An Unusual Presentation of Cerebellar Ataxia with Bilateral Vestibulopathy Syndrome: A Case Report

Sir,

The clinical syndrome of cerebellar ataxia with bilateral vestibulopathy (CABV) was first reported by Bronstein *et al*. in 1991.[1] Its characteristic clinical sign is the impairment of visually enhanced vestibulo-ocular reflex (VVOR).[2] There is combined failure of all three compensatory eye movement systems: the vestibulo-ocular reflex (VOR), optokinetic reflex (OKR), and smooth pursuit (SP). Gaze stabilization during natural activities like walking or running is attained by the combination of visual and vestibular reflexes (Grossman *et al*., 1989).[1] Visual reflexes such as SP and OKR are most obvious during the low-frequency, predictable head rotations, and VOR comes into play during high-frequency head rotations. Patients with cerebellar ataxia have impaired SP and OKR, but generate a near normal VVOR using their VOR. Patients with bilateral vestibulopathy produce a near normal VVOR below 1 Hz using SP and OKR. Therefore, the impairment of the VVOR below 1 Hz indicates involvement of vestibular as well as cerebellar pathways. An accurate diagnosis of this condition requires a high index of suspicion, as some of the etiologies like malignancies can masquerade as CABV syndrome.

A 56-year-old gentleman presented to the audio vestibular clinic of our tertiary care hospital with 6 months history of imbalance while walking, dizziness, apparent motion of objects while walking, and abdominal fullness. There was no family history of ataxia or any other chronic progressive neurological disorder. He neither had any hearing loss nor had any history of ototoxic drug intake in the past. Oto-neurological examination revealed a broad-based gait and spontaneous downbeat nystagmus. Corrective saccades were observed during the examination of smooth pursuit. Finger nose test incoordination and dysdiadochokinesia also were present. These findings suggested a central vestibular dysfunction, in addition his head thrust test was positive bilaterally and there was an impaired dynamic visual acuity, which suggested a peripheral vestibular dysfunction. An impaired VVOR was noted by observing compensatory saccadic eye movements when his head was slowly (at about 0.5 Hz) turned from side-to-side while he fixated at the examiner's nose. Romberg's sign was positive. On systemic examination there was a palpable abdominal mass involving the epigastric, umbilical, and left hypochondriac region, which moved with respiration. The patient had normal audiogram and tympanogram. Electronystagmogram (ENG) showed saccadic intrusions of smooth pursuit, asymmetry of optokinetic nystagmus, and bilateral hypoactive labyrinth [Figure 1]. Magnetic resonance imaging (MRI) brain [Figure 2a] was normal. Nerve conduction velocity and electromyographic study of upper and lower limbs were normal. The abdominal mass was further evaluated by the surgical team with a Computed tomogram (CT) of the abdomen and an Ultrasound (USG)-guided biopsy. Abdominal CT showed a large heterogeneously enhancing necrotic mass lesion in epigastric and left hypochondriac regions extending inferiorly till left iliac fossa (LIF) measuring 31 × 19 × 16 cm. Mass was seen engulfing the entire stomach [Figure 2b]. Biopsy of the mass was suggestive of a high-grade neuroendocrine tumor. The tumor cells were positive for pancytokeratin, CAM5.2, synaptophysin, very scatteredly positive for CD 56.CK 7, and negative for CK20, Chromogranin, Desmin, SOX-10, DOG-1, CD-117. The serum assays for the paraneoplastic antineuronal antibodies (Hu, Yo, Ri, CV2, Ma, amphiphysin, Recoverin, titin, Tr, AntiGAD-65, SOX1, Ta) were negative. The clinical findings of concurrent cerebellar ataxia and bilateral vestibulopathy were consistent with the diagnosis of CABV. Counselling for vestibular physiotherapy, and use of the assistive device such as walker was prescribed. He was started on six cycles of chemotherapy (Inj.Granisetron, Atezolizumab, Etoposide, Carboplatin, Pegfilgrastin) for the neuroendocrine tumor, but despite repeated cycles of chemotherapy, he succumbed to his illness after 6 months of treatment.

Migliaccio *et al*. studied in detail, 4 patients diagnosed as CABV with magnetic search coil oculography, and they were found to have impairment of all 3 compensatory eye movement reflexes: The VOR, smooth pursuit, and optokinetic response.[1] A retrospective study by Pothier *et al*. identified 33 patients matching the CABV clinical syndrome.[3] In 2004, Szmulewicz *et al*. proposed cerebellar ataxia with bilateral vestibulopathy as a distinct syndrome with a characteristic clinical sign - an impaired visually enhanced vestibulo-ocular reflex (VVOR; also called the "doll's head" or "doll's eye" or "oculo-cephalic reflex) known as Cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS).[4] In their study, three of the four patients had clinical and electrophysiological evidence of sensory peripheral neuropathy. Since then, patients with various combinations of bilateral vestibulopathy, cerebellar ataxia and peripheral neuropathy have been described. There is no discernible sequence to the onset of the 3 cardinal features of CANVAS (cerebellar impairment, bilateral vestibular hypofunction, and a somatic sensory deficit), and patients may manifest only 2 of the 3 for many years before fulfilling the minimal diagnostic requirements of this syndrome.[5] The major differential diagnoses are spinocerebellar ataxia type 3 (SCA 3) (Machado-Joseph disease), Friedreich's ataxia (FRDA), multiple system atrophy of cerebellar type (MSA-C), Wernicke's encephalopathy, SCA's 4 and 25, and occasionally SCA's 1, 8, and 27. Spinal sensory

