casts and no abnormal epithelial cells. Leucocyte esterase and nitrite were negative.

The rheumatology division graded the lupus as severely active, with a Mexican Systemic Lupus Erythematosus Disease Activity Index of 14 attributed to mononeuritis, haematuria and the antiphospholipid syndrome, and continued azathioprine 50 mg three times daily, vitamin D 10,000 international units on alternate days and rivaroxaban 20 mg once daily. It is worth noting, against the entries in Table 2, that the neurological domain of that activity score was assigned to mononeuritis rather than to the optic neuropathy, a judgement that proved consistent with the final attribution of the attack.

Table 2. Haematological, biochemical, immunoserological and urinary results obtained in July 2025, with the reporting laboratory's reference intervals.

Investigation	Result	Reference interval	Interpretation
Haematology			
Haemoglobin	12.3 g/dL	12.0-15.0 g/dL	Normal
Haematocrit	40.5%	36-46%	Normal
Erythrocytes	5.15 × 106/µL	4.0-5.2 × 106/µL	Upper normal
Leucocytes	9.6 × 103/µL	4.0-10.0 × 103/µL	Normal
Platelets	333 × 103/µL	150-450 × 103/µL	Normal
Inflammatory, hepatic, renal and metabolic			
Erythrocyte sedimentation rate	27 mm/hour	<20 mm/hour	Mildly raised
Aspartate aminotransferase	18 U/L	<34 U/L	Normal
Alanine aminotransferase	11 U/L	<34 U/L	Normal
Fasting blood glucose	79 mg/dL	70-100 mg/dL	Normal
Serum urate	4.2 mg/dL	2.4-5.7 mg/dL	Normal
Urea / creatinine	27 / 0.73 mg/dL	17-43 / 0.51-0.95 mg/dL	Normal
Estimated glomerular filtration rate	108 mL/min/1.73 m2	≥ 90 mL/min/1.73 m2	Normal
Lipids and vitamin D			
Total cholesterol	208 mg/dL	<200 mg/dL	Raised
Low-density lipoprotein cholesterol	129 mg/dL	<100 mg/dL	Above desirable
High-density lipoprotein cholesterol	55 mg/dL	>50 mg/dL	Normal
Triglycerides	81 mg/dL	<150 mg/dL	Normal
25-hydroxyvitamin D	32.3 ng/mL	30-100 ng/mL	Sufficient, near lower limit
Immunoserology			
Serum AQP4-IgG (June 2025)	Positive	Negative	Diagnostic; titre and assay method not recorded
Anticardiolipin IgG / IgM†	8 / <2	<12 / <12	Negative
Anti-β2-glycoprotein I IgG	Positive	Negative	Positive
Anti-β2-glycoprotein I IgM	Negative	Negative	Negative
Lupus anticoagulant (dRVVT screen / confirm / normalised ratio)	1.06 / 0.99 / 1.07	Normalised ratio <1.20	Not detected
Complement C3 / C4	130.2 / 30.4 mg/dL	90-180 / 10-40 mg/dL	Both normal
Urinalysis			
Specific gravity	1.034	1.005-1.030	Raised
pH	6.0	4.6-8.0	Normal
Protein (albumin)	25 mg/dL (1+)	Negative	Mild albuminuria
Blood	25/µL (2+)	Negative	Positive dipstick with 0-1 erythrocytes per high-power field
Urobilinogen	1 mg/dL (1+)	≤ 1 mg/dL	Borderline
Leucocyte esterase / nitrite	Negative / negative	Negative	Negative
Microscopy	0-1 erythrocytes and 0-2 leucocytes per high-power field; bacteria and amorphous urates present; no casts	0-2 / 0-5 per high-power field	No active sediment

AQP4-IgG, aquaporin-4 immunoglobulin G; dRVVT, dilute Russell viper venom time.

** Values in bold red fall outside the reference interval or carry diagnostic weight.*

† The laboratory reported the anticardiolipin antibodies as bare numbers; the conventional units are GPL-U/mL for the IgG isotype and MPL-U/mL for the IgM isotype, and the reference interval is quoted here as the laboratory stated it.

‡ The rheumatology service graded lupus activity as severe with a Mexican Systemic Lupus Erythematosus Disease Activity Index of 14, attributed to mononeuritis, haematuria and the antiphospholipid syndrome; the optic neuropathy was not scored as a lupus manifestation.

Neuroimaging

The neuroimaging available for this episode is detailed in Figure 2. Magnetic resonance imaging of the brain and orbits performed on 30 July 2025 in axial, coronal and sagittal planes was reported as demonstrating findings consistent with right optic neuritis; the visualised left optic nerve showed no apparent abnormality of calibre or signal. No cerebral infarct, intracranial haemorrhage or space-occupying lesion

was identified. Incidental findings were a leftward nasal septal deviation and hypertrophy of the right inferior nasal concha.

During the admission the patient underwent contrast-enhanced and unenhanced magnetic resonance imaging of the cervical and lumbosacral spine together with magnetic resonance myelography. As shown in Figure 2C and Figure 2D, the cervical study demonstrated a grade I posterior spondylolisthesis at C5-C6, multilevel disc dehydration and diffuse disc bulging at C4-5 and C5-6 with mild canal stenosis, without abnormal cord signal; the lumbosacral study and the myelogram in Figure 2E showed multilevel degenerative change, including disc dehydration, facet joint abnormality, an L3-4 bulge, an L4-5 central protrusion with grade II canal stenosis and an L5-S1 foraminal protrusion with mild right neural foraminal stenosis. No new inflammatory cord lesion and no radiological progression were identified.

Two limitations of this imaging record should be stated plainly at the outset, because they bear on the interpretation offered later. The studies survive in the file only as photographic reproductions of the reporting workstation, so the optic nerve signal change described in the radiological report cannot be independently resolved in Figure 2A or Figure 2B; and no fat-suppressed coronal orbital sequence was retained, so the length of the affected optic nerve segment was never measured.

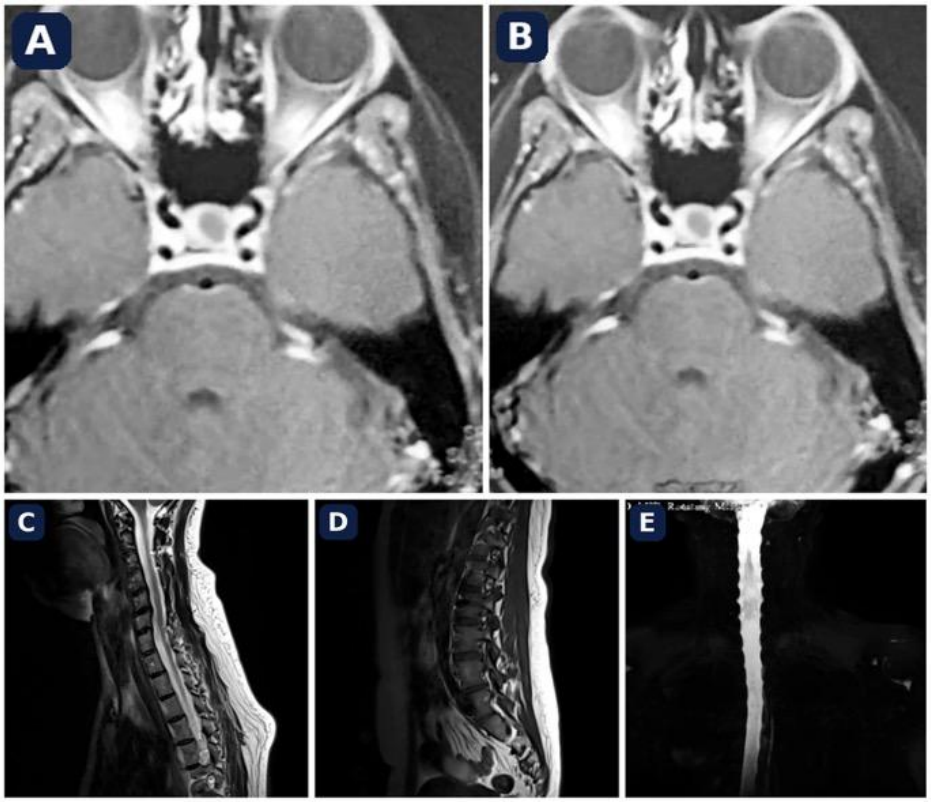

Figure 2. Neuroimaging. (A, B) Two adjacent contrast-enhanced axial T1-weighted sections through the orbits acquired on 30 July 2025 and reported as consistent with right optic neuritis; no infarct, haemorrhage or space-occupying lesion was identified. (C) Sagittal cervical and (D) sagittal lumbosacral images obtained during the admission, showing multilevel degenerative change without abnormal cord signal. (E) Magnetic resonance myelogram, with no cord lesion and no evidence of longitudinally extensive transverse myelitis. All images are reproductions of the reporting workstation; every burned-in patient identifier has been removed by cropping. At this reproduction quality the optic nerve signal change described in the radiological report cannot be independently resolved, and no fat-suppressed coronal orbital sequence was retained in the file.

