Progressive ataxia and palatal tremor (PAPT) Clinical and MRI assessment with review of palatal tremors

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Summary
Palatal tremor has been subdivided into essential (EPT) and symptomatic palatal tremor (SPT). A subgroup of the SPT form has a syndrome of progressive ataxia and palatal tremor (PAPT). Published details of cases of PAPT are sparse and the disorder appears heterogeneous. We present clinical and MRI features of six patients with sporadic PAPT who attended The University Health Network between 1991 and 2002. Eye movements were recorded using a magnetic search coil technique. We review previously reported cases of PAPT from the English language literature and relate this disorder to EPT and SPT. PAPT may be divided into sporadic and familial forms. We identified 22 other prior reported cases of sporadic PAPT. Sporadic PAPT is a subtype of SPT in which progressive cerebellar degeneration is the most symptomatic feature. A combination of vertical nystagmus and palatal tremor was found in one of our patients. Internuclear ophthalmoplegia, a new finding, was present in two of our patients and indicated additional brainstem dysfunction. Inferior olivary high signal abnormalities were present on MRI in all of our cases. The cause of sporadic PAPT remains uncertain. In some previous reports of sporadic PAPT, the combination of brainstem or pontine atrophy, parkinsonism, autonomic dysfunction or corticospinal tract abnormalities suggests a diagnosis of multiple system atrophy, although pathological verification is lacking. Familial PAPT is associated with marked brainstem and cervical cord atrophy with corticospinal tract findings, but the typical olivary MRI abnormalities have not been reported. A substitution in the glial fibrillary acidic protein (GFAP) gene has been described in a family with PAPT, raising the possibility of Alexander’s disease. One other familial syndrome of PAPT, termed ‘dark dentate disease’, has also been reported. PAPT is a subgroup of SPT in which ataxia progresses and is not usually the result of a monophasic illness. Eye movement abnormalities suggest a disorder of both the cerebellum and brainstem. Familial PAPT differs from sporadic PAPT in having marked atrophy of cervical cord and brainstem with corticospinal signs but without hypertrophic olivary appearance on MRI.

Keywords: progressive ataxia; palatal tremor; eye movement

Abbreviations: EPT = essential palatal tremor; GFAP = glial fibrillary acidic protein; INO = internuclear ophthalmoplegia; OPCA = olivopontocerebellar atrophy; OPT = oculopalatal tremor; PAPT = progressive ataxia and palatal tremor; SCA = spinocerebellar ataxia; SPT = symptomatic palatal tremor; VOR = vestibulo-ocular reflex; VVOR = visually enhanced vestibulo-ocular reflex

Introduction
Palatal tremor, formerly called palatal myoclonus, has been subdivided into essential (EPT) and symptomatic (SPT) forms (Deuschl et al., 1994). A syndrome of progressive ataxia with palatal tremor (PAPT) has also been rarely described, but in some reports clinical details are sparse and the disorder appears heterogeneous. Here we describe detailed clinical, ocular motility and imaging features of six patients with sporadic PAPT and review the English language...
Methods

The six patients attended the Movement Disorders Centre at the Toronto Western Hospital between 1991 and 2002 for neurological, radiological and other examinations.