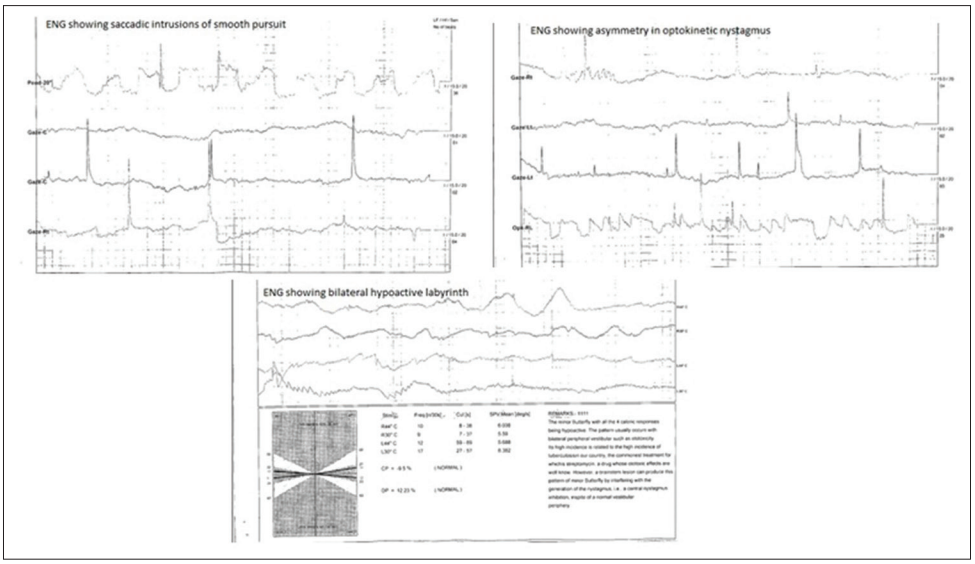

Figure 1: ENG showing saccadic intrusions of smooth pursuit, asymmetry of optokinetic nystagmus and bilateral hypoactive labyrinth

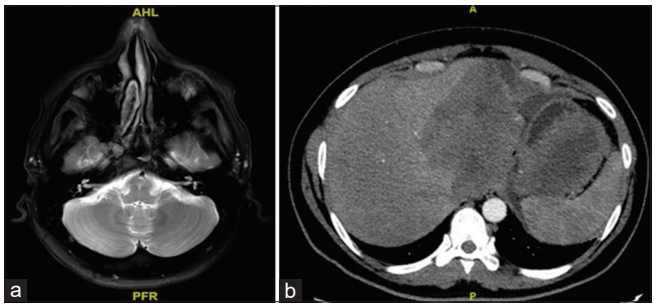

Figure 2: (a) Normal MRI brain of the patient. (b) CT abdomen showing large heterogeneously enhancing necrotic mass noted in greater and lesser omentum, completely encasing stomach

neuronopathies can be found in paraneoplastic diseases, immune disorders (Sjogren's syndrome, Miller-Fisher syndrome, and Bickerstaff's brainstem encephalitis), Friedreich ataxia, and history of intake of drugs such as cisplatin and pyridoxine.[4] Chronic cough and autonomic dysfunction are found to be variable features of CANVAS.[6] Management of CABV and CANVAS syndromes is symptomatic. Patients with dysphagia as seen in pure cerebellar syndromes and/or sensory impairment should be taught behavioral techniques and may require modification of food consistency. Measures should be taken for prevention of falls, such as educating regarding possible risks, advising patients to modify their home conditions to bulid fall free bathrooms, hand rails, etc. Individualized combination of neurological and vestibular rehabilitation may benefit the patient. Our patient had concurrent malignancy and abdominal high-grade neuroendocrine tumor along with CABV syndrome. The possibility that CABV was a paraneoplastic manifestation of the coexisting malignancy was duly considered, but the antibodies were negative. However, the possibility that malignancy is a potential cause cannot be dismissed summarily as the antibody tests done early in the disease process may still become positive later in the disease course.

Patients presenting with imbalance, dizziness, and ataxia could be having CABV syndrome. A head impulse test should be a routine part of every patient presenting with dizziness, and cerebellar signs should be looked for. Where suspected an MRI brain along with vestibular test should be performed. CABV syndrome could represent paraneoplastic syndrome, and therefore more sinister manifestation of systemic malignancy.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 27-Nov-2019 **Revisied:** 06-Jan-2020 **Accepted:** 22-Jan-2020
Published: 09-May-2020

DOI: 10.4103/aian.AIAN_601_19