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Severe Vitamin A Deficiency with Predominant Scotopic Dysfunction: Electrophysiological Recovery After Supplementation

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Case Report

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Abstract

Purpose

To describe a patient with acquired nyctalopia in whom full-field electroretinography (ffERG) provided a key diagnostic clue to severe vitamin A deficiency (VAD), with marked electrophysiological recovery after replacement therapy.

Methods

Retrospective review of the patient's medical history, multimodal imaging, visual fields, and electrophysiological findings.

Results

A 51-year-old man presented with progressive decline in distance and near vision and bilateral nuclear cataracts. Following uncomplicated cataract surgery, best-corrected visual acuity (BCVA) improved only to 0.5 in both eyes, and severe acquired nyctalopia became evident. ffERG demonstrated moderate-to-severe generalized retinal dysfunction with marked scotopic predominance. Serum vitamin A was profoundly reduced (< 0.02 mg/L), and systemic evaluation disclosed previously unrecognized alcohol-related cirrhosis (Child-Pugh class A6). Vitamin A replacement was followed by resolution of nyctalopia and near-normalization of visual fields. At approximately three months, ffERG showed striking recovery, with the overall response considered within normal limits. After 10 years of continued supplementation, the patient remains asymptomatic, with normal visual fields and BCVA of 1.0 in both eyes.

Conclusions

Severe rod-predominant electrophysiological dysfunction in acquired nyctalopia may provide an important clue to a potentially reversible retinal disorder. In this patient, ffERG redirected the diagnostic work-up toward profound VAD and ultimately led to recognition of clinically significant systemic disease. Marked functional recovery despite unchanged OCT findings further illustrates the value of electrophysiology for documenting reversibility.

Introduction

Acquired nyctalopia with minimal fundus abnormalities represents a diagnostic challenge, overlapping with inherited retinal disorders and autoimmune or paraneoplastic retinopathies. In this setting, full-field electroretinography (ffERG) substantially narrows the differential diagnosis by characterizing the pattern and severity of retinal dysfunction.

Vitamin A deficiency (VAD) is a rare, reversible cause of acquired retinal disorder in developed countries, usually associated with intestinal malabsorption or chronic liver disease. [1–3] Electrophysiological abnormalities predominantly affect rod function (markedly reduced or absent dark-adapted responses), though photopic responses may also be affected in severe disease. [4, 5] Recognizing this electrophysiological phenotype provides a crucial diagnostic clue and prompt investigation for a potentially reversible systemic cause.

We report a patient with acquired nyctalopia in whom severe rod-predominant ffERG abnormalities redirected the diagnostic work-up toward profound VAD secondary to previously unrecognized alcohol-related cirrhosis, followed by marked electrophysiological recovery after vitamin A replacement.

Case report

A 51-year-old man presented with progressive deterioration of vision. His medical history included arterial hypertension and anxiety. Best-corrected visual acuity (BCVA) was 0.63 in the right eye (OD) and 0.4 in the left eye (OS). Slit-lamp examination revealed bilateral nuclear cataracts; funduscopy was unremarkable. OCT demonstrated reduced retinal thinning, with central macular thicknesses of 196 µm OD and 204 µm OS, and mild retinochoroidal folds in OD (Fig. 1). As visual loss was attributed to cataracts, he underwent uncomplicated sequential phacoemulsification with intraocular lens implantation in both eyes (OU).

Despite successful surgery, visual recovery was limited (postoperative BCVA 0.5 OU). The patient also reported progressively disabling acquired nyctalopia. Insufficient visual recovery, night blindness, and an unremarkable fundus raised suspicion of an underlying retinal disorder (e.g. retinitis pigmentosa sine pigmento), prompting electrophysiological evaluation.

Electrophysiological testing followed International Society for Clinical Electrophysiology of Vision (ISCEV) protocols. [6] ffERG was recorded using a Roland Consult system (subconjunctival HK-Loop electrodes) after maximal pupil dilation. Dark-adapted (DA) rod and mixed responses, light-adapted cone and 30-Hz flicker responses, and oscillatory potentials were recorded. Multifocal ERG (mfERG) was obtained using 103 segments with HK-Loop electrodes.