Horizontal and vertical eye movements were recorded using a magnetic search coil technique (C-N-C Engineering, Seattle, WA) (Robinson, 1963). Subjects sat in a vestibular chair and wore scleral contact lens coils in both eyes. Recordings were done with binocular viewing unless the patient had diplopia, in which case one eye was covered. Patients were instructed to look at or follow a rear-projected laser dot target subtending 0.25°, on a featureless screen. Analogue signals of target and eye position were displayed on an inkjet rectilinear polygraph and digitized on-line, at 200 samples/s, using a PDP 11/73 computer. Initially, fixation of a stationary target was recorded in the light. Patients also attempted fixation of an imaginary target in darkness. Saccades to targets of predictable timing (3 s interval) were recorded at 10 and 20° amplitudes; the target was driven horizontally by mirror galvanometers. Smooth pursuit of a sine wave target of ±10° amplitude from mid-position at frequencies of 0.5–2 Hz was recorded. In patients 1 and 5, the vestibulo-ocular reflex (VOR) was also recorded during active head shaking at 0.5–2 Hz about the vertical axis, in time to an auditory beep. A head coil taped to the forehead recorded the input of the reflex and the eye coil recorded the output of the reflex. The VOR was recorded both in the light, with a laser dot fixation target 1.24 m away from the cornea (visually enhanced VOR; VVOR), and in the dark with an imaginary stationary target at the same target distance. VOR gain was measured by the ratio of smooth eye movement/ head movement amplitude, after saccades were removed (Wong and Sharpe, 2002).

The clinical features of our six patients are summarized in Tables 1 and 2, and are described in detail below.

Results

Patient 1
This 41-year-old man complained of a 1 year history of progressive right more than left hearing loss accompanied by bilateral tinnitus. Over this time, he described progressive difficulty with coordination on reaching for objects, climbing stairs and walking, but with no falls. He described diplopia but no change in visual acuity. His wife, in retrospect, felt that he may have been clumsy for 15–20 years. There was no relevant past medical history or family history.

Examination revealed visual acuity of 20/20 bilaterally, which decreased to 20/300 with horizontal head shaking at ~2 Hz, indicating a defective VOR. There was concomitant esotropia and left hypertropia and full ductions of each eye.

He had gaze-evoked and rebound nystagmus. Pursuit was saccadic. Left eye adduction was slow, indicating a left internuclear ophthalmoplegia (INO).

A 2 Hz palatal tremor was seen without extension to other facial muscles. Other cranial nerves were normal. Limb examination was normal except for bilateral arm and leg dysmetria. He walked with a wide-based gait and could not heel–toe walk. Deep tendon reflexes were present but diminished, except for ankle jerks which were absent. Plantar responses were flexor.

Investigations revealed normal routine blood analysis, thyroid-stimulating hormone (TSH), vitamin B12, antinuclear antibodies, lactate and pyruvic acid. Creatine kinase (CK) was mildly raised on two occasions (316 and 399 U/L, normal <225 U/L). Genetic tests for spinocerebellar ataxia (SCA) 1, 2, 3, 6, 7 and 8, Friedrich’s ataxia and Leigh’s syndrome/NARP (neuropathy, ataxia and retinitis pigmentosa) were negative. Left deltoid EMG showed a few minor myogenic potentials, and nerve conduction studies excluded a neuropathy. Audiological testing showed mild bilateral sensorineural hearing loss and bilaterally reduced cold and warm calorics. Muscle biopsy was declined by the patient. Brain MRI showed enlargement and increased signal intensity of both inferior olives on proton density- and T2-weighted images and cerebellar atrophy on T1-weighted images. There were no other focal lesions.

Magnetic search coil recording revealed square wave jerks in a primary position. At both amplitudes, adducting saccades of the left eye were slow, confirming the left INO. Rightward saccades of the right eye were hypermetric. Pursuit was saccadic. Horizontal VVOR gain was reduced (<0.9) but much more reduced in darkness almost to zero.

Patient 2
This 54-year-old man developed oscillopsia which worsened over ~12 months, making it impossible for him to read. Subsequently, he complained of difficulty in walking, followed by dysarthria, loss of arm coordination and tinnitus. He had a significant depression in his past medical history but no other symptoms. Family history was negative.

Clinical examination of his eyes in the primary position revealed vertical pendular nystagmus with a torsional component, which appeared to be synchronous with a 2 Hz palatal tremor. Saccades were hypermetric to the left. Lateral gaze increased the amplitude of his vertical nystagmus. Pursuit was saccadic. He had slow and irregular dysarthria. Limb examination was normal apart from dysmetria and slow and irregular fine finger movements. He walked with a wide-based gait and could not heel–toe walk.

