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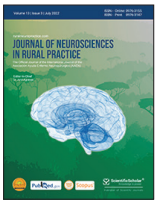
Journal of Neurosciences in Rural Practice

Article in Press



Case Report

Anti-SOX1 antibody-associated paraneoplastic cerebellar degeneration without detectable tumor

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ABSTRACT

A 56-year-old male presented with complaints of insidious onset difficulty in speech and head tremors for 2 years and imbalance while walking for 1 year. He did not have autonomic dysfunction and had a negative family history. The cerebrospinal fluid examination was normal and the workup for autoimmune disorders was negative. Brain magnetic resonance imaging showed mild superior cerebellar atrophy. The serum paraneoplastic antibody panel showed anti-Sry-like high mobility group box (SOX1) antibodies positivity. He was treated with steroids and steroid-sparing immunosuppressants resulting in mild improvement. Extensive workup for underlying malignancy was negative. Our case illustrates a small subset of individuals with anti-SOX1 antibody positivity who also exhibit neurological symptoms indicative of paraneoplastic cerebellar degeneration without having any underlying tumor and responded to immunotherapy.

Keywords: Anti-SOX1 antibody, Difficulty in speech, Head tremors

INTRODUCTION

Anti-Sry-like high mobility group box (SOX1) antibodies are partly characterized as onconeural antibodies due to their association with neoplastic diseases. Lambert-Eaton myasthenic syndrome and paraneoplastic cerebellar degeneration are commonly associated with these antibodies. Small cell lung cancer is the most common underlying tumor associated with these antibodies. Our case illustrates a small subset of individuals with anti-SOX1 antibody positivity, who also have neurological symptoms consistent with paraneoplastic cerebellar degeneration in the absence of an underlying tumor and who respond to immunotherapy.

CASE REPORT

A 56-year-old male presented with complaints of insidious onset difficulty in speech and head tremors for the past 2 years. He was giving undue stress on each syllable and was having scanning speech. There was no history of neologisms, paraphasia, agrammatism, nasal twang to his voice, or difficulty in swallowing. 2 years back, he also noticed tremors involving his head manifesting as side-by-side movements of his head. It was occurring throughout the day and used to stop during sleep. For the past 1 year, he felt swaying toward either side while he was negotiating through narrow passages. There was no history of postural syncope, urinary urgency, or incontinence. There was no history of such illness in his family members. On examination, he was having staccato speech, head tremors, mild impairment of finger-nose-finger test as well as impairment in tandem walking. Motor and sensory systems were normal. A clinical diagnosis of gradually progressive cerebellar ataxia was considered. Routine blood investigations were normal including vitamin B12, folate, and thyroid function test. Spinocerebellar ataxia panel was negative. Antinuclear antibodies, extractable nuclear antigens, antineutrophil cytoplasmic antibodies, anti-glutamic acid decarboxylase antibodies, and anti-transglutaminase antibodies were negative. Cerebrospinal fluid (CSF) examination showed normal pressure 8 cm of H_2O with 0 cells, protein 50 mg/dL, and CSF glucose 80 mg/dL. Brain magnetic resonance imaging showed mild superior cerebellar atrophy [Figure 1]. Autonomic function tests were normal. The serum paraneoplastic antibody panel showed anti-SOX1 antibodies positivity. Positron emission tomography scan did not show any evidence of malignancy. Hence, a diagnosis of paraneoplastic cerebellar degeneration (PCD) associated with anti-SOX1 antibody was made. The patient was given intravenous methylprednisolone 1 g pulse for 5 days followed by oral steroids and was started on azathioprine 50 mg twice daily for long-term immunosuppression. At the time of the

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Received: 21 January 2025 **Accepted:** 01 April 2025 **Epub ahead of print:** 02 May 2025 **Published:** XXXXXXX **DOI:** 10.25259/JNRP_18_2025