Diagnosis, corticosteroid therapy and its failure

Table 3 details the treatment sequence, the institutional plasma exchange protocol and the documented response of the right eye, with days counted from the onset of visual loss on 12 July 2025. On 5 August 2025, day 24, the patient was admitted and started on intravenous methylprednisolone 250 mg every six hours in 100 mL of 0.9% sodium chloride, a daily dose of 1 g, together with calcium supplementation, folic acid, intravenous ranitidine, oral citicoline and topical lubricants to both eyes. The course was completed on 8 August 2025, day 27.

As detailed in Table 3, no meaningful improvement in acuity or in any other measure of visual function followed the corticosteroid course. Taken with the positive AQP4-IgG result and the clinical phenotype, the diagnosis was revised to atypical optic neuritis associated with NMOSD in the right eye, with pre-existing optic atrophy in the left.

Table 3. Treatment sequence, the institutional plasma exchange protocol applied, and the documented response of the right eye. Day 0 is 12 July 2025, the day visual loss began.

Day	Date	Intervention	Documented response
24	5 August 2025	Admission. Intravenous methylprednisolone 250 mg every 6 hours in 100 mL of 0.9% sodium chloride (1 g daily), with calcium supplementation, folic acid, intravenous ranitidine, oral citicoline and topical lubricants to both eyes	BCVA 3/60; Ishihara 0 of 25
27	8 August 2025	Corticosteroid course completed	No measurable change in acuity or colour vision; diagnosis revised to NMOSD-associated optic neuritis
28	9 August 2025	Oral prednisone 1 mg per kg body weight started; double-lumen central venous catheter inserted	Escalation to therapeutic plasma exchange agreed
29	10 August 2025	Therapeutic plasma exchange, session 1	No improvement; no adverse event
30	11 August 2025	Therapeutic plasma exchange, session 2	No improvement; no adverse event
33-36	14-17 August 2025	Observation on oral prednisone and azathioprine	BCVA 6/60 on day 33, 6/6 on day 35; Ishihara 2 of 25; discharged day 36
38-40	19-21 August 2025	Readmission on 19 August; therapeutic plasma exchange, session 3, on 20 August	BCVA maintained at 6/6; Ishihara 5 of 25
Institutional plasma exchange protocol			
	Step 1. Preparation	Assessment of haemodynamic stability, vital signs and clinical status; haemoglobin, haematocrit, platelet count, electrolytes, calcium, coagulation profile and fibrinogen as required; insertion of a double-lumen central venous catheter, internal jugular or femoral	Applied; internal jugular access used
	Step 2. Separation	Blood withdrawn through one catheter lumen to the apheresis device and separated into cellular components and plasma by centrifugation or membrane filtration; the plasma fraction carries the pathogenic AQP4-IgG	One total plasma volume exchanged per session
	Step 3. Replacement	Plasma containing autoantibodies and inflammatory mediators is discarded and the cellular components returned with replacement fluid	5% human albumin used as the replacement fluid
	Step 4. Post-procedure care	Monitoring of blood pressure, heart rate, oxygen saturation, signs of hypocalcaemia, allergic reaction and catheter patency; both lumens flushed; calcium and fibrinogen rechecked as required; clinical response assessed	No hypotension, hypocalcaemia, allergic reaction or catheter complication recorded across the three sessions

AQP4-IgG, aquaporin-4 immunoglobulin G; BCVA, best-corrected visual acuity; NMOSD, neuromyelitis optica spectrum disorder.
** Values in bold red mark the functional end-points and the safety outcome.*
† The record does not state the patient's body weight, so the milligram dose of prednisone actually administered cannot be recovered from it.

Escalation to therapeutic plasma exchange

The whole course from documented seropositivity to structural follow-up is detailed in Figure 3A. Because the response to intravenous methylprednisolone was inadequate, therapeutic plasma exchange was undertaken after insertion of a double-lumen central venous catheter, following the four-step institutional protocol detailed in Table 3. Oral prednisone at 1 mg per kilogram of body weight was begun on 9 August 2025, day 28, alongside the previous supportive medication. The first exchange was performed on 10 August 2025, day 29, and the second on 11 August 2025, day 30. One total plasma volume was exchanged at each session and 5% human albumin was used as the

replacement fluid, in accordance with the protocol reproduced in the lower half of Table 3.

Figure 3B shows the patient during a session, with the apheresis device and the double-lumen central venous access in view. No procedure-related adverse event was recorded at any session: specifically, no hypotension, no symptomatic hypocalcaemia, no allergic reaction and no catheter complication appear anywhere in the record, as the final row of Table 3 states.

One symptom was not tracked. Ocular pain on eye movement was the presenting complaint and is recorded at the first assessment, but no entry anywhere in the subsequent record states when, or whether, it resolved. Pain is the symptom patients themselves use to judge whether an attack is settling, and its disappearance is ordinarily the earliest sign of response; its absence from the record means that the first four days after the initial exchange, during which acuity did not move, cannot now be assessed for an early symptomatic signal.

Figure 3. (A) Course of the attack from documented seropositivity to structural follow-up, with the day counted from the onset of visual loss on 12 July 2025. The interval from onset to the first plasma exchange was 29 days and the interval from onset to the first dose of intravenous methylprednisolone was 24 days. (B) The patient during a plasma exchange session, with the apheresis device and the double-lumen central venous access in view; the periocular region has been masked.

Clinical course and visual outcome

The functional trajectory is illustrated in Figure 4A, which plots best-corrected acuity of the right eye in logMAR against days from onset, with the Ishihara score on the second axis and the treatment epochs shaded. No improvement followed the first exchange, and none was apparent immediately after the second. Recovery then began. On 14 August 2025, day 33, acuity in the right eye had improved to 6/60. On 15 August, day 34, acuity remained 6/60 while the Ishihara score rose from 0 to 2 of 25 plates. By 16 August, day 35, best-corrected acuity had reached 6/6, although the Ishihara score was still 2 of 25.

The patient was discharged on 17 August 2025, day 36, with a best-corrected acuity of 6/6 and her oral medication continued. She was readmitted on 19 August for a third exchange, performed on 20 August, day 39, again without any adverse event. At review on

21 August 2025, day 40, best-corrected acuity in the right eye remained 6/6 and colour vision had improved further to 5 of 25 plates, as the last plotted points in Figure 4A show. Expressed as the interval from onset, the sequence recorded in Figure 3A was 24 days to corticosteroid, 29 days to the first exchange, four days from the first exchange to the first measurable gain on day 33, and six days from the first exchange to a normal high-contrast acuity on day 35.

