Movement Disorders
CLINICAL PRACTICE

CASE REPORT

Oro-Bucco-Lingual Dyskinesia, Weight Loss, and Cognitive Decline in Anti-DPPX Antibody-Mediated Encephalitis

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Anti-dipeptidyl-peptidase-like protein 6 (DPPX) encephalitis is a rare autoimmune disorder caused by antibodies against DPPX, a neuronal cell surface protein. DPPX is a regulatory subunit of Kv4.2 potassium channels and widely expressed in the cerebellum, hippocampus, striatum, and myenteric plexus.[1–3] Loss of DPPX modulation of potassium currents leads to neuronal hyperexcitability by increased dendritic back propagation of action potentials.[2,4] The spectrum of clinical manifestations in this disorder is thus representative of multifocal neuronal activation in the gastrointestinal tract and throughout the central nervous system. Consistent with the pattern of DPPX expression, neurological symptoms may include seizures, myoclonus, tremor, rigidity, hyperekplexia, and ataxia and generally involve some degree of cognitive decline and behavioral disturbance.[2,5–7] Here, we describe a gentleman with prominent oro-bucco-lingual dyskinesia, a symptom rarely reported in anti-DPPX encephalitis, in addition to the common neuropsychiatric and gastrointestinal features.

Case Report

We evaluated a 77-year-old retired electronic technician with a past medical history of subclinical coronary atherosclerosis, hypertension, and pulmonary artery stenosis for progressive cognitive decline, involuntary oro-bucco-lingual movements, and gait instability. These symptoms began 18 months prior with an abnormal "skin crawling" sensation in the arms without rash, which resolved spontaneously. During the subsequent months, his wife noted cognitive decline and erratic behavior, with increasing irritability and irrational accusations toward her. His gait, fine motor skills, and speech became notably slower, and he exhibited involuntary movements of the mouth and tongue. His examination showed mild bradykinesia throughout, with bilateral intention tremor. He had persistent oro-bucco-lingual dyskinesia, but no myoclonus or hyperekplexia. Extraocular movements appeared full in all planes, although testing was complicated by an inability to consistently follow commands. Casual gait was wide-based with decreased stride length, although he could ambulate independently. Postural reflexes were diminished. Additional symptoms included a 60-pound unintentional weight loss (without diarrhea), anorexia, sialorrhea, anhedonia, insomnia with daytime hypersomnolence, and postural lightheadedness. Fewer than 2 years after symptom onset, he had declined to the point that he could barely communicate, ambulate, or perform most activities of daily living without assistance.

A thorough evaluation included magnetic resonance imaging of the brain, dopamine transporter scan, and basic laboratory analysis, which all returned normal. Cerebrospinal fluid (CSF) analysis showed normal cell count, protein, and glucose. An autoimmune encephalitis panel was initially sent from the serum and subsequently from the CSF; serum studies did not reveal any abnormalities, whereas anti-DPPX antibodies were positive in the CSF on reflex cell-based assay (Mayo Clinic Laboratories, Rochester, MN, USA). There were 5 unique oligoclonal bands in the CSF, with the immunoglobulin G index at the upper level of normal (0.84).

He was admitted to the hospital and treated acutely with 5 days of intravenous methylprednisolone and plasma exchange. An induction dose of rituximab was initiated shortly after at 1000 mg on days 0 and 15, followed by maintenance therapy of 1000 mg every 6 months thereafter. Computed tomography scan of the chest, abdomen, and pelvis did not reveal malignancy, nor did whole-body positron emission tomography–computed tomography. He was found to have a monoclonal B cell lymphocytosis on peripheral cytology and flow, prompting a hematology consultation; subsequent testing demonstrated normalized cytology and flow.

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During the next 10 months, clinical examination showed gradual improvement with increased verbal output, reduced facial dyskinesia, and successful participation in activities of daily living. Montreal Cognitive Assessment showed objective improvement: he was unable to complete the test prior to immunotherapy, but scored 8/30 at 2 months, 16/30 at 6 months, and 18/30 at 9 months after initiation of rituximab.

Discussion

Anti-DPPX encephalitis remains a rare autoimmune condition, although it is growing in recognition in part as a result of its unique symptomatology. Fewer than 50 cases have been reported in the literature, consistently featuring subacute cognitive decline (80%–100%), diarrhea (30%–80%), weight loss (60%–100%), and neurological dysfunction (nearly 100%).[2,3,5–7] Myoclonus, tremor, rigidity, and hyperekplexia are among the most common hyperkinetic movement disorders described. This antibody has also been found in association with progressive encephalomyelitis with rigidity and myoclonus.[6,7] Our case features the rare finding of oro-bucco-lingual dyskinesia, which is seen in the accompanying Video S1, likely the result of central nervous system hyperexcitability. Another unique aspect includes the prodrome of diffuse pruritus, which has been reported in few patients.[6,8]

Immunotherapy remains the most effective treatment for anti-DPPX encephalitis. In a review of reported cases of anti-DPPX encephalitis, treatment with immunotherapy led to "moderate" or "substantial" improvement in 60% of patients.[5] It is important to note that although 23% reportedly had no improvement, most of those patients had not been treated with any immunotherapy. Fortunately, this gentleman has experienced marked clinical improvement after a 10-month follow-up period on maintenance rituximab. He will have ongoing assessments to evaluate the need for continued therapy, with the goal to taper off in the next 2 years if clinically stable. It is important to recognize that the relapse rate for DPPX antibody-mediated autoimmune encephalitis is reported at 23%,[5] and some patients do require chronic maintenance immunotherapy.

Patients with confirmed anti-DPPX encephalitis should be screened for malignancy given the known association with B cell neoplasms.[7] This patient had evidence of a monoclonal B cell lymphocytosis, but a thorough follow-up did not reveal a malignancy.

In conclusion, it is important to consider anti-DPPX antibody encephalitis in the differential diagnosis for a patient with subacute cognitive decline, weight loss with or without diarrhea, and signs of central nervous system hyperexcitability. Fast recognition of these symptoms can lead to prompt diagnosis and effective treatment as well as appropriate screening for malignancy.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

L.M.D.: 1A, 1B, 1C, 2A
C.H.Y.: 1A, 1B, 1C, 2B
C.L.V.: 1A, 1B, 1C, 2B
A.L.P.: 1A, 1B, 1C, 2B

Disclosures

Ethical Compliance Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. The patient and his wife provided verbal and written consent for publication of this video. The authors confirm that the approval of an institutional review board was not required for this work.

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Supporting Information

Supporting information may be found in the online version of this article.

Video S1. The video highlights the progressive decline in neurological and neuropsychological function in a 77-year-old gentleman with anti-DPPX encephalitis, followed by improvement after a long course of immunotherapy. Segment 1 shows the patient at the time of initial presentation approximately 18 months after symptom onset, with prominent oro-buccolingual dyskinesia, cognitive impairment, and functional decline. Segment 2 shows the patient 3 months later, when he was diagnosed with anti-DPPX encephalitis and admitted to the hospital for treatment. Segment 3 shows the patient after 10 months of receiving immunotherapy, with improvement in speech production, cognition, and involuntary movements.