Baseline ffERG revealed moderate-to-severe generalized retinal dysfunction, with marked scotopic predominance (Fig. 2; Table 1). DA 0.01 ERG b-wave amplitudes were profoundly reduced to 17.1 µV OD and 10.6 µV OS. DA 3.0 ERG responses were also markedly decreased, with a-wave amplitudes of 29.6 and 28.3 µV and b-wave amplitudes of 43.8 and 38.1 µV in OD and OS, respectively. Although the b:a ratios were reduced (1.48 OD and 1.34 OS), an unequivocal electronegative configuration could not be established because of low amplitudes. Photopic responses were decreased, although less severely. mfERG demonstrated diffuse abnormalities in OD and milder abnormalities with peripheral predominance in OS. Pattern visual evoked potentials (VEP) showed borderline prolonged latency with reduced amplitude in OD and delayed latency in OS. Automated perimetry showed diffuse depression in OD (Visual Field Index [VFI] 96%; Mean Deviation [MD] -5.86 dB) and a more pronounced diffuse, arcuate-

like defect in OS (VFI 87%; MD -9.28 dB) (Fig. 3). The severe rod-predominant electrophysiological dysfunction, acquired onset of nyctalopia, and absence of characteristic fundus abnormalities redirected the differential diagnosis from an inherited retinal degeneration toward acquired retinal disorders, including cancer-associated retinopathy (CAR) and VAD. Anti-recoverin antibodies were negative, whereas serum vitamin A was profoundly reduced at < 0.02 mg/L (reference range, 0.30–0.80 mg/L). Laboratory testing also showed macrocytosis (MCV 105.8 fL), thrombocytopenia (65 × 10^9/L), and elevated liver enzymes (AST 100 IU/L, ALT 58 IU/L, GGT 215 IU/L). Abdominal ultrasonography demonstrated hepatic steatosis and splenomegaly. Subsequent hepatological evaluation established the diagnosis of previously unrecognized alcohol-related cirrhosis (Child–Pugh class A6).

Oral vitamin A replacement was initiated (100,000 IU daily for 3 days). Maintenance therapy with 20,000 IU daily was insufficient to maintain target serum concentrations and was increased to 50,000 IU daily, under serum monitoring. Following treatment, BCVA improved to 1.0 OD and 0.8 OS, nyctalopia resolved, and visual fields nearly normalized (VFI 99% OU; MD -1.98 dB OD and − 2.33 dB OS) (Fig. 3). Funduscopy remained unremarkable and OCT findings were unchanged.

At three months, follow-up ffERG demonstrated striking recovery of retinal function (Fig. 2; Table 1). DA 0.01 ERG b-wave amplitudes increased to 236 µV OD and 173 µV OS, while DA 3.0 ERG a-wave amplitudes increased to 189 and 178 µV and b-wave amplitudes to 289 and 235 µV, respectively. DA 10.0 responses and oscillatory potentials also showed marked recovery. Photopic and 30-Hz flicker responses also improved substantially. Follow-up ffERG demonstrated marked recovery of retinal function, with only minor residual abnormalities. Serum vitamin A reached 0.4 mg/L. Complete clinical recovery has been sustained over 10 years of continued vitamin A supplementation with regular serum vitamin A monitoring. The patient remains asymptomatic, with BCVA of 1.0 bilaterally and normal visual fields.

Table 1

ffERG findings before and after vitamin A supplementation. Baseline ffERG was performed on December 11, 2018, and follow-up ffERG on March 12, 2019. Laboratory reference values represent mean amplitudes obtained using a Roland Consult™ system with subconjunctival HK-Loop electrodes, according to ISCEV protocols. *Laboratory reference values were obtained from González and Vilela [7]

ffERG response	Parameter	Baseline OD	Baseline OS	Follow-up OD	Follow-up OS	Laboratory normal mean*
DA 0.01	b-wave amplitude (μV)	**17.1**	**10.6**	**236**	**173**	**116.83**
	b peak time (ms)	76.3	115.5	80.2	88.1	—
DA 3.0	a-wave amplitude (μV)	**29.6**	**28.3**	**189**	**178**	—
	b-wave amplitude (μV)	**43.8**	**38.1**	**289**	**235**	**224.58**
	a peak time (ms)	17.6	16.6	22.5	21.5	—
	b peak time (ms)	28.4	28.4	48.9	42.1	—
	b:a ratio	**1.48**	**1.34**	**1.53**	**1.32**	—
DA 10.0	a-wave amplitude (μV)	32.7	34.7	257	230	—
	b-wave amplitude (μV)	40.5	30.8	326	300	—
Oscillatory potentials	Sum amplitude (μV)	**38.3**	**43.7**	**127**	**146**	**129.01**
LA 3.0	a-wave amplitude (μV)	12.9	14.8	18.7	21.0	—
	b-wave amplitude (μV)	**39.6**	**39.4**	**79.3**	**84.3**	**95.11**
	a peak time (ms)	13.5	13.2	13.8	13.5	—
	b peak time (ms)	32.6	30.8	32.0	31.7	—