Initial CT and evoked potentials were normal. Brain MRI showed high signal in the inferior olives bilaterally (Fig. 1A). Repeat MRI 40 months later showed this abnormality to persist (Fig. 1B) but he had developed cerebellar atrophy (Fig. 1C).

References

(Wong and Sharpe, 2002).

...results were normal. There was a high signal intensity of both inferior olives on proton density- and T2-weighted images and cerebellar atrophy on T1-weighted images. There were no other focal lesions. Magnetic search coil recording revealed square wave jerks in a primary position. At both amplitudes, adducting saccades of the left eye were slow, confirming the left INO. Rightward saccades of the right eye were hypermetric. Pursuit was saccadic. Horizontal VVOR gain was reduced (<0.9) but much more reduced in darkness almost to zero.
## Table 1 Clinical and imaging details of our six sporadic PAPT cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Presenting age (years)</th>
<th>Duration (years)*</th>
<th>Frequency of palatal tremor (if recorded)/other cranial findings</th>
<th>Ocular disorders</th>
<th>Cerebellar disorder</th>
<th>Other features</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>M 54</td>
<td>4.3</td>
<td>2 Hz/eyelid tremor</td>
<td>Oscillopsia. V-nystagmus&lt;sup&gt;P&lt;/sup&gt; + torsional component. Hypermetric saccades. Saccadic pursuit.</td>
<td>Dysarthria, arm dysmetria, leg ataxia</td>
<td>Tinnitus, depression</td>
<td>T1: cerebellar atrophy. T2 and PD: IOH.</td>
</tr>
<tr>
<td>3</td>
<td>M 64</td>
<td>6.3</td>
<td>2–3 Hz/nop</td>
<td>Failure of accommodation. Macrosaccadic oscillations. Saccadic pursuit. Hypermetric saccades.</td>
<td>Dysarthria, dysmetria, tremor, trunk and leg ataxia</td>
<td>SHL dementia, bradykinesia, rigidity, HT, sensory loss</td>
<td>T1: cerebellar atrophy. PD- IOH.</td>
</tr>
<tr>
<td>5</td>
<td>M 71</td>
<td>11</td>
<td>1–2 Hz/chin tremor</td>
<td>Exotropia. Bilateral INO. Hypermetric saccades. Saccadic pursuit. ↓VOR</td>
<td>Dysarthria, arm and leg dysmetria, trunk ataxia</td>
<td>Neuropathy, AF, HT</td>
<td>T1: cerebellar atrophy. T2 and PD: IOH.</td>
</tr>
<tr>
<td>6</td>
<td>M 58</td>
<td>7</td>
<td>1–2 Hz/tongue and pharyngeal</td>
<td>Saccadic pursuit. Hypermetric saccades. Nystagmus + torsional component.</td>
<td>Dysarthria, arm and leg dysmetria, trunk ataxia</td>
<td>Dysphagia + incontinence. FHx deafness. Alcohol abuse</td>
<td>T1: cerebellar, cerebral and pontine atrophy. T2: inferior olive high signal which resolved</td>
</tr>
</tbody>
</table>

M = male; * = duration from the history of first symptoms to the longest available follow-up. H-nystagmus<sup>GE</sup> = horizontal gaze-evoked nystagmus; V-nystagmus<sup>P</sup> = vertical pendular nystagmus; INO = internuclear ophthalmoplegia; VOR = vestibulo-ocular reflex; SHL = sensorineural hearing loss; T1 = T1 weighted; T2 = T2 weighted; PD = proton density = proton density MRI; IOH = inferior olive hypertrophy and high signal; AF = atrial fibrillation; HT = hypertension; FHx = family history.
Magnetic search coil recording revealed a pendular predominantly vertical nystagmus in the dark. Saccades were hypermetric leftward. No gaze-evoked nystagmus was present. Pursuit had superimposed vertical nystagmus.

