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Case report: Coexistence of optic neuritis and primary anti-PLA2R-positive membranous nephropathy

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Abstract

Background Optic neuritis (ON) is an inflammatory optic neuropathy characterized by acute vision loss. Primary anti-PLA2R-positive membranous nephropathy, an autoimmune disease, has been reported to be related to neurological diseases. However, the co-occurrence of ON and primary membranous nephropathy (PMN) has not been reported.

Case presentation A 57-year-old male presented with acute bilateral vision loss. Laboratory tests indicated proteinuria, hypoalbuminemia, hyperlipidemia, and a significantly increased level of anti-phospholipase A2 receptor antibody (PLA2RAb). Orbital MRI revealed inflammatory changes in the posterior segments of both optic nerves. Following treatments with corticosteroids and immunosuppressants, there was a significant improvement in the patient's vision and proteinuria.

Conclusion This case suggests that early identification and intervention for multisystem autoimmune damages are crucial for improving patient prognosis.

Keywords Optic neuritis, Membranous nephropathy, Anti-phospholipase A2 receptor antibody, Case report

Introduction

Optic neuritis (ON) is an inflammatory optic neuropathy with various possible causes. It can arise from idiopathic demyelinating conditions, as well as from inflammatory, infectious, or autoimmune disorders [1]. Membranous nephropathy is an autoimmune disease specific to the kidneys, which can sometimes undergo spontaneous remission [2, 3]. Primary membranous nephropathy (PMN) is a leading cause of nephrotic syndrome in adults [4], and approximately 70% of PMN patients exhibit antibodies against phospholipase A2 receptor (PLA2R), a glycoprotein from the mannose receptor family and is highly expressed in glomerular podocytes [5]. Patients with PMN with positive PLA2R antibodies (PLA2RAb) have been reported to present with clinical symptoms related to neurological diseases. However, to the best of our knowledge, the co-occurrence of PLA2RAb-positive PMN and ON has not been reported. In this report, we present a case of ON accompanied by PLA2RAb-positive PMN in a patient who experienced bilateral vision loss on neurological examination. Laboratory tests revealed proteinuria, hyperlipidemia, and an elevated level of PLA2RAb. This case underscores the significance of

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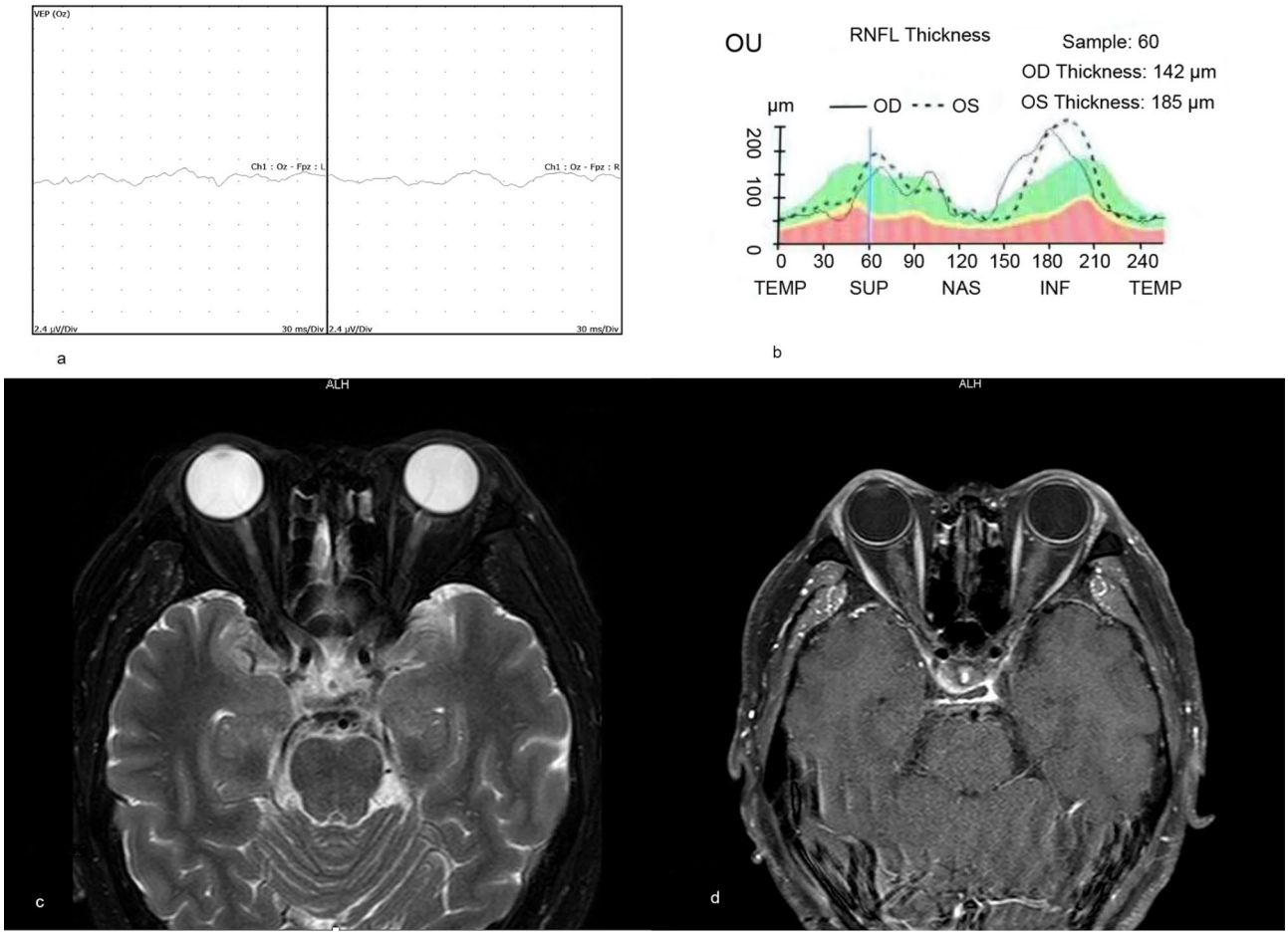

