SOX1 autoantibody-associated optic neuritis: Coincidence or correlation?

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Anti-Sry-like high mobility group box (SOX) 1 antibodies are the antibodies associated with paraneoplastic neurological disorders with the background of small-cell lung carcinoma. The most common of these paraneoplastic disorders are Lambert–Eaton myasthenic syndrome, cerebellar degeneration, and limbic encephalitis. Here, we report a novel case of an elderly diabetic lady with optic neuritis who had an elevated erythrocyte sedimentation rate and SOX1 antibody positivity by line blot essay along with cerebellar hypometabolism in fluorodeoxyglucose positron emission tomography imaging. We also discuss the management and treatment response of the patient.

Key words: Optic neuritis, paraneoplastic, SOX-1 autoantibody

A 53-year-old diabetic woman developed subacute sequential vision loss, first in the right eye (RE), followed 5 days later by the left eye (LE). Vision loss was static at 6/60 in RE and 2/60 in LE after 4 days of progression. Acute optic neuritis (ON) was diagnosed after clinical examination showing relative afferent pupillary defect (RAPD) in the left eye [Fig. 1], mild left disc edema in fundus, supplemented by visual evoked potential (VEP) test showing prolonged bilateral P100 latencies and optical coherence tomography (OCT) showing retinal nerve fiber layer (RNFL) thickening [Supplementary Fig.]. Her neurological examination was normal except for the impaired tandem gait. She underwent routine blood and imaging investigations for optic neuritis including complete blood count (CBC), erythrocyte sedimentation rate (ESR), renal and liver function tests, glycated hemoglobin (HBA1c), thyroid profile, Lyme's serology, Angiotensin converting enzyme (ACE) level, anti-nuclear antibodies (ANA), and Anti-Neutrophil cytoplasmic antibody (ANCA). Her magnetic resonance imaging (MRI) brain with contrast showed normal bilateral optic nerve intensity with cerebellar atrophy disproportionate for age. Blood investigations suggested a markedly elevated erythrocyte sedimentation rate (ESR). That, paired with cerebrospinal fluid (CSF) analysis revealing elevated protein (76 mg/dL) and normal cells, negative ANA, ANCA, myelin oligodendrocyte glycoprotein (MOG) and aquaporin 4 (AQP 4) antibodies, normal ACE levels, and negative Lyme's serology, leads to the further investigation with whole-body fluorodeoxyglucose (FDG) positron emission tomography (PET) imaging and paraneoplastic antibody testing. Her PET study showed cerebellar hypometabolism [Fig. 2] but no evidence of primary or metastatic malignancy. Serum paraneoplastic antibody test revealed strong Anti-SOX1 antibody positivity (high band intensity in line blot assay) (presence of other paraneoplastic antibodies including Ampiphysin, CV2, MA2/TA, Ri, Yo, Hu, Recoverin, Titi, Zic 4, GAD 65, Tr, NMDA, AMPA, GABA -B, LGI 1, CASPR ruled out). She received intravenous methylprednisolone 1 gm/day for 5 days followed by 1 mg/kg oral steroids tapered over 6 months and overlapped with azathioprine 25 mg BD initially and then 50 mg BD as a secondary immunosuppressant. Partial vision improvement (LE 6/18, RE 6/6) was noted at 2 months, and complete recovery was achieved by 4 months. At 1-year follow-up, her tandem gait remained impaired and a repeat line blot assay for SOX1 antibody was persistently positive (high band intensity) with no new evidence of malignancy in FDG whole-body PET.