ffERG response	Parameter	Baseline OD	Baseline OS	Follow-up OD	Follow-up OS	Laboratory normal mean*
LA 3.0 flicker 30 Hz	N1–P1 amplitude (μV)	**44.3**	**53.2**	**69.9**	**67.9**	**93.82**
	P1 peak time (ms)	63.3	63.9	63.3	62.6	—

Discussion

The main finding in this case was the diagnostic value of electrophysiology in acquired nyctalopia with limited structural retinal abnormalities. ffERG demonstrated severe generalized retinal dysfunction with scotopic predominance, narrowing the diagnostic pathway toward an acquired, potentially reversible retinal disorder and ultimately contributed to the recognition of an unsuspected systemic disease.

Vitamin A is essential for photoreceptor function through its role in the visual cycle. Severe deficiency preferentially impairs rod-mediated vision, resulting in nyctalopia, reduced retinal sensitivity, visual field defects, and marked attenuation of scotopic ERG responses. [3, 8] VAD occurs in up to two thirds of patients with cirrhosis, particularly in alcohol-related or decompensated disease, where several mechanisms may impair vitamin A homeostasis. [9, 10]

Ophthalmic manifestations of VAD are heterogeneous. Xerophthalmia, Bitot's spots, peripheral white punctate retinal lesions, the "double carrot" sign, and outer retinal OCT abnormalities are described but not consistently present. [1, 5, 11, 12] Generalized macular thinning has also been reported and was present in our patient. [4, 13] An unremarkable fundus may coexist with substantial functional abnormalities. [4, 14, 15] This dissociation between structural and functional findings was particularly evident in our patient: OCT abnormalities remained unchanged after treatment, despite striking clinical and electrophysiological recovery. Acquired nyctalopia, visual field abnormalities, and retinal thinning may also resemble inherited retinal degeneration or autoimmune and paraneoplastic retinopathies. [16–18]

In this setting, electrophysiology provides information that cannot be inferred from structural examination alone. In VAD, ffERG typically demonstrates markedly reduced or absent DA rod responses, and electronegative configurations have also been reported. [4] In our patient, DA responses were profoundly reduced, with b:a ratios of 1.48 OD and 1.34 OS. Very low response amplitudes precluded characterization of the waveform as unequivocally electronegative; the predominant feature was severe scotopic dysfunction. Cone involvement is generally less pronounced, although photopic responses may become reduced in severe or prolonged deficiency. [5] Macular electrophysiology may be abnormal, with reduced pattern ERG amplitudes and delayed or reduced mfERG responses. [4, 19] Pattern VEP abnormalities, including prolonged P100 latency and reduced amplitude, have also been reported. [3, 20] In our patient, the profound scotopic dysfunction, with less severe photopic involvement, was

considerably more informative than nonspecific structural abnormalities, directing the subsequent etiological investigation.

Recognition of this acquired functional phenotype prompted metabolic investigation and led to identifying profound VAD. In turn, the deficiency triggered systemic evaluation and ultimately disclosing previously unrecognized alcohol-related cirrhosis. Electrophysiology provided an efficient bridge between the ocular phenotype and systemic disease.

Rapid functional recovery following vitamin A replacement is documented in the literature. Serial electrophysiological studies show recovery of retinal responses beginning within days and substantial improvement within weeks after supplementation. [2, 4, 21, 22] Visual field improvement after treatment has likewise been documented, with recovery occurring over days to months. [23, 24] Consistent with these reports, our patient showed complete resolution of nyctalopia and near-normalization of visual fields, followed by striking recovery of ffERG responses at three months. In contrast, OCT findings remained unchanged. This marked functional recovery in the absence of structural improvement emphasizes the value of electrophysiology for documenting treatment response and supports the causal relationship between VAD and the retinal dysfunction.

