Tremor in Paraneoplastic Cerebellar Degeneration: Beyond Intention Tremor

Sir

A 68-year-old female diagnosed with metastatic endometrial cancer one year ago was seen in the neurology clinic with a tremor in her hands and slurring of speech which started two months ago. In addition, she complained of binocular double vision and was seeing the objects one above the other only while driving. Her gait was unsteady which required the use of cane because of multiple falls. Her symptoms had begun insidiously and have been progressive in course. The endometrial cancer was treated with 7 cycles of carboplatin and paclitaxel along with surgery.

Her general examination was normal. On neurological examination, she was alert and oriented to time, place, and person. Cranial nerve examination was unremarkable except for the presence of saccadic pursuits, upbeat nystagmus, and gaze-evoked nystagmus (while looking towards the right). Her facial expressions were normal, but the speech was slurred and and had a scanning quality. Her strength examination, sensory examination, and deep tendon reflexes were unremarkable. She had a bilateral flexor plantar response. She had dysmetria on finger-nose-finger testing, and an impairment of rapid alternating movements, finger chase, and heel-knee-shin on both sides (right >left). There was a low-frequency rest tremor in both hands (right >left) which was present with posture as well. No kinetic or intention tremor [Video 1] was found on finger-nose-finger testing.

Brain MRI showed cerebellar atrophy, and there was no enhancement with contrast [Figure 1]. The following investigations in the serum were either negative or normal: celiac disease panel, GAD antibody, TPO antibody, ANA, SSa, SSb, and vitamin E. A serum paraneoplastic evaluation sent to Athena Diagnostics® showed a mild elevation in anti-Yo antibody (1:200). This panel includes CASPR2, GAD65, VGCC type P/Q, LGI1, amphiphysin, CV2, Hu, Ma, Ta, Yo, Ri, Zic4, and ganglionic AchR antibodies. Cerebrospinal fluid (CSF) cell count, protein, and glucose were normal. Further evaluation showed four oligoclonal bands (OCBs) in the CSF while there were no OCBs in the serum and CSF IgG index was elevated at 0.90 (normal range: 0.3–0.6). FDG-PET scan did not show any evidence of recurrence. She received five doses of intravenous methylprednisolone and five sessions of plasma exchange with no improvement in her symptoms.

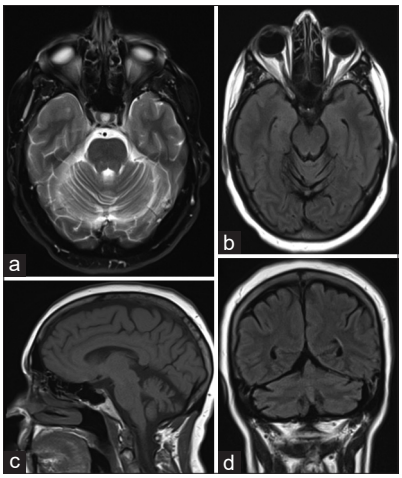

Figure 1: Brain MRI shows cerebellar atrophy on T2 axial [a], axial fluid-attenuated inversion recovery (FLAIR) [b], sagittal FLAIR [c], and coronal FLAIR [d]

Discussion

The highlights of this case are the symptoms and signs of underlying cerebellar pathology. Cerebellar atrophy on MRI further reinforced cerebellar involvement. Routine laboratory investigations to rule out the common reversible causes of late-onset cerebellar ataxia (hypothyroidism, vitamin E deficiency, celiac disease) were unremarkable as described above. There was a strong suspicion towards paraneoplastic etiology as the patient had an established history of malignancy. The elevated level of anti-Yo antibody in the serum confirmed the diagnosis of paraneoplastic cerebellar degeneration (PCD).

PCD is a rare complication of nonmetastatic malignancy. The set of cerebellar signs and symptoms associated with anti-Yo antibody or Purkinje cell cytoplasmic antibody type 1 is the most commonly reported variant of PCD.[1] More than 90% of the patients with cerebellar symptoms and anti-Yo antibody have underlying cancer, most often in the breast, lungs, or in the pelvic organs.[2] While the patient had symptoms expected in the setting of PCD (i.e., gait ataxia, gaze-evoked nystagmus, scanning speech, etc.), what is intriguing is the presence of mild rest and postural tremor without any evidence of intention or kinetic tremor. There is a traditional belief that tremor in the background of cerebellar pathologies, if present, is usually intentional. In fact, the term "cerebellar tremor" has been used synonymously and interchangeably with "intention tremor." Although the presence of intention tremor has been documented in a majority of case reports on PCD,[3-5] the phenomenology is not limited to intention tremor. Several studies have also reported the emergence of Holmes tremor in patients with PCD.[6] The complete absence of intention tremor, kinetic tremor, or Holmes tremor, as described in previous reports, is an interesting aspect of this case. The tremor in our patient can be best characterized as "Holmes-like" tremor based on the frequency; however, the kinetic component was absent, so it does not fit the diagnostic criteria for Holmes tremor.[7] One possible explanation for the

emergence of this kind of tremor is the involvement of dentate or inferior olivary nucleus as shown in an autopsy case with anti-Yo with cerebellar degeneration.[6] This further expands the clinical phenomenology of tremor emerging in the setting of cerebellar pathologies and reinforces the fact that "cerebellar tremor" is not limited to intention tremor.[8]

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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Conflicts of interest

There are no conflicts of interest.

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