Anti-SOX1 antibodies have been previously linked to a few known paraneoplastic neurological syndromes, Lambert–Eaton myasthenic syndrome (LEMS) being the most common, followed by paraneoplastic cerebellar degeneration (PCD), paraneoplastic limbic encephalitis (PLE), and neuropathy [Table 1].[1,2] SOX1 antibodies are primarily associated with small-cell lung carcinoma (SCLC) (present in 36.5% cases) and serve as a serological marker of this malignancy.[3] These antibodies can be detected in 49% of patients with PCD because of underlying SCLC.[4] Paraneoplastic optic neuropathies (PONs) are rare conditions

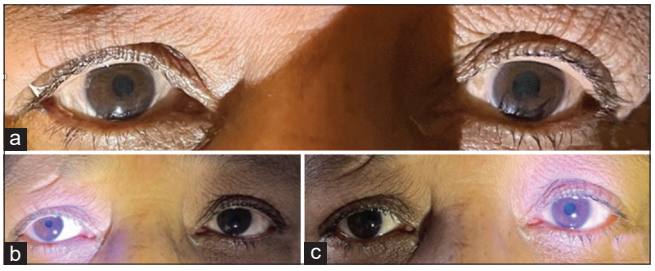

Figure 1: Swinging flashlight test (a) shows progressive constriction of right eye (b) and dilation of left eye (a, c) suggesting relative afferent pupillary defect

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Table 1: A summary of SOX1 antibody-associated paraneoplastic syndromes

Condition	Description	Comments	References
LEMS	Autoimmune disorder causing muscle weakness due to impaired neuromuscular transmission.	Most frequently associated with SOX1 antibodies.	[1]
PCD	Progressive cerebellar dysfunction, including ataxia and impaired coordination.	Found in 49% of patients with PCD and SCLC.	[2,4]
PLE	Inflammation of the limbic system presenting with memory deficits, seizures, and psychiatric symptoms.	Rare association with SOX1 antibodies.	[2]
Neuropathy	Peripheral nerve dysfunction presenting with sensory or motor deficits.	Associated in select paraneoplastic cases.	[2]

LEMS: Lambert–Eaton myasthenic syndrome, PCD: Paraneoplastic cerebellar degeneration, PLE: Paraneoplastic limbic encephalitis, SCLC: Small cell lung carcinoma, SOX1: Sry-like high mobility group box 1

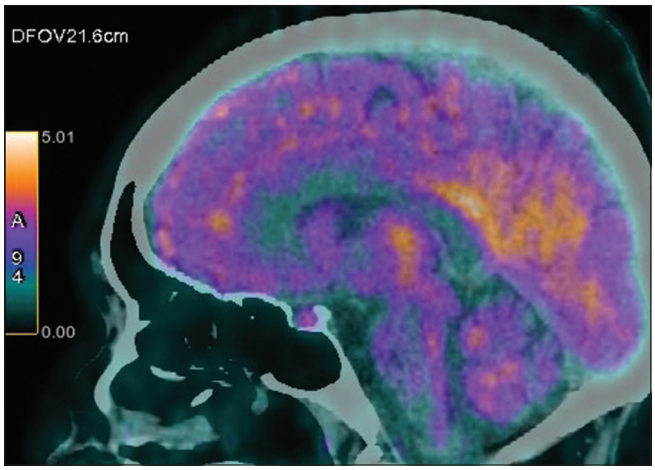

Figure 2: FDG PET showing cerebellar hypometabolism

most frequently associated with SCLC and less commonly with lymphoma and bronchial carcinoma. PON typically presents as painless subacute, progressive, bilateral visual loss, with the optic disk either normal or edematous.[5] It is often linked to cerebellar and brainstem syndromes in paraneoplastic contexts. This combination of PCD with PON has been most commonly observed with SCLC.[5,6]