Fig. 1 (**a**). Visual evoked potential (VEP) shows unclear differentiation of VEP waves of both optic nerves in this patient. (**b**). The superior quadrants of the retinal nerve fiber layer (RNFL) of both eyes thickened slightly, and the inferior quadrants are thickened. (**c** and **d**). Axial (**c**) and Coronal (**d**) T1 weighted contrast and fat saturated MRI sections showed enhancement of the retrobulbar segment of the bilateral optic nerves in the patient

considering multisystem damage when autoimmune impairments are present.

Case description

In July 2023, a 57-year-old Chinese male patient presented to our neurology department with a sudden onset of bilateral visual loss that had lasted for 2 days. He denied having any previous ocular disease history or other neurological symptoms. Best-corrected visual acuity was counting fingers for both eyes. The intraocular pressure was measured to be 18 mmHg in the right eye and 19 mmHg in the left eye. The fundus examination revealed optic disc edema and a flat retina, with no hemorrhage or exudates in both eyes. The retinal nerve fiber layer (RNFL) thickness was measured by OCT (optical coherence tomography), and showed that the superior quadrants of both eyes are thickened slightly, and the inferior quadrants are thickened (Fig. 1A). Furthermore, the visual evoked potential (VEP) test showed an indistinct differentiation of VEP waves in both optic nerves (Fig. 1B).

His urine tests showed a high level of urine protein (3+) and a 24-hour urine total protein of 11.30 g. Blood tests showed a decreased level of albumin (22.3 g/L) and high-density lipoprotein (0.79 mmol/L), while an increased level of triglycerides (3.11 mmol/L), cholesterol (8.79 mmol/L), and low-density lipoprotein (6.62 mmol/L). Creatinine and estimated glomerular filtration rate (eGFR) were within normal limits (4.75 µmol/L and 99.58 mL/min/1.73m^2, respectively). Tests for rheumatoid factor and tests for immune antibodies related to Sjögren's syndrome (antigens A and B), antinuclear antibody, and anti-neutrophil cytoplasmic antibody, anti-double-stranded DNA, and anti-cyclic citrullinated peptide antibodies all yielded negative results. Given the presence of significant proteinuria, hypoalbuminemia, and hyperlipidemia, which indicates nephrotic syndrome, further screening revealed a significantly elevated level of

PLA2RAb (422.30 RU/ml) through immunofluorescence assay (IFA).

Cerebrospinal fluid (CSF) analysis showed normal pressure, normal cell counts and cytological assessment, and a protein concentration within the normal range. Tests for aquaporin-4 antibody (AQP4-Ab), myelin oligodendrocyte glycoprotein antibody (MOG-Ab), glial fibrillary acidic protein antibody (GFAP-Ab), myelin basic protein antibody (MBP-Ab), and oligoclonal bands in both serum and CSF yielded negative results. Brain and orbital MRI revealed enhancement of the retrobulbar segment of both optic nerves (Fig. 1C and D). Brain Magnetic Resonance Venography (MRV) showed narrowing of the left transverse sinus, and digital subtraction angiography confirmed that the narrowing was likely due to developmental delay and ruled out left transverse sinus thrombosis.