The magnitude of recovery provided additional differential diagnostic information, as progressive inherited retinal degenerations would not show such restoration of retinal function after vitamin A supplementation. Electrophysiology was informative both in redirecting the etiological investigation and in documenting reversibility after treatment.

Importantly, therapeutic response was sustained over 10 years of continued vitamin A supplementation and serum monitoring. The patient remains asymptomatic, with BCVA of 1.0 in OU and normal visual fields. Although long-term electrophysiological normalization cannot be inferred without serial ffERG recordings throughout follow-up, sustained clinical recovery supports durability of functional benefit when deficiency is adequately corrected.

Conclusion

This case highlights the pivotal role of electrophysiology in evaluating acquired nyctalopia when structural findings are limited or nonspecific. The severe rod-predominant ffERG abnormality redirected the diagnostic work-up toward an acquired, reversible retinal disorder, leading to identification of profound VAD and previously unrecognized alcohol-related cirrhosis.

Marked restoration of electrophysiological function after vitamin A replacement, together with resolution of nyctalopia and visual field abnormalities, provided objective evidence of reversibility and supported the causal diagnosis. Thus, appropriate recognition of the electrophysiological phenotype helps distinguish treatable retinal dysfunction from progressive retinal disease, revealing clinically significant systemic disease beyond the eye.

Declarations

Data Availability Statement

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request. Data are located in controlled access data storage at Manises Hospital.

Author Contribution Statement

[AJC]: Conceptualization, Data Curation, Investigation, Writing – Original Draft.

[ESM]: Investigation, Conceptualization, Supervision, Formal Analysis, Writing – Review & Editing.

[EGG]: Investigation, Conceptualization, Supervision, Validation, Writing – Review & Editing.

[MMM]: Supervision, Validation, Data Curation

[ARB]: Supervision, Validation, Data Curation

[DSA]: Supervision, Validation, Conceptualization, Data Curation

All authors have read and agreed to the published version of the manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

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References

1. Breazzano M, Oh JK, Batson SA, Kucherich JA, Karani R, Rohrmann CM, Sparrow J, Fragiotta S, Tsang SH (2022) Vitamin A deficiency and the retinal double carrot sign with optical coherence tomography. Eye 37:1489–1495. https://doi.org/10.1038/s41433-022-02137-9
2. Pereira A, Wright T, Weisbrod DJ, Ballios B (2024) Vitamin A deficiency retinopathy in the setting of celiac disease and liver fibrosis. Doc Ophthalmol 149:125–131. https://doi.org/10.1007/s10633-

