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Tremor and Other Hyperkinetic Movements

Letters

Purkinje Cell Cytoplasmic Antibody (PCA-2)-related Chorea–Dystonia Syndrome

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There are several causes of adult-onset chorea, with Huntington's disease (HD) being the most common. We report a patient who developed a complex movement disorder consisting of chorea and dystonia associated with caudate atrophy on brain magnetic resonance imaging (MRI) because of a paraneoplastic etiology that can be easily confused with HD. He was found to have elevated titers of Purkinje cell cytoplasmic antibody (PCA-2) in the serum and cerebrospinal fluid (CSF).

A 70-year-old Caucasian male with no pertinent past medical history was referred for complaints of unintentional weight loss, weakness, and involuntary movements. Over the past year, he had experienced progressive weakness in his legs such that he required a walker. As his weakness progressed, he developed bladder and bowel incontinence, further gait decline, and 60-pound (27-kg) weight loss. During the course of his weight loss and gait decline, he developed involuntary movements of the mouth, abnormal posturing of the hands, and dysarthria. His involuntary movements disappeared during sleep and while he was eating or drinking. The tongue did not push food out and he was able to eat and swallow without difficulty. There was no history of medication intake that could cause these involuntary (tardive) movements. The family history was negative for neurodegenerative disorders. He had a 30 pack-year smoking history and prior history of heavy alcohol intake. Clonazepam was prescribed to help with the involuntary movements, which resulted in mild improvement as seen in the latter half of the video (Video 1).

His general examination was significant for cachexia. On neurological examination, he was alert and oriented. Cranial nerves were intact with the exception of the involuntary movements discussed below. Ocular motor examination did not reveal any impairment in saccades or smooth pursuit. Strength and reflexes in the upper extremities were normal. Strength testing in the lower extremities showed bilateral hip flexors (Medical Research Council [MRC] grade 2/5), knee flexors (MRC grade 2/5), knee extensors (MRC grade 3/5), ankle dorsiflexors (MRC grade 4/5), and plantar flexors (MRC grade 4/5). Reflexes were increased in the lower extremities with clonus and bilateral extensor plantar responses. Sensory testing was normal. Coordination was found to be normal on finger–nose–finger testing. As far as his involuntary movements were concerned, overall they could be best described as a combination of dystonia and chorea. He had involuntary, irregular, continuous, and partially suppressible dystonic movements around the mouth leading to opening of the jaw and protrusion of the tongue. His left eye closure was suggestive of unilateral blepharospasm. His hands assumed dystonic posturing while holding a towel to clear oral secretions. His movements in the neck, upper limbs, and trunk appear to be choreiform in nature (Video 1).

MRI of the brain showed bilateral caudate atrophy along with global parenchymal loss (Figure 1). MRI studies of the cervical, thoracic, and lumbar spine with and without contrast were normal. Electromyography and nerve conduction studies did not show evidence of neuropathy or motor neuron disease. A movement neurophysiology study showed co-contraction of agonist and antagonist muscles in the upper extremities suggestive of dystonia. The following investigations were negative or normal: human immunodeficiency

virus 1/2 antibody, Human T-cell lymphotropic virus (HTLV) I/II antibody, copper, vitamin B12, ceruloplasmin, ferritin, peripheral smear for acanthocytes, antinuclear antibody, thyroid stimulating hormone, thyroperoxidase antibody, celiac disease panel, creatine kinase, aspartate transaminase, alanine transaminase, vitamin E, antiphospholipid antibody, syphilis antibody immunoglobulin (Ig)G, and glutamic acid decarboxylase (GAD65) antibody. A polymerase chain reaction-based assay was utilized to detect cytosine–adenine–guanine (CAG) repeat expansions in exon 1 of the *HTT* gene (Huntingtin), which showed 19/20 CAG repeats. A paraneoplastic antibody panel performed in both the serum and CSF showed elevated titers of PCA-2 (1:15,360 in the serum and 1:512 in the CSF). Computed tomography scan of the chest, abdomen, and pelvis demonstrated left mediastinal adenopathy and a positron emission tomography scan showed hypermetabolism in the same area that was suspicious for malignancy. A biopsy of the lymph node was negative for malignancy and the patient chose to be transferred to a hospice after seven sessions of plasma exchange failed to show any benefit. Owing to recurrent infections, treatment with other immunosuppressive agents was not considered.

Video 1. Neurologic Examination Demonstrating a Complex Movement Disorder. The video shows dysarthria and jaw opening as well as tongue protrusion dystonia that improves while drinking and is suppressible. There is dystonic posturing of the hands while using the towel and blepharospasm on the left side. The chorea is evident in the neck, trunk, and upper limbs. The latter part of the video shows some improvement of the above-mentioned movements with clonazepam.