Though this is the first reported instance of SOX1 antibody detected in a patient of optic neuropathy as per our literature review, other antibodies such as anti-CV2, also known as anti-collapsin responsive mediator protein-5 (CRMP-5) antibodies, are found to be associated with PON with or without PCD.[7,8] The method of antibody testing in our patient remained commercially available line blot assay. Secondary confirmation with cell-based assay (CBA) could not be done due to its scarce commercial availability. A drawback of SOX1 positivity in line blot assay is the high rate of false positivity. However, Arnaldos-Pérez *et al*.[9] in their study of 34 patients have shown that despite the high false positivity of line blot assay for SOX1 antibody, the band intensity data are helpful in predicting the replication of results in CBA. For our patient, we performed the antibody testing twice, 1 year apart, and the band intensity was detected high both the times. Apart from that, all the common causes of optic neuritis including neuromyelitis optica (NMO) and myelin oligodendrocyte glycoprotein-associated disease (MOGAD), Lyme's disease, and sarcoidosis were ruled out; there was no history suggestive of exposure to oculotoxic drugs; and her clinical onset, progression, and treatment response were not indicative of anterior ischemic optic neuropathy (AION). The presence of subtle cerebellar signs, cerebellar atrophy on MRI brain, and cerebellar hypometabolism in FDG PET clinically and radiologically correlated with cerebellar degeneration and are likely SOX1 antibody-associated. Cerebellar findings were crucial in directing the diagnosis as routine optic neuritis is scarcely subjected to paraneoplastic workup. Elevated ESR provided an additional diagnostic clue. Despite significant nadir vision loss, timely initiation of treatment yielded favorable outcome. Treating the underlying malignancy generally improves optic neuropathy in such cases.[1] In our case, azathioprine was added to the oral steroids as the primary malignancy was not detected in paraneoplastic evaluation. Follow-up whole body PET at 6 and 12 months also did not show any evidence of malignancy. Ongoing follow-up has been planned for any new symptoms or radiological findings, mainly focusing on detecting SCLC.

To conclude, with the background of mild clinical cerebellar deficits and raised ESR, a SOX1 positivity was detected in a patient of optic neuropathy which responded well to the immunosuppression. The case opens the discussion on necessity of paraneoplastic workup in optic neuropathy after ruling out the common etiologies. Subtle accompanied neurological and other systemic features should be paid attention to. High inflammatory markers in the absence of underlying rheumatological and infective conditions should be diligently evaluated, and constitutional symptoms should be inquired for.

Author contribution

Dr. Monalisa Vegda: Conceptualisation, data collection, manuscript writing- original draft and editing. Dr. Ekta Singh Dahiya: Manuscript writing and editing, Formal analysis. Dr. Abhishek Dixit: Formal analysis, data collection and curation. Dr. Nishant Tomar: Data collection. Dr. Man Mohan Mehndiratta: Visualisation, manuscript editing, supervision

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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References

1. Titulaer MJ, Klooster R, Potman M, Sabater L, Graus F, Hegeman IM, *et al*. SOX antibodies in small-cell lung cancer and Lambert-Eaton myasthenic syndrome: Frequency and relation with survival. J Clin Oncol 2009;27:4260-7.
2. Ruiz-García R, Martínez-Hernández E, García-Ormaechea M, Español-Rego M, Sabater L, Querol L, *et al*. Caveats and pitfalls of SOX1 autoantibody testing with a commercial line blot assay in paraneoplastic neurological investigations. Front Immunol 2019;10:769.
3. Hardy-Werbin M, Arpí O, Taus A, Rocha P, Joseph-Pietras D, Nolan L, *et al*. Assessment of neuronal autoantibodies in patients with small cell lung cancer treated with chemotherapy with or without ipilimumab. Oncoimmunology 2017;7:e1395125.
4. Sabater L, Höftberger R, Boronat A, Saiz A, Dalmau J, Graus F. Antibody repertoire in paraneoplastic cerebellar degeneration and small cell lung cancer. PLoS One 2013;8:e60438.
5. Chan JW. Paraneoplastic retinopathies and optic neuropathies. Surv Ophthalmol 2003;48:12-38.
6. Sun X, Tan J, Sun H, Liu Y, Guan W, Jia J, *et al*. Anti-SOX1 antibodies in paraneoplastic neurological syndrome. J Clin Neurol 2020;16:530-46.
7. de la Sayette V, Bertran F, Honnorat J, Schaeffer S, Iglesias S, Defer G. Paraneoplastic cerebellar syndrome and optic neuritis with anti-CV2 antibodies: Clinical response to excision of the primary tumor. Arch Neurol 1998;55:405-8.
8. Cross SA, Salomao DR, Parisi JE, Kryzer TJ, Bradley EA, Mines JA, *et al*. Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. Ann Neurol 2003;54:38-50.
9. Arnaldos-Pérez C, Vilaseca A, Naranjo L, Sabater L, Dalmau J, Ruiz-García R, *et al*. Algorithm to improve the diagnosis of paraneoplastic neurological syndromes associated with SOX1 antibodies. Front Immunol 2023;14:1173484.