It is worth stating the magnitude of that gain in the units the comparator literature uses. Best-corrected acuity moved from 1.30 logMAR to 0.00 logMAR, a gain of 1.30 logMAR, which is 13 lines on a logarithmic chart. Series that classify response as an improvement of at least two acuity levels[12] or as a final acuity better than 20/40[11] would each have counted this attack as a responder several times over, and a study defining incomplete recovery as an acuity worse than 0.1 logMAR would have classified the right eye as fully recovered.[15] The colour vision result, discussed below, is the reason that classification would have been incomplete.

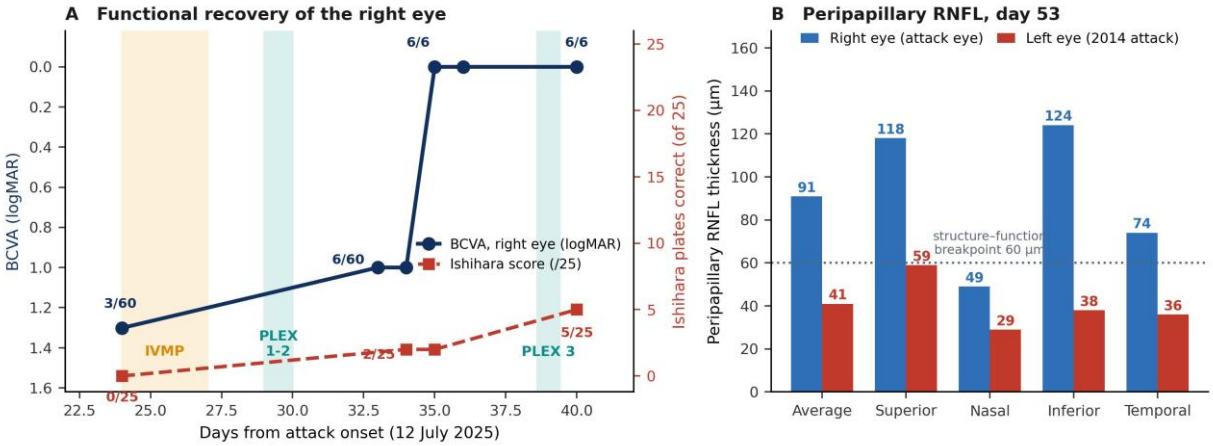

Figure 4. (A) Best-corrected visual acuity of the right eye in logMAR, with the Snellen equivalent above each point, and the Ishihara score on the right axis, against days from the onset of visual loss. Shaded bands mark the intravenous methylprednisolone course and the three plasma exchange sessions. Acuity was unchanged through the corticosteroid course and through the first two exchanges, then improved from 3/60 to 6/60 on day 33 and to 6/6 on day 35; colour vision lagged, reaching 5 of 25 plates only on day 40. (B) Peripapillary retinal nerve fibre layer thickness by sector on day 53. The dotted line marks the 60-micrometre structure-function breakpoint reported for this population.

Structural and functional follow-up

Figure 5 shows the follow-up examination on 3 September 2025, day 53. Fundus photography of the right eye in Figure 5A showed a disc of normal calibre with a preserved neuroretinal rim, whereas the left disc in Figure 5B was pale with extensive peripapillary change. Peripapillary retinal nerve fibre layer analysis, detailed in Figure 5C, gave an average thickness of 91 micrometres in the right eye, classified by the device as within normal limits, and 41 micrometres in the left, classified as outside normal limits, with an inter-eye symmetry of 0%.

Quadrant values, detailed in Figure 4B, followed the same pattern. In the right eye the superior, nasal, inferior and temporal quadrants measured 118, 49, 124 and 74 micrometres; in the left eye the same quadrants measured 59, 29, 38 and 36 micrometres. The printout reproduced in Figure 5C additionally reports the superior and inferior hemisphere values, which are not plotted in Figure 4B: 94 and 89 micrometres on the right, whose mean of 91.5 rounds to the reported average of 91, and 46 and 36 micrometres on the left, whose mean is exactly the reported 41. Optic nerve head morphometry gave a horizontal cup-to-disc ratio of 0.55 and a vertical ratio of 0.53 on the right against 0.57 and 0.64 on the left, with disc areas of 2.44 and 2.90 mm^2 and cup areas of 0.68 and 1.12 mm^2. The left cup area was therefore 1.65 times the right within a disc only 1.19 times larger, and the vertical cup-to-disc ratio and the cup area were the two parameters that differed materially between the eyes; the horizontal cup-to-disc ratio, 0.55 against 0.57, did not. The printout records a scan pattern of 6.0 × 6.0 mm sampled at 512 × 128, a scan quality index of 2 of 5 for both eyes, signal strength indices of 9 of 10 and 10 of 10, and the manufacturer's default Gullstrand assumption for axial length rather than a measured value.

Automated static perimetry of the right eye was performed on the same day using a 24-2 SITA-Standard program with a size III white stimulus on a 31.5 apostilb background, a pupil diameter of 3.0 mm, a refractive correction of -7.00 dioptres sphere and a test duration of 6 minutes 33 seconds, with a false-positive rate of 14%. The glaucoma hemifield test was reported as within normal limits. As stated in the legend to Figure 5, the perimetric printout survives only as a photograph of the reporting screen, and the mean deviation, pattern standard deviation and visual field index could not be resolved from it at any level of enhancement; those global indices are therefore not reported here, and the perimetry panel is deliberately not reproduced.

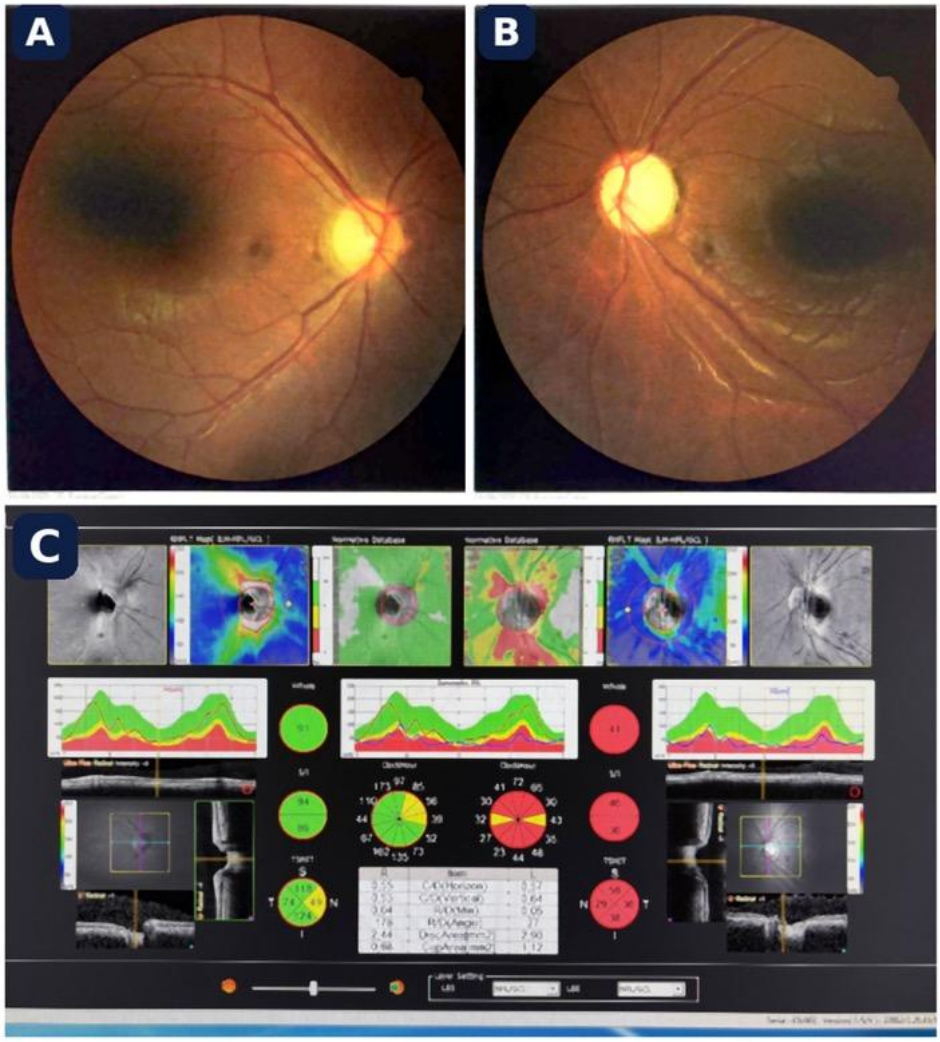

Figure 5. Follow-up on day 53. (A) Right and (B) left fundus; the left disc is pale with extensive peripapillary change, the right disc retains a normal calibre neuroretinal rim. (C) Peripapillary retinal nerve fibre layer analysis of both eyes, showing an average thickness of 91 micrometres on the right and 41 micrometres on the left with an inter-eye symmetry of 0%. The patient banner has been cropped from every panel. The Humphrey 24-2 printout obtained on the same day existed only as a photograph of the reporting screen and remained illegible under every enhancement attempted; it is therefore not reproduced, and only the parameters that could be read from it are reported in the text.

