Case Report

Steroid-responsive dual neuronal antibody-positive paraneoplastic encephalitis

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ABSTRACT

Here, we report the case of an elderly African male with multifocal neuraxial involvement in the form of progressive parkinsonism and ataxia over a year. On evaluation, dual neuronal antibody positivity was detected. A diagnosis of paraneoplastic encephalitis was made without any detection of primary neoplasm. He was successfully managed with pulse steroid therapy followed by oral steroid and steroid-sparing oral immunosuppressive drug without any need for intravenous immunoglobulin or plasma exchange.

Key words: Anti-Yo and Anti-Zic-4, Paraneoplastic encephalitis

Paraneoplastic neurologic syndromes (PNS) are a diverse group of neurologic disorders associated with a systemic neoplasm outside the central nervous system. Neurologic dysfunction in PNS is the result of a probable immune mechanism, as suggested by the association with onconeural antibodies. Treatment options include early identification and definitive management of the tumor along with immunotherapy. However, in the absence of a tumor, immunotherapy forms the cornerstone of management.

CASE REPORT

A 64-year-old African male presented with complaints of gradually progressive difficulty in walking with a slow and short stepping gait, postural dizziness on standing, and monotonous speech abnormality for a year. The patient was dependent for all his activities of daily living and was unable to stand without support for the past 2 months.

On examination, supine blood pressure (BP) and pulse recorded were 140/70 mmHg and 74/min, respectively, whereas, standing BP and pulse were 100/60 mmHg and 88/min respectively with a scanning speech. Motor examination revealed reduced knee jerk, absent ankle jerk, with intact power. Impaired finger-nose-finger test with mild postural and intention tremors were detected. Gait was broad-based with slow and short steps with positive Romberg's sign.

The hemogram and routine biochemical tests were normal. Magnetic resonance imaging (MRI) brain revealed predominant cerebellar atrophy with chronic white matter ischemic changes. MRI spine revealed degenerative spine changes without any cord involvement. The nerve conduction study was suggestive of sensory demyelinating polyneuropathy. Cerebrospinal fluid analysis reported glucose 64 mg/dl, protein 63 g/dl, seven cells (lymphocytes predominant), and no malignant cells. Tuberculosis polymerase chain reaction routine staining and culture were normal.

The erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, antineutrophilic cytoplasmic antibody, and serum Angiotensin-converting enzyme levels were normal. The whole body fluorodeoxyglucose (FDG)-positron emission tomography FDG scan (Fig. 1) for occult malignancy was negative but revealed hypermetabolism in the cerebellum. Neuronal (paraneoplastic) antibody profile was reported positive for Anti-Yo and Anti-Zic4.

A provisional diagnosis of paraneoplastic encephalitis with multifocal involvement (cerebellar, extrapyramidal, and large fiber sensory nerve) was made.

He was started on pulse steroid therapy. By the 5th day, he started to show signs of improvement as he was able to stand for 5 min for his basic needs, like going to the washroom for self-care. He was discharged on oral steroids, steroid-sparing agents (mycophenolate mofetil), Vitamin D supplements, and compression stockings.

DISCUSSION

Paraneoplastic encephalitis has an incidence of 0.86/100,000 and a prevalence of 4.37/100,000 cases [1]. Paraneoplastic encephalitis comprises several neurologic syndromes including

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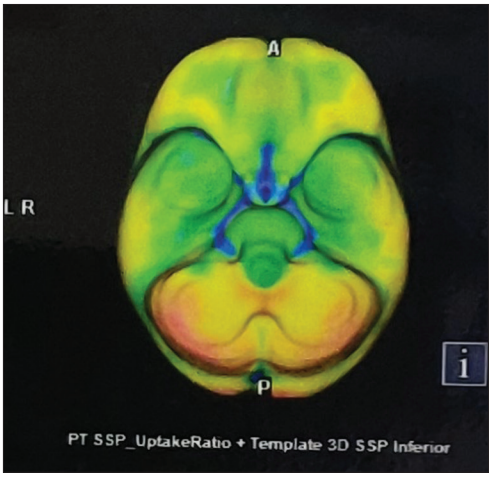

Figure 1: Fluorodeoxyglucose positron emission tomography Brain showing inferior axial view with relative cerebellar hypermetabolism

paraneoplastic cerebellar degeneration (PCD), limbic encephalitis, paraneoplastic encephalomyelitis (PEM), brain stem encephalitis and opsomyoclonus syndrome. These are associated with onconeural antibodies such as Hu, Yo, and Ri which classically attack intracellular neural components. Each onconeural antibody is associated with different tumor types.

Approximately, 50% of these PNS cases are noted in the middle age group with 67% of patients subsequently found to have malignancy within a few years. Suggesting that PNS may be a presenting feature of an occult tumor. Rarely, do these tumors emerge only months or years after the neurologic syndrome, necessitating the need for continuous follow-up of patients with repeated screening to detect the malignancy at the earliest [2]. Of these PNS, PCD is the most common. Because PCD can present much before the cancer is discovered, the nature of antibodies guides the quest for the primary cancer [3].

Anti-Yo antibodies are usually associated with malignancy in more than 90% of cases commonly including uterine, ovarian, and breast cancers. A few recent case reports have reported its association with adenocarcinoma (stomach, esophageal, parotid, lung) in males. Anti Yo is also associated with paraneoplastic sensory peripheral neuropathy, opsoclonus myoclonus syndrome, and PEM [4]. In our case, the presence of cerebellar findings and sensory involvement favored Anti-Yo-associated PNS. Hence far, Anti-zic4 antibodies have been found in PNS patients with small cell and non-small cell lung cancer, ovarian, and endometrial cancer. The clinical spectrum described with anti-zic-4 has been in the form of PCD and rhombencephalitis leading to dysautonomia [5].

With the varying prognosis, treatment of antibody-mediated paraneoplastic syndrome remains uncertain without any standard protocol. Treatment of PNS usually involves tumor removal, anti-tumor therapy, intravenous immunoglobulin (IVIG), and plasmapheresis. As neuronal damage is cell-mediated, it is hard to treat classic PE. On the other hand, T cell-directed therapies have been shown to have a modest effect in some cases such as cyclophosphamide, steroids, mycophenolate mofetil, and tacrolimus. However in our patient, initial therapy with high-dose steroid therapy showed drastic symptomatic improvement without necessitating the need for plasmapheresis or IVIG.

In a case series of 55 patients with Anti Yo positivity, 22 patients treated with plasma exchange sustained mild-moderate improvement only. The same study reported that only two out of 17 patients showed mild-to-moderate improvement when treated with high-dose corticosteroids [4]. Another case series of 16 patients suggested no improvement with either steroid therapy or plasmapheresis [6].

Our case is unique for the occurrence of multifocal neurological involvement and the presence of dual antineuronal antibodies corroborating with the neurological condition. Extrapyramidal involvement in the form of parkinsonism has not been described either with anti-Yo or anti-Zic-4. Dual neuronal antibody positivity has been reported previously and such an exquisite response to pulse methylprednisolone has not been documented in such cases [7]. Detection of paraneoplastic antibodies should not rob the patient for a cost-effective treatment and a pulse methylprednisolone trial should always be considered before IVIG and plasma exchange.

CONCLUSION

Rapid onset progressive parkinsonism with multi-neuraxial involvement should alarm for a possible immune-mediated etiology. Antibody detection helps to prove the diagnosis but with newer antibody tests being commercially available, chances of multiple antibody positivity may be a common future occurrence. Treating the patient depending on the disability and clinical response may be a better way to decide the therapy rather than treating it as per antibody positivity results.

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