Patient 3
One year prior to presentation, this 64-year-old man developed difficulty with focusing when changing fixation from far to near and he complained of dysarthria. He had hearing loss related to previous exposure to loud noise, but denied other symptoms. His wife noted mild but progressive gait impairment over 4 years, and more recently memory impairment, minor behavioural and personality changes and some hallucinations. He had treated hypertension for 14 years and suffered a traumatic concussion 47 years earlier and traumatic ankle fracture 24 years earlier. There was a family history of stroke in his mother.

Ocular examination revealed normal acuity. Fixation was disrupted by saccadic intrusions. Saccades were hypermetric and pursuit was saccadic but without nystagmus. A 2–3 Hz palatal tremor was observed. Speech was slow and irregular. Muscle bulk and power were normal. Tone was rigid in the right arm, and bradykinesia was present on foot tapping. There was a fine postural tremor, and finger movements were clumsy. He had difficulty with heel–toe walking and fell back into the chair on attempted rising. He had impaired pain and vibration sensation to the knees and absent ankle reflexes.

Mini-mental test score was 20 out of 30. He showed palomental, pout and grasp reflexes. Apraxia was absent. Formal neuropsychometric testing revealed deficits in verbal, visual immediate, recent and remote memory, along with deficits in arbitrary associations, forward planning, switching tests and word-finding difficulties, with little insight into his difficulties. He was generally slow but had otherwise appropriate behaviour.

Investigations for cerebellar degeneration (including a paraneoplastic cause) and cognitive decline were negative. Audiological tests showed sensorineural hearing loss. EMG and nerve conduction studies were normal. Proton density MRI showed bilateral inferior olivary high signal intensity, which persisted 2 years later, and mild cerebellar atrophy.

Search coil recording showed macrosaccadic oscillations (Fig. 2A) that were present in both the light and darkness. He had hypermetric saccades, and pursuit was saccadic.

Patient 4
This 58-year-old man noted an abrupt onset of dysarthria and ataxia which progressed over 4 weeks to the point where he could not walk unaided. He denied other symptoms. Past medical history included treated hypertension. Family history

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Summary of course (where available) of progression of cerebellar symptoms and signs in our patients: for other features, see text on individual patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>Initial symptoms</td>
</tr>
<tr>
<td>1</td>
<td>Limb ataxia, diplopia and INO. Palatal tremor at first examination</td>
</tr>
<tr>
<td>2</td>
<td>Oscillopsia. Palatal tremor at first examination</td>
</tr>
<tr>
<td>3</td>
<td>Failure of accommodation. Dysarthria. Palatal tremor at first examination</td>
</tr>
<tr>
<td>4</td>
<td>Dysarthria and ataxia</td>
</tr>
<tr>
<td>5</td>
<td>Gait ataxia</td>
</tr>
<tr>
<td>6</td>
<td>Dysarthria and gait disturbance</td>
</tr>
</tbody>
</table>

INO = internuclear ophthalmoplegia; IOH = inferior olivary hypertrophy.
was negative. Investigations, including a search for a paraneoplastic cause, failed to find an aetiology. MRI was normal (Fig. 1D). His CSF analysis showed seven mature lymphocytes/ml.

Three years later, his stance had deteriorated further and he had developed transient oscillopsia. Head and palatal tremors were now evident. Visual acuity was normal. Eye examination in the primary position showed downbeat nystagmus. He had hypermetric saccades and saccadic pursuit. Neurological examination was normal except for limb ataxia bilaterally. With aid, he walked with a wide-based gait.

Extensive investigations for a malignancy were negative, including annual chest X-rays. Brain MRI 3 years after presentation revealed enlarged inferior olives which returned a high signal on T2- and proton density-weighted images (Fig. 1E). This abnormality persisted for another 2 years when he was re-scanned as part of his continued medical surveillance. Repeat T1 MRI showed the progression of cerebellar atrophy (Fig. 1F–H).