024-09978-7

3. León-Ruiz M, Benito-León J, Castañeda-Cabrero C (2025) Nyctalopia Due to Vitamin A Deficiency Secondary to Short Bowel Syndrome: When the Electroretinogram Is the Diagnostic Key. Brain Sci 15. https://doi.org/10.3390/brainsci15091019
4. McBain V, Egan C, Pieris S, Supramaniam G, Webster A, Bird A, Holder G (2007) Functional observations in vitamin A deficiency: diagnosis and time course of recovery. Eye 21:367–376. https://doi.org/10.1038/sj.eye.6702212
5. Pichi F, Aljneibi S, Neri P, Rishi P, Cicinelli M, Introini U, Sharma S, Munk M, Pasadhika S, González-López J, Lembo A, Nucci P, Choudhry N, Carreño E (2023) Multimodal Imaging Study of Patients With Vitamin A Deficiency Retinopathy. Ophthalmic surgery, lasers & imaging retina. 54(6):330–336. https://doi.org/10.3928/23258160-20230513-01
6. McCulloch DL, Marmor MF, Brigell MG, Hamilton R, Holder GE, Tzekov R, Bach M (2015) ISCEV Standard for full-field clinical electroretinography (2015 update). Documenta ophthalmologica. Adv Ophthalmol 130(1):1–12. https://doi.org/10.1007/s10633-014-9473-7
7. González E, Vilela C (2024) Electrorretinograma (ERG). Sociedad Española de Neurofisiología Clínica. Potenciales Evocados: Correlación clínica y neurofisiológica. Sociedad Española de Neurofisiología Clínica, Granada, pp 125–182
8. Arnett JJ, Li AL, Yassin SH, Miller R, Taylor L, Carter C, Shayan-Tabrizi K, Borooah S (2022) Dent disease presenting with nyctalopia and electroretinographic correlates of vitamin A deficiency. Am J Ophthalmol Case Rep 29. https://doi.org/10.1016/j.ajoc.2022.101781
9. Saeed A, Dullaart R, Schreuder T, Blokzijl H, Faber K (2017) Disturbed Vitamin A Metabolism in Non-Alcoholic Fatty Liver Disease (NAFLD). Nutrients 10. https://doi.org/10.3390/nu10010029
10. Koop A, Mousa O, Pham L-E, Corral-Hurtado JE, Pungpapong S, Keaveny A (2018) An Argument for Vitamin D, A, and Zinc Monitoring in Cirrhosis. Ann Hepatol 17(6):920–932. https://doi.org/10.5604/01.3001.0012.7192
11. Khan Z, Cox V, Creagmile J, Oboh-Weilke AM (2023) Nyctalopia and Xerophthalmia in a Patient With Crohn's Induced Vitamin A Deficiency. Cureus, p 15. https://doi.org/10.7759/cureus.42961
12. Chow C, Mieler W (2013) Vitamin A deficiency and xerophthalmic fundus in autoimmune hepatitis and cirrhosis. Retinal cases brief Rep 8(3):164–166. https://doi.org/10.1097/icb.0000000000000031
13. Berkenstock MK, Castoro CJ, Carey A (2020) Outer retina changes on optical coherence tomography in vitamin A deficiency. Int J Retina Vitreous. 6https://doi.org/10.1186/s40942-020-00224-1
14. Renner A, Dietrich-Ntoukas T, Jägle H (2015) Recurrent episodes of night blindness in a patient with short bowel syndrome. Doc Ophthalmol 131:221–230. https://doi.org/10.1007/s10633-015-9516-8
15. Oli A, Upadhyay S, Bhatia A, Rao BV (2024) Throwing light on night blindness associated with rare manifestation of vitamin A deficiency. Romanian J Ophthalmol 68:434–438. https://doi.org/10.22336/rjo.2024.78

16. Verbakel SK, Van Huet RV, Boon C, Hollander ADD, Collin R, Klaver C, Hoyng C, Roepman R, Klevering JB (2018) Non-syndromic retinitis pigmentosa. Prog Retin Eye Res 66:157–186. https://doi.org/10.1016/j.preteyeres.2018.03.005
17. Przeździecka-Dołyk J, Brzecka A, Ejma M, Misiuk-Hojło M, Solis T, Solís LF, Herrera A, Somasundaram SG, Kirkland CE, Aliev G (2020) Ocular Paraneoplastic Syndr Biomedicines 8. https://doi.org/10.3390/biomedicines8110490
18. Nguyen X, Moekotte L, Plomp A, Bergen A, Van Genderen MV, Boon C (2023) Retinitis Pigmentosa: Current Clinical Management and Emerging Therapies. Int J Mol Sci 24. https://doi.org/10.3390/ijms24087481
19. Hayashi T, Gekka T, Nakano T, Tsuneoka H (2011) Improvement in S-cone–mediated Visual Fields and Rod Function after Correction of Vitamin a Deficiency. Eur J Ophthalmol 21:657–660. https://doi.org/10.5301/ejo.2011.6337
20. Huang-Link Y, Mirabelli P, Lindehammar H, Link H (2021) Retinal changes associated with multivitamin deficiency before and after supplementation. Acta Neurol Scand 144. https://doi.org/10.1111/ane.13438
21. Poornachandra B, Jayadev C, Sharief S, Shetty R (2022) Serial ERG monitoring of response to therapy in vitamin A deficiency related night blindness. BMJ Case Rep 15. https://doi.org/10.1136/bcr-2021-247856
22. Yamada F, Kato K, Nagashima R, Yonekawa Y, Kashima Y, Kondo M (2024) Case of persistent corneal epithelial damage after cataract surgery leading to diagnosis of vitamin A deficiency. Doc Ophthalmol 1–8. https://doi.org/10.1007/s10633-023-09963-6
23. Hulzen RTD, Wagner IV, Decastro P-Y, Sullivan JP (2022) Visual field decline and restoration following vitamin A therapy for vitamin A deficiency. Am J Ophthalmol Case Rep 26. https://doi.org/10.1016/j.ajoc.2022.101471
24. Saenz-De-Viteri M, Sádaba L (2016) Optical Coherence Tomography Assessment Before and After Vitamin Supplementation in a Patient With Vitamin A Deficiency. Medicine 95. https://doi.org/10.1097/md.0000000000002680