3. Discussion

Scoring the diagnosis rather than asserting it

An item-by-item adjudication of the 2015 International Panel for NMO Diagnosis criteria against this record is detailed in Table 4. Those criteria require, in a seropositive patient, at least one core clinical characteristic, a positive AQP4-IgG assay by the best available method, and exclusion of alternative diagnoses; the six core characteristics are optic neuritis, acute myelitis, area postrema syndrome, acute brainstem syndrome, symptomatic narcolepsy or an acute diencephalic syndrome with typical lesions, and a symptomatic cerebral syndrome with typical brain lesions.[16] Scored against that list, this patient had one of six. Optic neuritis was present and unambiguous; the other five were absent, and the cord imaging summarised in Figure 2C to Figure 2E excluded the myelitis that would otherwise have been the most likely second characteristic.

One of six is enough. That is precisely the point worth making out loud, because it means the entire diagnostic weight of a decision to expose a young woman to central venous access and three plasma exchanges rested on a single qualitative antibody report. As Table 4 records, the assay method and the titre of that report appear nowhere in the file. Titre is not a bookkeeping detail: among 546 patients categorised by serum AQP4 antibody titre, those at 1:100 or below had significantly fewer severe optic neuritis attacks (false discovery rate-corrected $p < 0.001$), a lower incidence of visual disability, and an annual recurrence rate that differed significantly from that of patients at 1:320 or above, and the low-titre group was also less prone to severe relapse on conventional immunosuppressants and on rituximab.[4] A result recorded only as positive discards the prognostic information the test was capable of providing.

Table 4. Item-by-item adjudication of the 2015 International Panel for NMO Diagnosis criteria against this patient's record, followed by the competing diagnoses considered at the exclusion step.

Criterion or competing diagnosis	Verdict	Evidence in this record
Core clinical characteristics (at least one required)		
1. Optic neuritis	Present	Painful subacute visual loss in the right eye with acuity 3/60 and Ishihara 0 of 25; magnetic resonance imaging reported as consistent with right optic neuritis; a further episode had affected the left eye in 2014
2. Acute myelitis	Absent	Contrast-enhanced and unenhanced cervical and lumbosacral imaging with magnetic resonance myelography showed no abnormal cord signal and no new inflammatory lesion
3. Area postrema syndrome	Absent	No intractable hiccups, nausea or vomiting documented
4. Acute brainstem syndrome	Absent	No brainstem signs documented; brain imaging unremarkable
5. Symptomatic narcolepsy or acute diencephalic syndrome with typical lesions	Absent	Not documented; no diencephalic lesion reported
6. Symptomatic cerebral syndrome with typical brain lesions	Absent	No infarct, haemorrhage, space-occupying lesion or typical brain lesion reported
Serological and exclusionary requirements		
Positive AQP4-IgG by best available detection method	Met, incompletely documented	Serum AQP4-IgG reported positive in June 2025; the assay method and the titre are not recorded anywhere in the file
Competing diagnoses considered		
Lupus-associated optic neuropathy	Considered, not favoured	Serum C3 and C4 were both within the reference interval and the lupus anticoagulant was not detected; the rheumatology service scored the neurological domain of disease activity to mononeuritis rather than to the optic neuropathy
Antiphospholipid-related anterior ischaemic optic neuropathy	Considered, not favoured	The presentation was painful and subacute rather than painless and abrupt, there was no disc swelling or altitudinal field loss, and the patient was anticoagulated with rivaroxaban
Myelin oligodendrocyte glycoprotein antibody-associated disease	Not tested	MOG-IgG was never requested; the absence of disc oedema is against it, but the exclusion rests on inference rather than on a result
Multiple sclerosis	Considered, not favoured	No disseminated brain or cord lesions on imaging; severe colour vision loss and poor corticosteroid response are atypical
Compressive, infiltrative or infectious optic neuropathy	Excluded	Imaging showed no mass or infiltrate; there was no systemic infective illness
Diagnostic outcome	Criteria met	One of six core clinical characteristics, which is all the criteria require in a seropositive patient; the diagnostic weight therefore rests almost entirely on a single qualitative antibody result

AQP4-IgG, aquaporin-4 immunoglobulin G; MOG-IgG, myelin oligodendrocyte glycoprotein immunoglobulin G; NMO, neuromyelitis optica.
** Adjudication performed by the authors against the published criteria[16]; bold red marks the items that carry the diagnosis and the documentation gaps within them.*

Why the differential diagnosis was not a formality

In a patient carrying lupus, antiphospholipid syndrome and AQP4 seropositivity at once, three mechanisms could each have produced this optic neuropathy, and Table 4 sets out how each was weighed. The association between NMOSD and systemic autoimmunity is not incidental: seropositive patients in a national registry carried a 5.2-fold higher odds of autoimmune comorbidity, and across that whole 136-patient cohort lupus was present in 5.1% and primary antiphospholipid syndrome in 2.9%,[5] and 1,425 of 16,360 inpatient episodes with neuromyelitis optica also carried lupus or Sjogren syndrome.[6] In an Oxford service cohort, 49 of 175 seropositive patients (28%) had at least one additional autoimmune disease, yet clinical and visual recovery did not differ between those with and without such comorbidity.[15] Coexistence is common; it does not by itself change the expected outcome, so the question is only which mechanism is driving the present attack.

Two entries in Table 2 answered that question. Serum C3 and C4 were both within their reference intervals, and the lupus anticoagulant was not detected. Normal

circulating complement is not what a complement-consuming systemic lupus flare would be expected to produce, whereas the complement-dependent injury of AQP4-IgG-positive disease is a local, tissue-level process that need not deplete serum complement; the clinical corollary of that mechanism is visible in treatment data, where C5 inhibition produced the lowest annualised relapse rate of any agent compared, 0 with a 95% confidence interval of 0 to 0.063.[17] The antiphospholipid alternative also fits poorly. Anterior ischaemic optic neuropathy does occur in antiphospholipid-positive patients, but among 117 persistently antibody-positive patients only 10 had any antiphospholipid-attributable ocular manifestation, and the authors' emphasis was that most ocular findings in that cohort were iatrogenic, corticosteroid exposure carrying an odds ratio of 9.0 with a 95% confidence interval of 2.2 to 37.7.[18] This patient's presentation was painful and subacute rather than painless and abrupt, there was no disc swelling or altitudinal defect, and she was already anticoagulated.

The one gap in that reasoning is recorded honestly in Table 4: myelin oligodendrocyte glycoprotein immunoglobulin G was never requested. Its exclusion here rests on inference, supported by the absence of disc oedema, rather than on a result. That inference has quantitative backing. In an international study of 111 adults imaged within two weeks of a first attack, a peripapillary nerve fibre layer increase of more than two standard deviations, indicating disc oedema, was present in 73.4% of eyes with myelin oligodendrocyte glycoprotein antibody-associated disease but in only 11.1% of the 36 NMOSD eyes, and a cut-off of 117.5 micrometres separated the two with 92.9% specificity.[19] The pale, non-swollen disc seen in Figure 1C is therefore the phenotype expected of NMOSD rather than of the antibody that was not tested.