Magnetic search coil recording confirmed the primary position downbeat nystagmus with superimposed square wave jerks (Fig. 2B). Saccades were hypermetric (Fig. 2C) and pursuit was saccadic.

Five years after his initial presentation, he had no other new symptoms. He was still unable to walk and had persistent palatal tremor and eye movement abnormalities. Genetic testing for SCA1, 2, 3, 6, 7 and 8 and Friedreich’s ataxia was negative. Eleven years after onset, his symptoms continued to deteriorate very slowly and he could not stand unassisted.

Patient 5
When 63 years old, this man developed mild unsteadiness, first noted by his wife. Over the next 8 years, this slowly progressed and he had several falls. Four years into his illness, he developed a lateral rectus palsy acutely which was thought to be vascular in origin. Three years later, he developed tingling and numbness of the feet. A slurring dysarthria and bilateral INO were noted. He was referred to our hospital at the age of 71 years. He had a history of treated hypertension and a family history of coronary heart disease, hepatic carcinoma, pernicious anaemia and cerebrovascular disease in his parents when they were elderly.

Examination revealed normal mental status, a mild distal peripheral sensorimotor neuropathy but preserved reflexes. He had a left exotropia, bilateral INO, hypermetric saccades and saccadic pursuit. Tongue movements were slow and he had a 1–2 Hz palatal tremor. Occasionally, a chin tremor was seen, but the rest of his cranial nerves were normal. Limb examination was normal apart from bilateral finger–nose
ataxia and poor coordination of rapid finger movements. Heel–toe walking was impaired and he had a wide-based gait.

When seen again 11 years after symptom onset, he complained of worsening balance and speech and he used a wheelchair. His symptoms had gradually worsened over the years with no history of discrete episodes of deterioration. However, he had developed atrial fibrillation, and an echocardiogram showed an enlarged left ventricle without intraventricular clot. Examination now confirmed the severe dysarthria, persistence of the ocular motility abnormalities, palatal tremor and the limb cerebellar and sensory features, severe gait ataxia, but no pyramidal tract features.

Routine blood investigations were normal. Brain MRI revealed some high signal T2 lesions in the deep white matter, consistent with cerebrovascular disease; similar lesions were not evident in the brainstem or cerebellum. Magnetic resonance angiography was normal. T2-weighted MRI 7 years into his illness showed the presence of high signal and hypertrophy of the inferior olives. T1-weighted MRI scans showed cerebellar atrophy.

Magnetic search coil recording showed no nystagmus or saccadic intrusions in light and dark during fixation. He had bilaterally slow adducting saccades (Fig. 2D) and saccadic pursuit. The VOR at 0.5 Hz in light was normal but with low gain in the dark.

**Patient 6**

This 58-year-old man had a 7 year history of difficulty with balance and slurred speech. He had a history of high alcohol intake but had discontinued this 3 years prior to his neurological symptoms and had remained abstinent. Five years into the illness, he had severe dysarthria and had become wheelchair bound because of ataxia. There was a 12

