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A Rare Case of Familial Progressive Ataxia with Palatal Tremors

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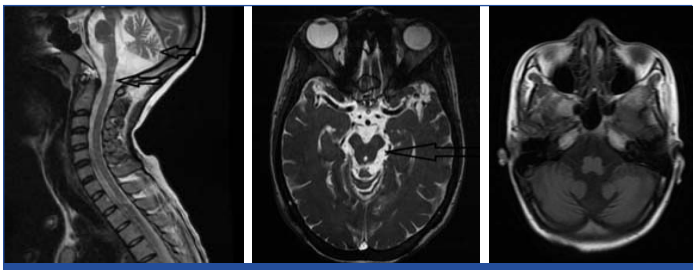
A 25-year-old female patient presented with insidious onset progressive difficulties of gait and balance. Onset of these symptoms first appeared nine years prior and evolved to include changes in speech, increased occurrence of falls and spastic paraparesis. There were no complaints of ear clicks, blurring of vision, urinary incontinence, seizures. She had visited a family clinician for the above-mentioned complaints and was advised to visit higher centers but because of economic constraints she did not avail further opinions. It was after the increase in disease progression that led to significant impairment of daily communication and activities, the parents brought her to this hospital.

There was no history of developmental delay or cognition abnormality. There was no history of alcohol intake, neurotropic drug ingestion, or exposure to any toxin. There was a positive family history of imbalance and gait instability in one of her siblings which was not investigated.

General examination did not reveal any abnormality. There was no postural hypotension. A comprehensive neurological examination revealed higher functions to be normal, PTs [Video 1], bilateral ankle clonus [Video 2] and knee reflexes were exaggerated and bilateral plantars were extensor, appendicular ataxia was present, including dysdiadochokinesia [Video 3], past pointing, ataxic dysarthria and vertical nystagmus were more prominent in downward gaze [Video 4]. Sensory system was intact. A provisional diagnosis of Multisystem Atrophy; Cerebellar Type (MSA-C) was kept.



[Table/Fig-1]: Sagittal T2 weighted MRI image reveals thinning and atrophy of upper cervical spine and cerebellum with prominent CSF spaces and cisterna magna. **[Table/Fig-2]:** High Resolution 3 Dimentional Fast Imaging Employing Steady-state Acquisition Magnetic Resonance Imaging (3D FIESTA MRI) image showing atrophy of midbrain. **[Table/Fig-3]:** T(Time)1 weighted Axial image showing cerebellar and vermis atrophy. (Images from left to right)

MRI brain with cervical spine revealed diffuse cerebellar atrophy with hypoplastic inferior cerebellar vermis with upper cervical spine and midbrain atrophy [Table/Fig-1-3]. A Glial Fibrillary Acidic Protein (GFAP) analysis and Genetic study for Spinocerebellar Ataxias (SCA 1-17) were negative in this case. SCA 20 was also negative. A final diagnosis of familial PAPT was entertained.

Patient was treated with Baclofen 10 mg thrice a day and Clobazam 5 mg in night before going to bed. After two months follow-up of treatment, the spasticity decreased but there was no effect on other signs and symptoms.

PT was earlier called as palatal myoclonus. Palatal tremor are classified as essential (EPT) and symptomatic (SPT) [1,2]. Palatal myoclonus was renamed as 'PT' during the First International Congress of Movement Disorders to justify the continuous and rhythmic nature of the palatal movement as opposed to non rhythmic jerky movements of myoclonus. SPT originate from lesions in the Guillain Mollaret Triangle (GMT) which triggers the contraction of Levator Veli Palatini muscle (LVP) supplied by the 9th and 10th cranial nerves [3].

The GMT is a hypothetical triangle in the brainstem formed by the ipsilateral red nucleus in the midbrain, the inferior olive in the medulla and the contralateral dentate nucleus in the cerebellum, forming the dentato-rubro-olivary pathway. Any lesion in this triangular area activates the inferior olivary nucleus. This constant triggered activation leads to hypertrophy of the inferior olivary nucleus which constantly and rhythmically sends discharges leading to oculo-PT. With constant activation, finally the olivary nucleus may become atrophied overtime and PTs may be seen without documented hypertrophy also [4]. Progressive ataxia with PTs presents with gradually progressive bilateral cerebellar ataxia, PTs, diplopia, oscillopsia because of various abnormalities of eye movements like saccadic, pursuit disorder, gaze evoked and pendular nystagmus. Other features are due to brain stem and autonomic dysfunction. Familial PAPT includes Alexander disease, Polymerase Gamma (POLG) mutations, SCA 20 and Ganglioside Monosialic (GM) 2 gangliosidosis. The classic MRI finding of familial PAPT is brain stem and cervical spinal cord atrophy [5].

In SPT involuntary oscillations can affect posterior part of the soft palate in approximately 60 % of cases. In 30% of cases ocular and branchial muscles also may have oscillations [6]. Fibres from nucleus ambiguous supply the levatorveli palatini which is responsible for palatal movement and may be associated with ear clicks [7-10]. On MRI, hypertrophy of the olivary nucleus and an increase in T2 or proton density of the nucleus may be seen within six months of the initial insult [11]. It is believed that due to secondary, trans-synaptic deafferentation and inhibitory input loss from the contralateral dentate nucleus that olive develops pseudohypertrophic degeneration after a sufficient time has elapsed from the initial insult [12].

PT associated with familial PAPT is usually symptomatic but underlying mechanism is yet to be understood fully. Olivary hypertrophy is not seen frequently in familial PAPT as compared to sporadic PAPT. The index patient had PTs, pyramidal signs and neuroimaging was positive for atrophy of mid brain, pons, cerebellum and upper cervical cord [13]. There was positive family history that one of the siblings had ataxia but no other complaints. This might be suggestive of some genetic abnormality which most probably suggests autosomal dominant pattern of inheritance, but our genetic study was inconclusive. On MRI brain, there were no lesions of GMT and olivary hypertrophy so sporadic PAPT was unlikely. On the basis of all above findings patient was diagnosed as Familial PAPT. The closest differentials of PAPT are multiple system atrophy, spinocerebellar ataxia, progressive supranuclear palsy or adult-onset Alexander's disease and these conditions should be should be carefully ruled out.

As far as the management is concerned; Gluten free diet, nasal sumatriptan, lamotrigine, gabapentin has been used to treat ataxia but none showed any promise. Surgeries like tympanic membrane perforation with excision of levator and tensor veli palatini muscles, thalamotomy and deep brain stimulation to red neucleus has also been tried in vain [14-16].

PAPT is definitely a separate category of PT. Symptomatic PT can be sporadic or familial. Lesions in the hypothetical GMT along with hypertrophied olivary nucleus points towards symptomatic PT. The characteristic feature of Familial PT in MRI is brainstem and cervical cord atrophy. There is no definitive treatment for PAPT making this an area of future research.

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