The patient underwent a treatment regimen consisting of 1 gram of intravenous methylprednisolone daily for three days, followed by a gradual taper of 60 mg of oral prednisone daily and 1.5 mg of tacrolimus twice per day. After nine days of treatment, the patient experienced a significant improvement in bilateral vision, with a visual acuity of 0.3 in the right eye and 0.5 in the left eye. Additionally, the 24-hour urine total protein level decreased from 11.30 g to 2.72 g, indicating effective control of the patient's urine protein. Subsequently, he was discharged on July 24, 2023. By August 16, 2023, one month after treatment, the patient had already resumed work with nearly normal visual acuity, and his biochemical data had shown improvement, and the disease remission remained when he followed up two months later.

Discussion and conclusion

The patient's clinical course was consistent with optic neuritis. Alternative diagnoses, such as infectious, infiltrative, and compressive optic neuropathies, were excluded based on laboratory tests, neuroimaging, and clinical history. This patient also presented with significant proteinuria, hypoalbuminemia, and hyperlipidemia, which supports the manifestations of membranous nephropathy [6]. The quantitated PLA2RAb in serum using an enzyme-linked immunosorbent assay has been applied as a noninvasive test to aid in the diagnosis of PMN and to monitor treatment in patients with PMN [7]. With the significantly elevated level of PLA2RAb and the exclusion of other underlying causes, the patient was finally diagnosed with PMN. Based on recent guidelines, this patient was classified as being at high risk of progressive kidney injury due to the high level of PLA2RAb, necessitating immunosuppressive therapy [8]. Therefore, in addition to corticosteroids, the patient was also treated with tacrolimus, an immunosuppressant that is recommended as the first-line treatment for membranous nephropathy according to the 2020 KDIGO guideline [9]. The patient has shown a positive response to the treatments, with improvements in both visual acuity and urine protein control at follow-up.

Although the exact mechanism of ON with PMN was unclear, an association between PMN and neurological disorders has long been recognized. The neurological disorders that have been reported to coincide with PMN include inflammatory demyelinating polyneuropathy, multiple sclerosis, myasthenia gravis and neurological-related tumors [10, 11]. However, the coexistence of PLA2RAb-positive PMN with ON has not been reported before. In this particular case, both ON and PMN were closely linked to immune system damage. Although we cannot definitively establish a causal relationship between ON and PMN, the presence of PLA2RAb-related membranous nephropathy does confirm alterations in the immune system, and the good response of patient's vision loss to immunosuppressant therapy also indicated that immune-mediated damage occurred to the optic nerves. Genetic predisposition, immunologic regulation, interactions of multiple targets with autoantibodies, and shared common antigens triggering cross-immune responses all have a possibility to contribute to pathological changes.

Our findings emphasized the importance of early recognition and treatment of ON and PMN for favorable clinical outcomes and prognosis. The presence of PLA2RAb may provide insights into the underlying mechanisms of autoimmune ON. Further studies and more cases are needed to explore the potential underlying mechanisms of PMN with ON and the intrinsic nature of immune-related diseases.

Abbreviations

ON	Optic neuritis
PMN	Primary membranous nephropathy
PLA2RAb	Phospholipase A2 receptor antibodies
RNFL	Retinal nerve fiber layer
VEP	Visual evoked potential
eGFR	Estimated glomerular filtration rate
IFA	Immunofluorescence assay
CSF	Cerebrospinal fluid
MRV	Magnetic Resonance Venography
AQP4-Ab	Aquaporin-4 antibody
MOG-Ab	Myelin oligodendrocyte glycoprotein antibody
GFAP-Ab	Glial fibrillary acidic protein antibody
MBP-Ab	Myelin basic protein antibody

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Author contributions

WX, ZYP: Conceptualization, Data curation, Writing – original draft. ZYL: Data curation, Writing – review & editing. LBY: Investigation, Writing – review & editing. YJ: Conceptualization, Supervision, Writing – review & editing.Wang Xi and Zeng Yuping contribute equally to this work.All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Ethical approval is not required for this case report in accordance with local guidelines.

Consent for publication
Not applicable.

Consent for publication
Written informed consent was obtained from the patient's next of kin for publication. A copy of the written consent is available for review by the Editor of this journal.

Patient's view
The patient himself reports that he is happy that we could find a solution for his disease. He has been returning to work normally already for 12 months. He has noticed that his visual acuity and biochemical data have improved noticeably since we initiated the treatments.

Competing interests
The authors declare no competing interests.

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