An absent pupillary defect in the eye that was inflamed

The most instructive single sign in Table 1 is a negative one. The acutely inflamed right eye, with an acuity of 3/60 and no colour vision at all, showed no relative afferent pupillary defect, while the asymptomatic left eye showed one. This is not a paradox but a direct consequence of what the test measures. The swinging flashlight test reports the difference in afferent input between the two eyes, not the absolute damage in either. Where that asymmetry has been quantified with pupillometry, the correlation is with inter-eye difference and not with unilateral disease severity: in 81 patients with asymmetric glaucomatous optic neuropathy the pupillometric defect detected the clinical one with an area under the curve of 0.85 to 0.88, and its coefficient of determination against inter-eye asymmetry was 0.63 to 0.67 for the visual field and 0.35 to 0.45 for nerve fibre layer thickness,[20] while in 82 patients with macular disease the defect score correlated with the inter-eye difference in lesion dimensions at r = 0.84 in the 65 unilateral cases.[21]

In this patient the fellow eye had been reduced to light perception by an attack in 2014 and, as Figure 5C later confirmed, carried a peripapillary nerve fibre layer of 41 micrometres. The left afferent deficit still exceeded the right one even at the height of the right-sided attack, so the defect appeared on the left. Two practical consequences follow. First, in any patient with a previously damaged fellow eye, the absence of a relative afferent pupillary defect carries no reassurance whatever about the acutely symptomatic eye and must not be used to downgrade suspicion of an acute optic neuropathy. Second, the direction of the observed defect is itself quantitative information: that it remained left-sided while the right eye sat at 3/60 with an Ishihara score of 0 of 25 is a measure of how complete the 2014 injury had been, and it is consistent with the structural asymmetry shown in Figure 4B and with the disc appearances in Figure 1C and Figure 1D, where a right disc with indistinct margins sits beside a uniformly pale left one. Table 4 records that this asymmetry played no part in satisfying the diagnostic criteria, which the patient met on the acute attack alone.

Corticosteroid failure and the decision to escalate

The failure of a full Optic Neuritis Treatment Trial regimen in this patient, documented in the first two rows of Table 3, is neither unusual nor a sign that the corticosteroid was given badly. In a database study of acute treatment across both antibody-mediated diseases, high-dose corticosteroid alone improved NMOSD-associated optic neuritis on only 33.3% of occasions, a non-significant effect, in contrast to its clear effect in the myelin oligodendrocyte glycoprotein group.[22] Among 51 patients with atypical optic neuritis, 4 of the 7 who were AQP4-antibody positive had no recovery at all and only 2 recovered fully, while myelin oligodendrocyte glycoprotein positivity and intravenous methylprednisolone were the variables associated with full recovery.[23] Seropositive optic neuritis is, in short, the phenotype in which corticosteroid monotherapy is most likely to fail, and the escalation recorded in Table 3 was the appropriate response to that failure rather than a rescue of last resort.

The mechanistic case for the escalation is straightforward. Plasma exchange removes circulating pathogenic immunoglobulin along with complement components and proinflammatory mediators, and the removal is measurable: among 43 patients with acute attacks, the seropositive patients within the 29 who received corticosteroid plus plasma exchange showed a significant fall in AQP4 antibody concentration by day 10 ($p = 0.013$), accompanied by improvement in disability and daily-activity scores,[24] and in the 48-patient prospective arm of a 105-patient real-world series of steroid-refractory disease, lymphoplasmapheresis significantly reduced AQP4 antibody, fibrinogen, erythrocyte sedimentation rate, C-reactive protein, complement and immunoglobulin

levels together with interleukin-6, tumour necrosis factor alpha, interleukin-1 beta and interleukin-9.[25] A prospective comparison of 146 patients found double-filtration plasmapheresis, given alone or with methylprednisolone in 81 patients, and methylprednisolone alone in 65, to give indistinguishable response rates of 66.7% against 69.2%, with an unadjusted odds ratio of 0.89 and a 95% confidence interval of 0.45 to 1.77; only 21 of the 81 received apheresis without concomitant corticosteroid, so the comparison is of apheresis-containing therapy against corticosteroid alone rather than of one against the other.[26] In a propensity-score-matched analysis of 90 attacks, the 30 given apheresis in addition to methylprednisolone showed a more favourable shift in disability at six months, with an odds ratio of 0.499 and a 95% confidence interval of 0.309 to 0.806, and a better six-month visual acuity, a median of 0.35 against 1.00 logMAR.[27] No tool was available at the bedside to predict whether this particular patient would respond, and that remains a live research question: in 38 participants of a trial of apheresis for steroid-refractory *multiple sclerosis* relapses, a lower pre-procedural serum glial fibrillary acidic protein concentration and younger age predicted a favourable response at four weeks, and the ratio of serum neurofilament light to glial fibrillary acidic protein performed better than either marker alone, with an odds ratio of 1.924 and a 95% confidence interval of 1.073 to 3.451.[28] Whether that model transfers to seropositive NMOSD is untested.

Recovery after a 29-day delay

The published series against which this attack should be read are detailed in Table 5, ordered by the interval between onset and the first exchange. That ordering is the reason the case is worth reporting. The recommendation to treat early is well founded: in 395 attacks treated at a median of 2.6 weeks, a longer delay independently predicted a worse final acuity alongside worse acuity at the time of exchange and older age.[11] In the AQP4-antibody-positive stratum of a prospective cohort, 96 attacks in 95 patients drawn from 124 attacks overall, the time window to exchange entered models that discriminated a gain of at least two acuity levels with an area under the curve of 0.747 and recovery to better than 1.0 logMAR with an area under the curve of 0.834.[12] The corticosteroid literature says the same thing more sharply still: recovery of at least three Snellen lines at three months fell from 66.7% to 31.0% when treatment began beyond 14 days,[9] and failure to regain 0.0 logMAR was associated with an interval of 10 days or more to the first dose of methylprednisolone in 82 patients with an inaugural attack of myelin oligodendrocyte glycoprotein antibody-associated optic neuritis, 18 of whom also received plasma exchange.[29]

Against that background, the row for the present case in Table 5 is anomalous in the useful direction. Exchange began on day 29 and acuity nevertheless returned from 3/60 to 6/6, the ceiling of the measurement. The closest published comparator by delay is a paediatric series in which the median interval was also 29 days, with a range of 10 to 98 days, and in which only the single child treated on day 10 was judged to have improved clinically, the other five showing no change in disability.[30] The present case does not contradict that series; it shows that a delay of that length does not guarantee its outcome. One discrepancy inside that series should be declared: although its text states that the other five children showed no clinical improvement, its own per-patient table records small acuity gains in three of them, so the contrast with the present case is one of degree rather than of kind. Two larger studies point the same way. An apheresis service reviewing 54 patients treated an average of 23 days after onset found no relationship between the duration of symptoms before exchange and the result, with an average improvement of 2.9 on a five-point clinician-rated scale,[14] and a rescue study of 61 corticosteroid-unresponsive attacks, of which 22 received immunoadsorption and 24 plasma exchange, concluded explicitly that the effective period for immunoadsorption may be longer than previously thought.[13] As shown in Table 5, the two series that report no timing effect are also the two with the longest mean intervals, which is what one would expect if the relationship between delay and outcome flattens rather than continuing to fall. The practical inference is narrow and should be stated as such: lateness is a reason to hurry, not a reason to withhold.