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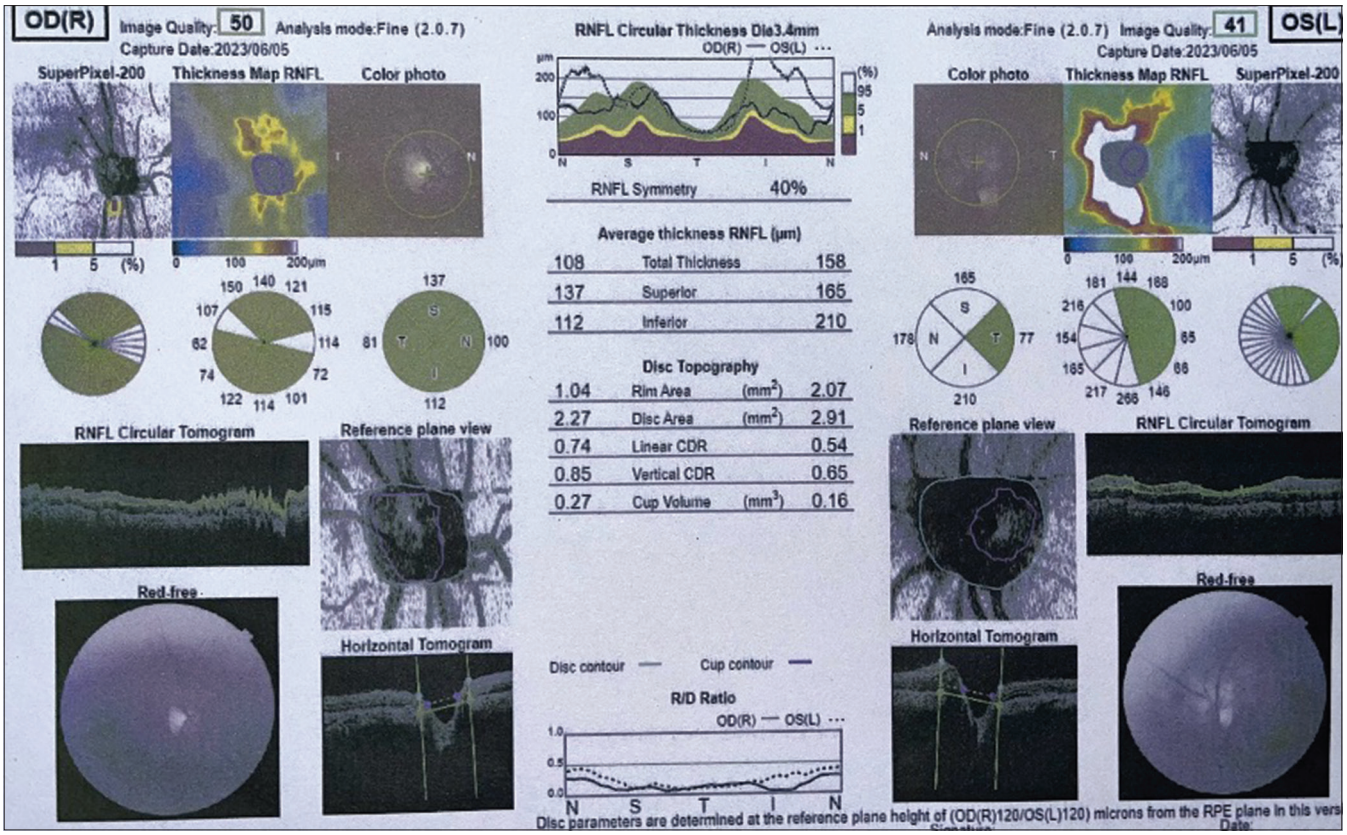

Supplementary Figure 1: Optical coherence tomography (OCT) showing increased retinal nerve fiber layer thickness in superior, nasal and inferior quadrant in the left eye