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**Fig. 2** Magnetic search coil recordings. The ordinate (vertical axis) records target and eye amplitude. The abscissa (horizontal axis) is time. The vertical bar in (A) represents 10° and the horizontal bar represents 0.4 s. Calibrations are the same in all panels. H = horizontal; V = vertical. (A) Case 3. Upper tracing: the target is stationary and appears as a straight line. The middle tracing shows right eye horizontal macrosaccadic oscillations. These straddle the intended point of fixation. Bottom tracing: no movement in the vertical plane. (B) Case 4. Middle tracing: horizontal square wave jerks are recorded from the right eye. Bottom tracing shows concurrent downbeat nystagmus. (C) Case 4. Upper tracing: the target steps 20° left of the central position. The middle tracing is from right eye horizontal movement. As the target moves by 20° to the central position, the subject’s eyes move by 32° horizontally in the same direction, overshooting the central position (hypermetric horizontal saccade) before regaining fixation with nystagmus. The bottom tracing is from right eye vertical movement. (D) Case 5. Upper tracing: the target is central, moves to the right, back to the centre, then moves to the left. Middle tracing: right eye adduction is slow [compare the slope of (iii) with the almost vertical slope of the left eye abducting saccade (iv)]. Lower tracing: left eye adduction is slow [compare the slope of (ii) with the almost vertical slope of the right eye abducting saccade (i)].
month history of mild urinary incontinence and mild swallowing difficulty, but no other autonomic features. Past medical history revealed only cataract surgery. His mother and a nephew both had early onset, non-progressive deafness of unknown aetiology. His mother died at the age of 80 years from a carcinoma. Ten other siblings had no relevant medical history.

Systemic and mental state examinations were normal, without evidence of orthostatic hypotension. Cranial nerve examination revealed a 1–2 Hz palatal tremor affecting the base of the tongue and posterior pharynx. In the primary position, he had torsional nystagmus in both eyes. Pursuit was saccadic and saccades were hypermetric. Cranial nerves and other neurological examinations were normal, except for bilateral limb ataxia, a wide-based gait (with support) and a liability to fall spontaneously. He could not stand without help.

Normal investigations included routine blood tests and CSF examination including lactate. Mutation analyses for SCA 1, 2, 3, 6, 7 and 8 and Friedreich’s ataxia were negative. MRI 2 years after symptom onset had shown normal size of olives but with high signal. The inferior pons was atrophic. MRI after 7 years revealed cerebral, pontine and cerebellar atrophy, but the inferior olives now appeared normal.

Magnetic search coil recording in the primary position showed torsional nystagmus in both eyes, hypermetric saccades and saccadic pursuit.

**Discussion**

Palatal tremor (formerly called palatal myoclonus) has been subdivided into essential (EPT) and symptomatic (SPT) forms according to clinical and aetiological features (Deuschl et al., 1990). A large series reviewing palatal tremors has been published previously (Deuschl et al., 1990). From this and more recent reports, we shall very briefly review EPT and SPT before considering how PAPT differs from these.

EPT is a syndrome in which there is typically isolated rhythmic movement of the anterior soft palate, often associated with ear clicks which can be heard by the patient and examiner and without identifiable aetiology. Structural neuroimaging with MRI is normal, although hyperactivity of the region of the inferior olives has been shown by fMRI in patients who had voluntary control over their palatal tremor (Boecker et al., 1994; Nitschke et al., 2001). EPT comprises ~25% of all reported cases of palatal tremor (Deuschl et al., 1990) but the true incidence relative to SPT is unknown since a reporting bias for EPT seems likely. Palatal movement is usually the result of activity of the tensor veli palatini muscle supplied by fibres from the trigeminal nucleus. This muscle arises from the lateral wall of the Eustachian tube and its rhythmic contraction is thought to be associated with repetitive opening and closing of the Eustachian tube, leading to the clicks (Slack et al., 1986; Deuschl et al. 1991).

In SPT, there is rhythmic involuntary oscillation of the posterior soft palate, with accompanying oscillations of other branchial and ocular muscles in 60 and 30% of cases, respectively (Deuschl et al., 1990). Palatal movement is the result of levator veli palatini activity, supplied by motor fibres from the facial nucleus or nucleus ambiguous. Levator veli palatini activity is also associated with ear clicks (Jamieson et al., 1996; Fabiani et al., 2000; Erickson et al., 2002), which were found in 8% of SPT in the early review (Deuschl et al., 1990). The presence of ear clicks alone, therefore, is not a reliable indicator to classify palatal tremor as EPT or SPT.