Figures

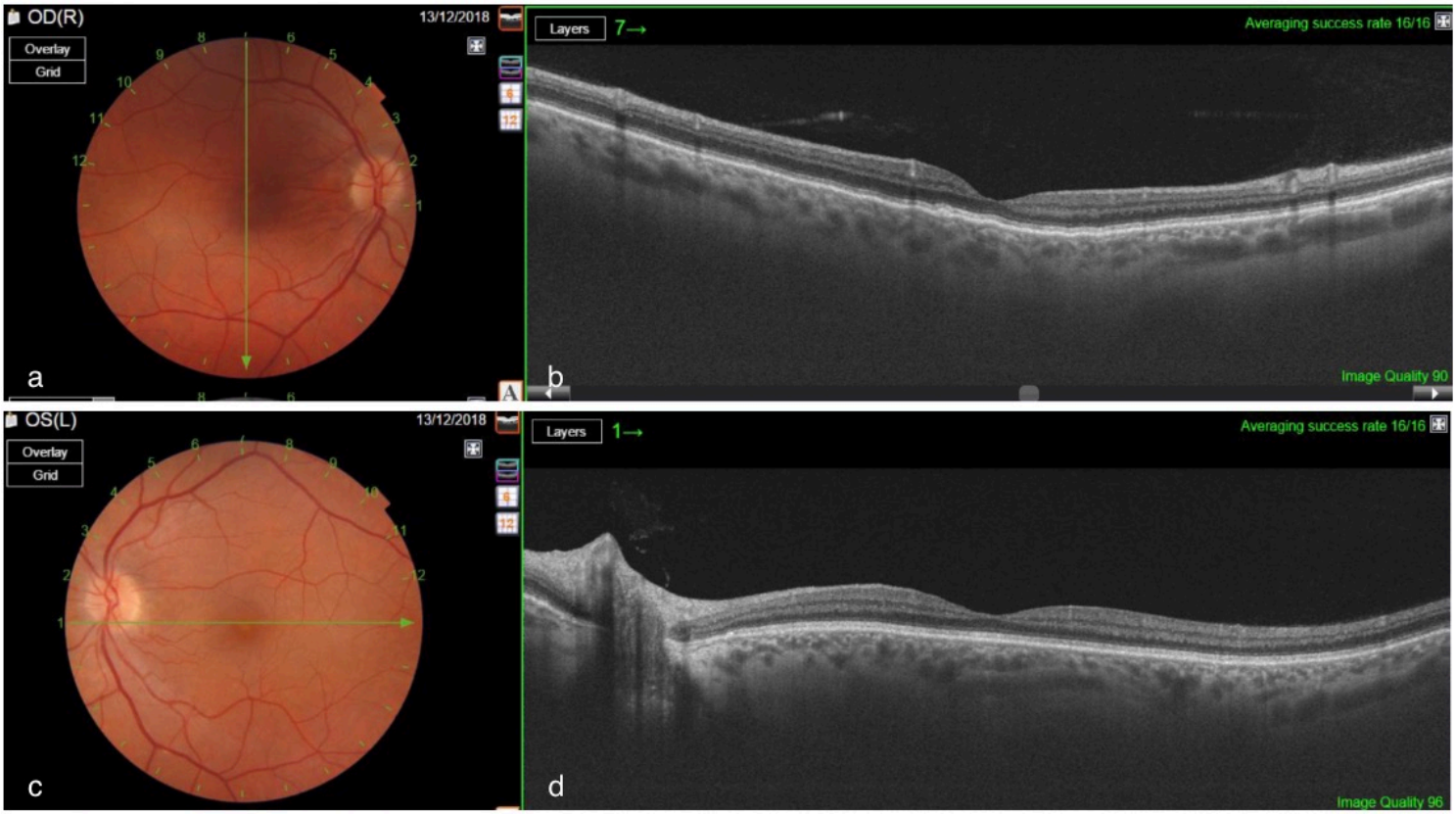


Figure 1

(a) Retinography of the right eye. (b) Macular OCT of the right eye showing retinal thinning, with a central macular thickness of 196 µm. (c) Retinography of the left eye. (d) Macular OCT of the left eye showing retinal thinning, with a central macular thickness of 204 µm