PCA-2 was identified by Vernino et al.[1] in 10 patients with subacute neurological syndrome associated with small cell lung cancer (SCLC). This antibody has been reported to cause ataxia, encephalitis, motor neuropathy, dysautonomia, and Lambert–Eaton myasthenic syndrome.[1,2] PCA-2 is specific for the presence of SCLC and it has not been reported to be associated with any other cancer. The biopsy for the presence of malignancy can initially be negative, as it was in our case.[1,2] The following antibodies were found in a review of 14 cases of paraneoplastic chorea: CRMP-5 (collapsin response-mediator protein 5)-Ig, amphiphysin-IgG, GAD65, VGCC-P/Q type (voltage-gated calcium channel), striational, anti-Hu, and anti-Ri.[3] Our case is the first in the literature to identify PCA-2 leading to a hyperkinetic movement disorder (chorea–dystonia in our case) associated with caudate atrophy on brain MRI. A case of chorea with caudate atrophy associated with SCLC was described in 1997. This patient was later

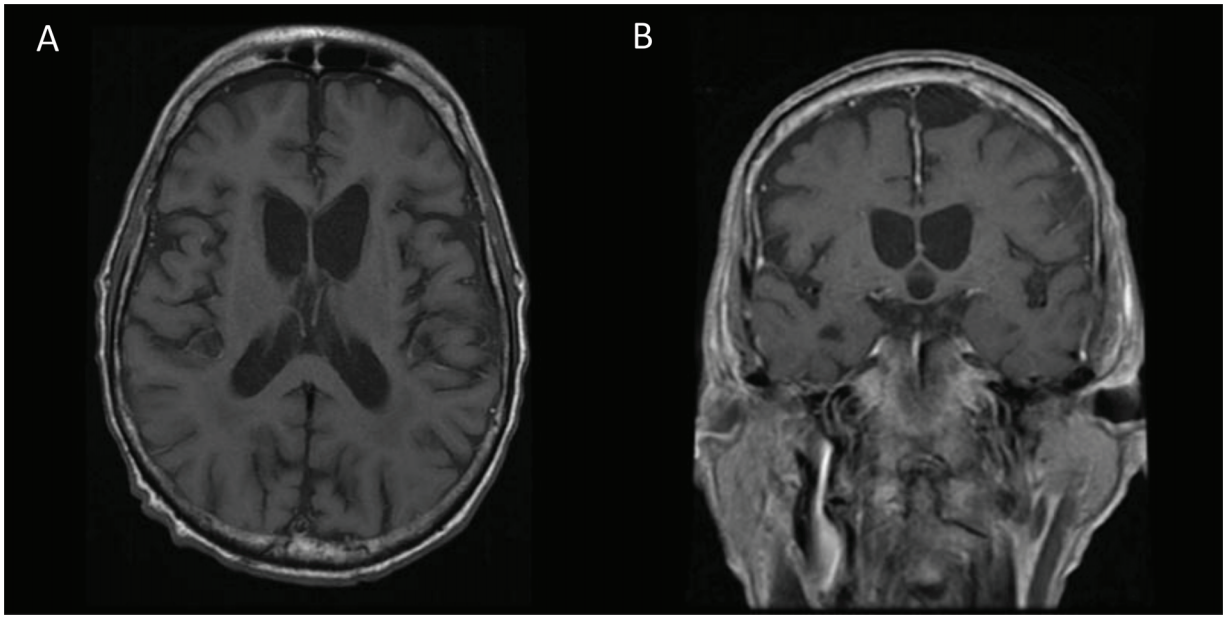

Figure 1. **Neuroimaging Study.** Magnetic resonance imaging of the brain axial T1 (A) and coronal T1 (B) Axial T1 and coronal T1: bilateral caudate atrophy with global parenchymal loss.

found to have anti-Hu antibody and showed transient improvement with intravenous corticosteroids.[4] It is rare for a paraneoplastic etiology to cause a combination of hyperkinetic movement disorder and caudate atrophy. Paraneoplastic etiology of chorea tends to be more common in older male patients with coexisting peripheral neuropathy or weight loss.[3] The two other disorders associated with chorea and caudate atrophy are chorea–acanthocytosis and McLeod syndrome.[5] These two conditions are usually associated with areflexia and muscle atrophy.[5] The presence of upper motor neuron signs, paucity of chorea in the lower extremities, lack of psychiatric features, and normal extraocular movements distinguish our patient's clinical picture from classic HD. The treatment of paraneoplastic neurologic disorders involves treating the underlying cancer and immunotherapy. If the antibody is directed towards the cell surface antigen (e.g. anti-*N*-methyl-D-aspartate receptor encephalitis) then plasma exchange or intravenous immunoglobulin may result in some improvement by removing the antibody. However, neurologic dysfunction can also be mediated by the cytotoxic T-cells when the antigen is intracellular (e.g. PCA-1, PCA-2, GAD65, etc.) as in our case. The response to immunotherapy in such cases can be variable and cyclophosphamide should be considered because it is directed at the cytotoxic T-cell response.[2,6]

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