Definable aetiologies for SPT most commonly include monophasic structural lesions of the brainstem or cerebellum. Similar to the previous review (Deuschl et al., 1990), our review of the English language literature on SPT over the last 13 years (Table 3) confirms that stroke (46%), trauma (11%), demyelinating lesions (10%) and posterior fossa tumours (6%) are the most common aetiologies. In contrast to the previous large series (Deuschl et al., 1990) in which degenerative diseases accounted for only 3% of cases of SPT, we found sporadic neurodegenerative diseases to compromise 17% of our reviewed cases. The higher incidence of progressive neurodegenerative diseases is likely to include patients in whom progressive ataxia and palatal tremor co-exist, some of whom could also possibly be classified as PAPT, in the absence of other clear aetiologies.

Cases of SPT associated with posterior fossa infarcts, haemorrhage or surgery are especially informative since, in these cases, a clear onset of pathology can be dated (Yanagisawa et al., 1999). Typically, cerebellar or brainstem syndromes are the most symptomatic feature of SPT, and early structural neuroimaging may reveal the aetiology, which is proposed to interrupt the inhibitory pathway from the dentate nucleus (via the superior cerebellar peduncle and central tegmental tract) to the contralateral inferior olivary nucleus (Lapresle, 1979). Palatal tremor typically develops 2–49 months after the initial insult (Matsuo and Ajax, 1979), although this may range from 1 month (Turazzi et al., 1977) to 8 years (Legros et al., 2001).

Typical radiological changes are associated with SPT (Goyal et al., 2000). There is an increase in T2 or proton density MRI signal within the olivary nucleus and hypertrophy of the nucleus which may be seen within 6 months of the initial insult when this was defined. Both of these changes persist for 3–4 years, although the high signal intensity may return to normal (Yanagisawa et al., 1999) (as in our case 6). It is postulated that sufficient time must elapse after the initial insult before the olives develop pseudohypertrophic degeneration which is believed to be the result of secondary, transsynaptic deafferentation and loss of the inhibitory input from the contralateral dentate nucleus. In support of this are the cases in whom the initial strokes or tumour spared the olives, but permitted a secondary olivary degeneration to occur following the onset of other clinical symptoms (Yanagisawa et al., 1999; Eggenberger et al., 2001). A recent clinicopathological study, however, demonstrated the persistence of palatal tremor despite the resolution of pseudohypertrophy and the subsequent development of atrophy of
the olives (Nishie et al., 2002). These correlations, along with
the known resolution of MRI abnormalities of the olivary
nuclei despite the persistence of SPT, question the cause and
effect relationship between pseudohypertrophy and palatal
tremor.
Recently, delayed and progressive worsening of cerebellar
function associated with SPT, secondary to identified struc
tural aetiologies (stroke, tumour and subarachnoid haemor-
rhage), has also been reported (Eggenberger et al., 2001).
The authors termed this ‘oculopalatal tremor with tardive ataxia’
(referring to its late onset, rather than to a relationship with
neuroleptic drugs). These patients could equally be classified
as PAPT syndromes with identifiable aetiologies. The
phenomenon of delayed-onset and progressive movement
disorders following a monophasic illness is rare but well
described (Louis et al., 1996; Scott and Jankovic, 1996) and
its acknowledgement should increase the realization that not
all progressive disorders arise from primary neurodegenera
tive processes. The clinical course of our patient 5 may have
suggested this possibility, although a structural causative
lesion could not be demonstrated on repeated imaging
studies. We prefer to restrict the term PAPT to a disorder of
an undetermined, presumed degenerative, aetiology (as below).

**PAPT**

Examples of degenerative progressive ataxia with palatal
tremor have been described previously, sometimes with
sparse details. The clinical spectrum of these disorders is
wide. As with other causes of progressive ataxia (Abele et al.,
2002), there are sporadic and familial cases. Our literature
review allowed us to divide previously published cases into
sporadic degenerative PAPT (Table 4) and familial PAPT
(Table 5).