The timing of the response, visible in Figure 4A and in the day counts of Figure 3A, is worth noting for its own sake. Nothing changed after the first exchange and nothing after the second. The first measurable gain came on day 33, four days after the first session, and normal acuity on day 35, six days after it. A clinician judging the intervention at the bedside 48 hours after the second exchange would have concluded that it had failed. That lag is consistent with a series of 10 patients with neuromyelitis optica in which four first improved only after the second or third cycle, although no patient in that series had visual involvement,[31] and it argues against abandoning a planned course on the basis of an early absence of response.

It is worth locating the delay precisely, because the two halves of it are not equally modifiable. Twenty-four of the 29 days elapsed before this institution saw the patient, along a referral chain the record documents step by step; the remaining five were spent inside the hospital completing and assessing the corticosteroid course. For comparison, in a national analysis of 11,209 patients hospitalised for optic neuritis between 2000 and 2020, plasma exchange use rose from 0.63% to 5.46%; within the 3,215-patient subset coded after 2015, use was highest in NMOSD at 21.21% and the median time to exchange was one day after admission.[35] The in-hospital interval here was therefore longer than that benchmark, but it was spent

on a therapy that had to be tried first, whereas the 24 days preceding admission were not spent on treatment at all. Shortening the interval in a system like this one means acting on the referral pathway rather than on the ward.

Table 5. The present case set against published series of plasma exchange for optic neuritis and for attacks of neuromyelitis optica spectrum disorder, ordered by the reported interval between attack onset and the first exchange.

Study	Design and size	Onset to first exchange	Principal outcome
Sahoo and colleagues31	Retrospective single centre, 10 patients	Abstract states within 5 days; the paper's own table gives 3-14 days	6 of 10 improved markedly in limb power, 2 showed no improvement and 2 died; no patient in the series had visual involvement; one procedure aborted for hypotension
Gonzalez and colleagues32	Prospective series, 83 patients and 558 sessions	Median 8 days (range 1-32)	82.4% improved by Keegan criteria and 78.3% gained at least one point on the visual outcome scale; low fibrinogen in 26% of sessions
Chen and colleagues11	International multicentre, 395 attacks in 317 patients, of which 75 attacks were AQP4-IgG positive	Median 2.6 weeks (IQR 1.4-4.0)	Median final acuity 20/25 across all attacks; 20.5% ended at 20/200 or worse; longer delay, worse acuity at exchange and older age each predicted a poorer result
Bhushan and colleagues14	Retrospective apheresis service review, 54 patients	Average 23 days	Average improvement 2.9 on a 1-5 clinician-rated scale; no relationship between symptom duration before exchange and outcome
Li and colleagues30	Paediatric case series, 6 children, all AQP4-IgG positive	Median 29 days (range 10-98)	Only the child treated on day 10 was judged to have improved; the other five showed no change in disability, although the paper's own per-patient table records small acuity gains in three of them
Present case	Single patient, AQP4-IgG positive, 3 sessions	29 days	3/60 to 6/6 by day 35; Ishihara 0 of 25 to 5 of 25 by day 40; no adverse event
Fu and colleagues12	Prospective cohort, 124 attacks in 122 patients; 96 attacks in 95 patients were AQP4-antibody positive	Not stated as a single figure	In the seropositive stratum, mean logMAR acuity improved after five cycles and was maintained (adjusted $p < 0.001$); the time window to exchange entered both prediction models, which reached areas under the curve of 0.747 and 0.834
Xu and colleagues27	Propensity-score-matched cohort, 90 attacks, 30 given apheresis	Matched on time to steroids	More favourable shift in disability at 6 months with apheresis (OR 0.499, 95% CI 0.309-0.806) and better 6-month acuity (median 0.35 versus 1.00 logMAR, $p = 0.002$); fibrinogen fell in 15 of the 30 apheresis-treated attacks, all in the immunoadsorption arm; no severe adverse event
Zhang and colleagues33	Observational study, 76 patients including 26 aged 60 or over, 25 analysable for response	Not stated	24 of the 25 analysable elderly patients improved functionally by 6 months; a severe optic neuritis attack independently predicted a poor response; transient hypotension was more frequent in older patients
Takai and colleagues34	Two-decade retrospective comparison, 39 patients (43 eyes) with AQP4-antibody-positive optic neuritis	Not stated	Plasmapheresis was used in 1 eye (3.8%) in the earlier decade and 7 eyes (41.1%) in the later one (OR 16.3, 95% CI 1.7-815); final acuity was better in the later, separate group, 0.10 versus 0.70 logMAR ($p = 0.042$)

AQP4-IgG, aquaporin-4 immunoglobulin G; IQR, interquartile range; logMAR, logarithm of the minimum angle of resolution.

** The present case is shown in bold red at its position in the ordering by treatment delay.*

† Studies that do not report a single interval between onset and the first exchange are listed after those that do, and are not assigned a rank.

‡ This table is a descriptive juxtaposition assembled for orientation, not a systematic review or a meta-analysis; the studies differ in population, in outcome definition and in the completeness with which the treatment interval is reported, and no pooled estimate should be inferred from it.

Acuity recovered before colour vision, and by a wide margin

The second axis of Figure 4A carries a message that the acuity curve alone conceals. On day 35 high-contrast acuity was 6/6 and the Ishihara score was 2 of 25. On day 40, with acuity still 6/6, the score had reached only 5 of 25, a fifth of the plates. Had this attack been assessed by acuity alone, as most acute inpatient reviews are, it would have been recorded as a complete recovery. It was not one.

This dissociation has a structural explanation and a measurement one. Structurally, high-contrast acuity depends on a small foveal projection that can be sustained by a minority of surviving axons, whereas colour discrimination samples a wider population of the papillomacular bundle. Across NMOSD, myelin oligodendrocyte glycoprotein antibody-associated disease and multiple sclerosis, the relation between visual function and nerve fibre layer thinning follows a broken-stick model with a breakpoint near 60 micrometres, and acuity loss per micrometre of thinning is steeper in NMOSD than in the myelin oligodendrocyte glycoprotein group.[36] The dotted line in Figure 4B marks that breakpoint, and the sector values plotted against it are worth reading carefully: the right eye lay above 60 micrometres in the superior, inferior and temporal sectors but below it nasally, at 49 micrometres, while the left eye lay below 60 micrometres in every sector, its highest value being 59 micrometres superiorly. In measurement terms, a study defining incomplete visual recovery as an acuity worse than 0.1 logMAR would have classified this patient as fully recovered on day 35,[15] which is a reminder that the outcome definitions used in the cohort literature are coarser than the deficits patients actually carry. Colour vision, and where possible automated perimetry and optical coherence tomography, should be part of the record of every optic neuritis attack, not an optional refinement.

What the structural follow-up can and cannot be made to say

Figure 5C shows an average peripapillary nerve fibre layer of 91 micrometres in the treated right eye, flagged by the device as within normal limits, against 41 micrometres in the left. It is tempting to read the right-eye value as proof that the attack left no structural trace. That reading is not supportable, for three reasons that should be stated before any inference is drawn from it.

First, the eye is myopic at -7.00 dioptres sphere and the analysis, as recorded in the printout and described in section 2.8, used the manufacturer's default Gullstrand axial length rather than a measured one. In 72 healthy eyes, the percentage difference between magnification-corrected and uncorrected circumpapillary nerve fibre layer thickness increased significantly with axial length globally and in every sector, and did so more strongly for nerve fibre layer thickness than for capillary density.[37] Second, high myopia shifts the normative comparison itself: among people with multiple sclerosis, baseline peripapillary retinal nerve fibre layer thickness was 5.3 micrometres lower (95% confidence interval -9.0 to -1.7) and ganglion cell-inner plexiform layer thickness 3.2 micrometres lower (95% confidence interval -5.5 to -0.8) in eyes with a refractive error of -6 dioptres or worse than in non-myopic eyes, with a reciprocal temporal increase of 7.1 micrometres and a similar pattern in healthy controls, and the authors of that work warned in terms that such cross-sectional differences can lead to false attribution of pathology when refractive error is not taken into account.[38] Third, the printout records a scan quality index of 2 of 5. Taken together, a classification of within normal limits against a normative database that excludes high myopia, obtained at that quality index and without a measured axial length, cannot carry the weight of a claim that the nerve was spared.