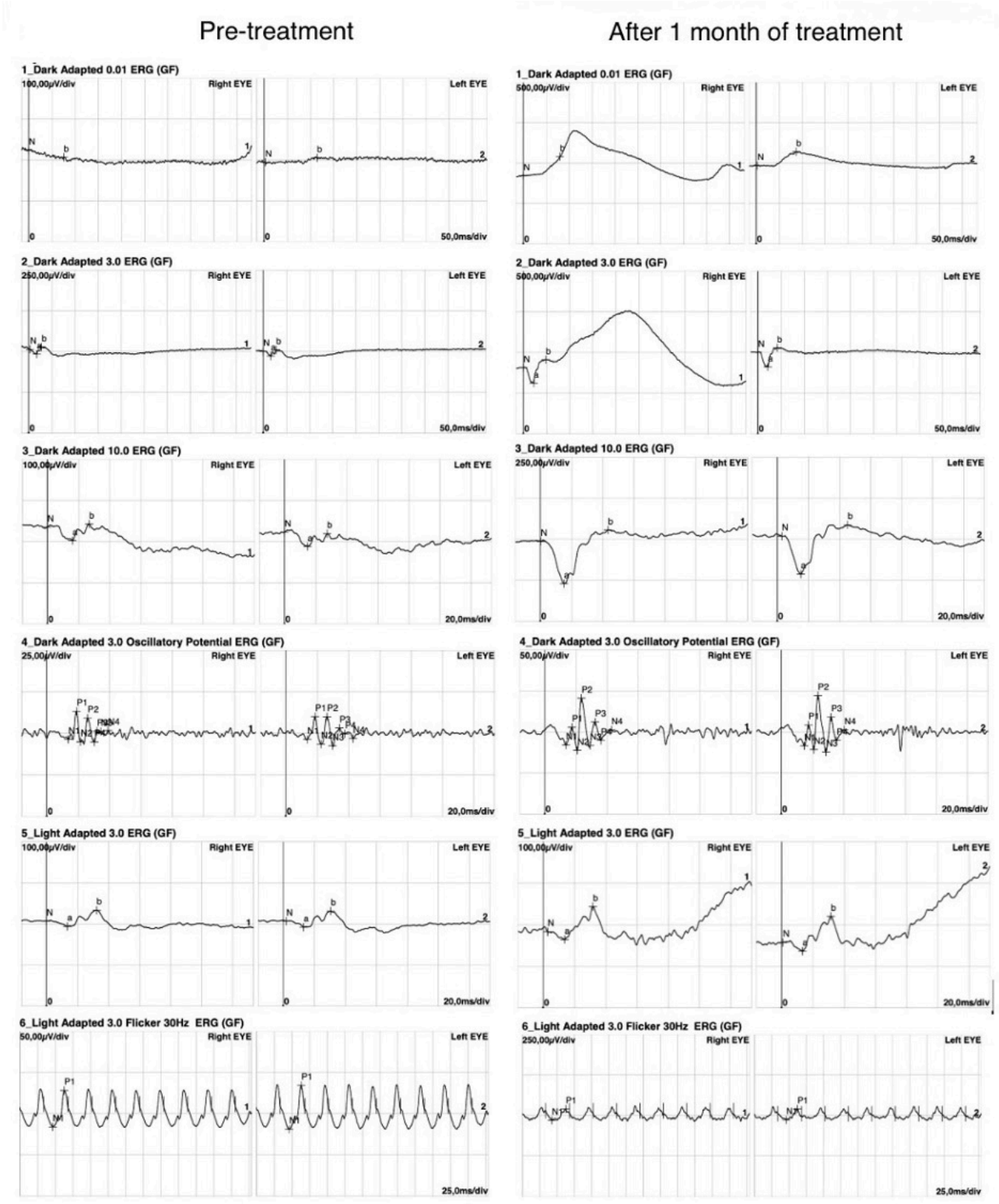


Figure 2

Full-field electroretinography before and after vitamin A replacement. Baseline testing (11 December 2018) demonstrated moderate-to-severe generalized retinal dysfunction, predominantly affecting scotopic responses. Follow-up testing (12 March 2019) demonstrated marked recovery, with only minor residual abnormalities; overall findings were within normal limits