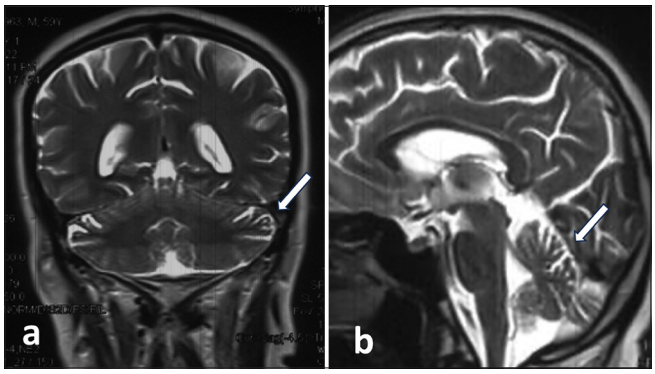

Figure 1: Brain magnetic resonance imaging (a) T2 coronal section (b) T2 sagittal section showing superior cerebellar atrophy.

last follow-up of 3 months, there was mild improvement in gait and head tremors.

DISCUSSION

Paraneoplastic neurological syndromes (PNS) are rare syndromes due to immune-mediated cross-reactivity between the tumor and nervous system due to various antibodies. Fewer than 1% of cancer patients develop PNS, but diagnosis of PNS will allow early detection of occult malignancy.[1] Classic PNS includes paraneoplastic limbic encephalitis, encephalomyelitis, PCD, Lambert-Eaton myasthenic syndromes, and sensory neuronopathy. PCD is the second most frequent paraneoplastic presentation as well as the second most common immune-mediated cerebellar ataxia.[2] Well-characterized antibodies associated with PCD are CRMP5, Hu, Ma2, Ri, Yo, and Tr. PNS associated with anti-SOX1 antibodies can involve the limbic system, cerebellum, neuromuscular junction, and peripheral nervous system.[1] PNS affecting the peripheral nervous system (Lambert-Eaten syndrome and paraneoplastic neuropathy) as well as the central nervous system PCD are linked to anti-SOX1 antibodies.[3] Anti-SOX1 antibodies are cancer-related onconeural antibodies and are often associated with underlying malignancy, the most common of which is small-cell lung cancer.[4] Its pathogenic role is unknown; however, it appears to be related to the immunological process.[4] Very few isolated cases of PCD linked with Anti-SOX1 antibodies have been documented in the literature.[5] Some patients such as the one in our case may acquire neurological symptoms despite the absence of an obvious underlying cancer. In some cases, even after several years of follow-up (up to 15 years), patients will have isolated neurological symptoms associated with anti-SOX1 antibodies without the presence of a tumor.[4] However, mandatory screening for cancer should be done and the patient should be followed up closely.

Although the specific pathogenic mechanism for PNS is unclear, anti-SOX1 antibodies are malignant neoplasm-related onconeural antibodies due to their relationship with tumors. The presence of SOX1 antibodies has been observed in both small-cell lung cancer and cerebellum. The presence of SOX1 antibodies is indicative of an immune response targeting these shared antigens, which has resulted in neuronal damage. Cytotoxic T cells also play a role in immune response. As SOX1 is involved in neuronal development and differentiation, autoimmunity against SOX1 could disrupt these processes leading to cerebellar dysfunction.[6]

We are describing a case of anti-SOX1 antibody-positive PCD who had no underlying cancer and responded to immunotherapy. Early immunotherapy administration before Purkinje cell necrosis and cerebellar atrophy may be related to improved patient outcomes. Our patient presented with a 2-year history; it may have been mistakenly labeled as a neurodegenerative disease which would prevent patients from receiving treatment.

CONCLUSION

Clinicians should be aware of the varied presentations of anti-SOX1 antibodies and proper screening for underlying malignancy should be done. The use of early immune therapy may result in better outcomes.

Ethical approval: Institutional Review Board approval is not required.
Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.
Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.
Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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How to cite this article: Mustafa F, Singh RK, Das A, Vibha D, Tripathi M. Anti-SOX1 antibody-associated paraneoplastic cerebellar degeneration without detectable tumor. J Neurosci Rural Pract. doi: 10.25259/JNRP_18_2025