What the study does support is the inter-eye comparison, which is internally controlled and does not depend on the normative database. The difference between the eyes was 50 micrometres in absolute terms and 54.9% in relative terms. The thresholds evaluated for this purpose in seropositive patients are an inter-eye absolute difference of 5 micrometres and a percentage difference of 5% for the peripapillary nerve fibre layer, and 4 micrometres and 4% for the ganglion cell-inner plexiform layer; the nerve fibre layer percentage difference separated seropositive patients with a previous unilateral attack from healthy controls with an area under the curve of 0.96, at 87% specificity and 89% sensitivity.[39] This patient's asymmetry exceeds those thresholds tenfold, and the device reported an inter-eye symmetry of 0%. Figure 5A and Figure 5B show the same asymmetry qualitatively, the left disc pale across its whole surface and the right retaining a neuroretinal rim of normal calibre. Attribution matters here: that asymmetry is the residue of 2014, not of 2025, since the left eye had already been reduced to light perception 11 years earlier. A further caution applies to the right eye even so, because in first unilateral attacks the clinically unaffected fellow eyes of NMOSD patients already showed significantly worse acuity, field mean deviation and nerve fibre layer thickness than healthy control eyes within two weeks of onset.[40] The absence of a pre-attack measurement in this patient means that no baseline exists against which the 91 micrometres can be read, and none can now be constructed. A single measurement at day 53 is in any case not an endpoint: in a prospective longitudinal study, clinically stable patients continued to lose ganglion cell-inner plexiform layer thickness at a median of 0.18 micrometres per year, and both macular nerve fibre layer and ganglion cell-inner plexiform layer thicknesses were already significantly lower in patients than in healthy controls, at 33.91 against 38.88 and 54.89 against 64.42 micrometres.[41] Serial rather than single imaging is what would answer the question

this study was asked. One further morphometric observation belongs here. The left disc carried a vertical cup-to-disc ratio of 0.64 against 0.53 on the right, and a cup area of 1.12 against 0.68 mm², in an eye with no history of raised intraocular pressure and an intraocular pressure of 12 mmHg at both visits. Cupping of the optic nerve head, classically a sign of glaucomatous optic neuropathy, can follow an episode of optic neuritis, and in a multicentre study of 86 patients imaged at least six months after a single unilateral attack, 35 with multiple sclerosis, 26 with NMOSD and 25 with myelin oligodendrocyte glycoprotein antibody-associated disease, cupping asymmetry was greatest in the NMOSD group on univariable analysis (coefficient 0.032, p = 0.017); it did not persist after adjustment for age, sex, race, follow-up time and either the nerve fibre layer or the ganglion cell complex thickness of the affected eye. That study reports no antibody status, so its NMOSD group is defined by the 2015 consensus criteria rather than by seropositivity.[42] The asymmetry here is best read as the structural residue of the 2014 attack rather than as evidence of a second, glaucomatous process.

An attack that occurred on treatment, in a patient already known to be seropositive

The most actionable finding in this case is not the recovery but the circumstance of the attack, recorded in the first two rows of Table 1 and in the first entry of Figure 3A. AQP4-IgG had been reported positive in June 2025. The attack began in July 2025. The relapse-prevention therapy in place was azathioprine 50 mg three times daily, alongside low-dose oral methylprednisolone prescribed for lupus.

Azathioprine is a legitimate agent in this disease, and in a registry of 493 patients with 1,247 treatment courses it was, with rituximab, the most widely used, and it reduced the risk of a subsequent attack in seropositive patients, although only marginally so, with a hazard ratio of 0.72 whose 95% confidence interval of 0.51 to 1.00 touches unity.[43] But among the agents compared directly in a cohort of 176 patients followed for a median of 9 years, azathioprine carried the highest annualised relapse rate, 0.34 with a 95% confidence interval of 0.18 to 0.56, while C5 inhibitors carried the lowest at 0, and relapse risk relative to rituximab was significantly lower with C5 inhibitors, inebilizumab and satralizumab.[17] Even rituximab is not a guarantee: in 605 seropositive patients from 22 centres followed for a median of 47 months, 117 (19%) relapsed at least once and 68, that is 11% of the whole cohort, had multiple or severe relapses.[44] The same registry that endorsed azathioprine also identified a prior attack while on the same therapy as an independent risk factor for further attacks,[43] and a nationwide cohort of 66 seropositive patients found that delayed immunosuppression after the first relapse was associated with a higher final disability score, that optic neuritis was associated with a higher relapse frequency, and that rituximab correlated with a lower final score.[45] The attack described here therefore did more than damage an optic nerve; it reclassified the patient's maintenance therapy as having failed, in an eye that was already her only functioning one.

One further omission belongs in this section. Azathioprine was prescribed without any recorded thiopurine methyltransferase or NUDT15 status. Among 1,403 adults newly started on the drug, poor or intermediate metabolisers were at substantially higher risk of discontinuation for myelotoxicity, with a hazard ratio of 2.90 and a 95% confidence interval of 1.58 to 5.31 in that unadjusted analysis.[46] The variant established as decisive in Chinese populations is NUDT15 R139C, associated with azathioprine-induced leukopenia at an odds ratio of 21.7 with a 95% confidence interval of 12.1 to 38.8, and prospective screening of 1,013 participants with substitution of an alternative immunosuppressant in carriers brought the incidence of leukopenia down to 0.4% against a historical incidence of 7.6%.[47] Whether the same variant frequency applies in an Indonesian population has not been established, which is itself an argument for measuring rather than assuming; in this patient, maintained on azathioprine for years, the genotype was never determined.

Safety of the procedure and of the access

No adverse event was documented across the three sessions, as the last row of Table 3 records, and this is consistent with contemporary series rather than fortunate. In an 11-year single-centre experience, 265 patients underwent 1,274 procedures for a presumed autoimmune neurological disease, five being excluded once their final diagnoses were known; the overall response rate was 81.3%, only one patient required termination of a procedure, and the commonest complication was an easily managed allergic reaction, although that case mix was dominated by Guillain-Barré syndrome, myasthenia gravis and multiple sclerosis rather than by NMOSD.[48] Among the 30 apheresis-treated attacks within a 90-attack propensity-matched analysis, no severe adverse event forced discontinuation, although fibrinogen fell in 15 of those 30, all of them in the immunoadsorption arm.[27] Hypofibrinogenaemia is a frequently reported laboratory effect, occurring in 26% of 558 sessions in one series,[32] and adverse reactions of mild or moderate intensity were recorded in 9.3% of procedures affecting 38% of patients in another.[49] Age modifies this: transient hypotension was significantly more frequent in patients aged 60 or over. The safety column of Table 5 makes the same point across the series collected there, in that the events reported are almost entirely laboratory or transient haemodynamic ones rather than events that ended a course of treatment.[33]

The access route deserves separate mention because it was a double-lumen central venous catheter in a patient with antiphospholipid syndrome. Among 9,863 discharges of adults treated with plasma exchange, a catheter was used in 5,988 (60%) and its use was

significantly associated with thrombosis, with an odds ratio of 1.23 and a 95% confidence interval of 1.04 to 1.46, as well as with red cell transfusion, in-hospital mortality and a longer stay.[50] Acute non-occlusive internal jugular vein thrombosis was one of four adverse-event occurrences, two rashes, one thrombosis and one thrombocytopenia, reported in a series of six children.[30] That this patient was already anticoagulated with rivaroxaban for her antiphospholipid syndrome is a plausible part of why nothing happened, and the combination of central access and a prothrombotic state is precisely the situation in which existing anticoagulation should be documented and continued deliberately rather than by default.

Auditing the record against the determinants of outcome

The surgery of this case, so to speak, was conventional and successful. What the case exposes is not a failure of treatment but a set of measurements that the determinants of outcome in the recent primary literature require, and that this record does not contain. Six are worth naming, because each corresponds to a quantity that a published study has shown to predict something.