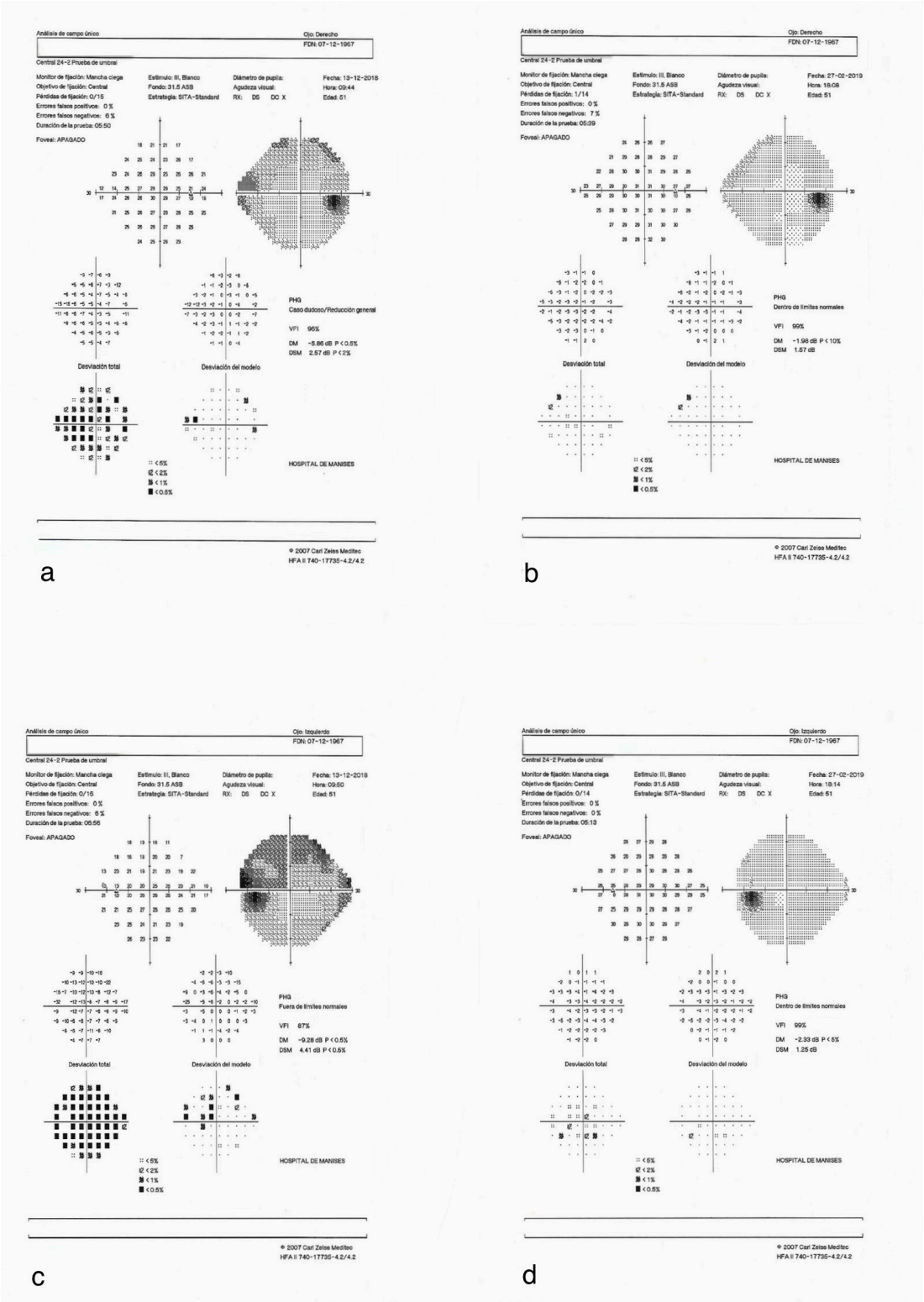


Figure 3

(a, c) Baseline automated perimetry showing diffuse depression in OD and a more pronounced diffuse, arcuate-like defect in OS. (b, d) Near-normalization of visual field parameters following vitamin A replacement