The AQP4-IgG titre was never recorded, although titre stratifies severe optic neuritis attacks, visual disability and recurrence rate.[4] The interval from onset to treatment was allowed to reach 24 days for corticosteroid and 29 days for exchange, in a referral chain that the record itself documents step by step, although delay beyond 14 days more than halves the rate of recovery of at least three Snellen lines at three months[9] and delay to exchange independently predicts a worse final acuity.[11] No fat-suppressed coronal orbital sequence was retained and no optic nerve lesion was measured, as Figure 2 makes plain, although a lesion extending from the intracanalicular optic nerve to the chiasm has been associated with worse acuity and a thinner ganglion cell-inner plexiform layer,[8] and chiasmal tissue damage measured by magnetisation transfer ratio is lower in AQP4-antibody-positive patients than in healthy controls both with and without a previous optic neuritis (28.55 ± 4.18 and 28.37 ± 7.27 against 31.65 ± 4.93, p = 0.020 and p = 0.035), while across the whole inflammatory demyelinating cohort a lower chiasmal ratio was associated with a higher number of optic neuritis episodes (regression coefficient -1.15, 95% confidence interval -1.82 to -0.49) and with worse acuity (-0.026, 95% confidence interval -0.041 to -0.011).[51] No optical coherence tomography and no automated perimetry were obtained at the acute visit, where a confrontation field was substituted, so the day-53 study in Figure 5C has no baseline; inter-eye metrics with validated thresholds exist precisely for this situation.[39] The thiopurine methyltransferase and NUDT15 status was never determined.[46,47] And the body weight on which the 1 mg per kilogram prednisone dose was calculated is absent, so the milligram dose actually given cannot be recovered from the file, as the footnote to Table 3 states.

These are not exotic investigations. Converted into a minimum data set for a seropositive optic neuritis attack, they read as follows. First, record the AQP4-IgG assay method and titre at the moment of diagnosis, because the titre carries prognostic information that a qualitative result discards. Second, record the date and hour of symptom onset, of first medical contact and of the first dose of each acute therapy, at admission, because the interval is the modifiable variable with the largest published effect on recovery. Third, obtain a fat-suppressed coronal orbital sequence and record the length of the affected segment, at the diagnostic scan, because lesion extent predicts the structural outcome. Fourth, obtain peripapillary optical coherence tomography of both eyes with a measured axial length and an accepted quality index, and an automated visual field, at the acute visit and again at three months, because without a baseline the follow-up study can only be read against a normative database that may not apply to the eye in front of you. Fifth, record the Ishihara or equivalent colour score alongside acuity at every visit, because acuity alone would have called this recovery complete on day 35. Sixth, determine thiopurine methyltransferase and NUDT15 status before or at the start of azathioprine, and record the maintenance decision explicitly at discharge after any breakthrough attack, because the attack has by definition redefined the adequacy of the maintenance.

Two of those six items were acted on for this patient after the attack. The AQP4-IgG result was referred back for titre and assay method, and the maintenance regimen was referred to the neurology and rheumatology services with a recommendation to move from azathioprine monotherapy to an agent with a lower published relapse rate, the choice constrained in practice by availability and cost.[17,44] The remaining four are prospective and cannot be applied retrospectively to this attack; they are offered here because the cost of omitting them only becomes visible, as it did in this patient, at the moment someone tries to interpret a follow-up measurement against a baseline that was never taken.

Limitations

This is a single patient, so no causal relationship between plasma exchange and the recovery can be established, and the contribution of the oral prednisone begun on day 28 cannot be separated from that of the exchanges. The optimal number and spacing of sessions cannot be inferred from one course of three. Follow-up extends only to day 53, which is long enough to document the functional outcome and a single structural measurement but not long enough to show whether the gain is durable or whether a further relapse follows; the annualised relapse rates cited above imply that a longer observation is needed before any statement about durability.[3] Several of the source

records were available only as photographs of reporting screens, which is why the perimetric global indices are not reported and why the orbital images in Figure 2 cannot be independently assessed. AQP4-IgG was not remeasured after the exchanges, so the antibody reduction that the mechanism predicts was not confirmed in this patient, although it has been demonstrated in cohorts.[24,25] The comparison assembled in Table 5 is descriptive and was not designed as a systematic review, so it establishes the position of this case within the published range rather than any pooled effect. The reference base was assembled to report original patient data wherever possible. Of the 51 sources cited, 48 report original research published within the last five years, one is a six-patient case series, one is a ten-patient consecutive apheresis series, and two are the international consensus documents whose criteria the manuscript scores the patient against and which cannot be replaced by primary research without leaving the diagnostic and apheresis classifications uncited; counted at its strictest, treating both series as series rather than as cohorts, 47 of 51 sources, or 92.2%, are original research published within five years. Finally, the audit in section 3.10 describes one institution's record at one moment and should be read as a proposal to be tested rather than as a general characterisation of practice.

4. Conclusion

A 34-year-old woman with AQP4-IgG-positive NMOSD, systemic lupus erythematosus and antiphospholipid syndrome recovered best-corrected visual acuity from 3/60 to 6/6 after three sessions of therapeutic plasma exchange begun 29 days after the onset of a corticosteroid-refractory optic neuritis attack, without any procedure-related adverse event. Recovery began four days after the first session and reached the measurement ceiling six days after it, so a judgement made at the bedside two days after the second exchange would have been wrong. Lateness is a reason to move quickly, not a reason to withhold treatment.

Three observations from this attack generalise beyond it. A relative afferent pupillary defect measures the difference between two eyes, so its absence in an acutely inflamed eye carries no reassurance when the fellow eye is already damaged, and here the defect sat on the asymptomatic side throughout. Colour vision recovered to only 5 of 25 plates while acuity was already 6/6, so an outcome recorded by acuity alone would have been recorded wrongly. And a peripapillary nerve fibre layer flagged as within normal limits in a highly myopic eye, measured against a default axial length at a low quality index and without a baseline, cannot be made to prove that the nerve was spared, although the inter-eye difference of 50 micrometres remains interpretable because it is internally controlled.

The attack itself occurred on azathioprine in a patient whose seropositivity had been documented a month earlier and whose thiopurine genotype had never been determined, which redefines the maintenance therapy as inadequate rather than merely unlucky. The six-item minimum data set proposed here, covering antibody titre, treatment intervals, orbital lesion length, paired structural and perimetric measurements, colour vision at every visit, and thiopurine genotyping with an explicit maintenance decision at discharge, is offered as the smallest set of measurements that would have allowed each of these judgements to be made on evidence rather than on inference.

Declarations

Ethical approval and consent to participate

This report describes the routine clinical care of a single patient and involved no change to management and no research intervention. The patient gave written informed consent to the publication of her clinical details and of the accompanying images. All identifying information has been removed from the text and from every image; the periocular region has been masked in the clinical photograph and every burned-in patient identifier has been cropped from the radiological, fundus and tomographic reproductions. The work was conducted in accordance with the Declaration of Helsinki and follows the CARE reporting guideline for case reports.

Consent for publication

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

Availability of data and materials

All data supporting the findings of this report are contained within the article. The underlying clinical record is held by the treating institution and is not publicly available because it contains information that could compromise patient privacy.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors contributed to the conception of the report, the acquisition and interpretation of the clinical data, and the drafting and critical revision of the manuscript. All authors have read and approved the final version and agree to be accountable for all aspects of the work.

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Reporting guideline

The CARE checklist for case reports was completed in full and every item is addressed in the manuscript: the title identifies the report as a case report, the abstract is structured, the introduction states what makes the case unique, the patient information, clinical findings, timeline, diagnostic assessment, therapeutic intervention, follow-up and outcomes each occupy a labelled part of the Case Presentation, the discussion states the strengths and the limitations of the management, and informed consent is documented above.

Generative AI disclosure

The authors declare that no generative artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

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