**Sporadic PAPT**

Our six patients would be classified as sporadic. By
definition, PAPT patients have progressive cerebellar
features, and this may partly explain their ocular motility
signs. We have been unable to characterize any other clinical
features that are predominantly or exclusively associated with
this syndrome. None of our six patients had ear clicks. We did
not perform EMG studies to document which palatal muscles
were active, but would argue that it was more likely to have
been levator veli palatini simply because of the absence of ear
clicks.

We believe that PAPT is a progressive disorder, as
evidenced by the clinical expression of new cerebellar signs

| Table 3 Causes and associations of sporadic SPT reported since the review of Deuschl et al. (1990) |
|---------------------------------|-----------------|
| Disease                        | n               |
| Brainstem infarcts or haemorrhages | 43              |
| Severe brainstem trauma        | 10              |
| Inflammatory/demyelinating lesions (including multiple sclerosis) | 9               |
| Posterior fossa tumours or extirpation of cerebellar tumours | 6               |
| With posterior circulation abnormalities (AVM, giant aneurysm, cavernous angioma, ectatic vertebral artery) | 6               |
| Behcet’s disease               | 3               |
| With partial epileptic status syndromes | 3               |
| Progressive supranuclear palsy  | 2               |
| Coeliac disease                | 2               |
| Sporadic disease with Rosenthal fibres | 2               |
| Krabbe disease                 | 1               |
| Cerebrotendinous xanthomatosis  | 1               |
| Hashimoto’s encephalitis       | 1               |
| Serum IgM abnormalities        | 1               |
| Antibodies to GAD               | 1               |
| Lipomembranous osteodysplasia   | 1               |
| Interstitial lymphoma          | 1               |
| Associated with fluoxetine*     | 1               |

n = number of cases; AVM = arteriovenous malformation; GAD = glutamic acid decarboxylase; *resolved on stopping fluoxetine. Normal imaging.
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex/age(^a) (years)</th>
<th>Duration (years)</th>
<th>Frequency of palatal tremor (Hz)/other cranial movements</th>
<th>Ocular disorders</th>
<th>Cerebellar disorder</th>
<th>Other disorders</th>
<th>Investigations and authors’ conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Nathanson (1956) Patient 5</td>
<td>F70</td>
<td>2–3</td>
<td>2.3–2.5 Hz/lower lip, head, neck, larynx, arms 1.87 Hz/pharynx</td>
<td>‘Cogwheel type of movement on pursuit’ Gaze-evoked nystagmus Spontaneous vertical and horizontal gaze-evoked nystagmus, torsional component</td>
<td>Dysarthria, ataxic limbs Dysarthria, gait and limb ataxia Dysarthria, ataxic limbs and gait</td>
<td>Parkinsonism?, dysphagia Hyper-reflexia, Babinski sign</td>
<td>‘Probably degenerative’* ‘Idiopathic’</td>
</tr>
<tr>
<td>2 Nathanson (1956) Patient 11</td>
<td>F56</td>
<td>3</td>
<td>1.87 Hz/pharynx</td>
<td>Upbeat nystagmus, OKN absent, ocular dysmetria, intermittent exotropia</td>
<td>Dysarthria, ataxic limbs, left limbs jerking</td>
<td>Dysphagia</td>
<td>Cerebellar atrophy on pneumo-encephalography</td>
</tr>
<tr>
<td>3 Herrmann and Brown (1967) Patient 3</td>
<td>M35</td>
<td>15</td>
<td>2.3 Hz/pharynx, larynx</td>
<td>‘Eyes’</td>
<td>Dysarthria, ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 Tahmoush et al. (1972) Patient 2</td>
<td>M53</td>
<td>3–4</td>
<td>2–2.3 Hz/head, larynx, pharynx, vocal cords</td>
<td>Horizontal pendular nystagmus</td>
<td>Dysarthria, ataxia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Kawahira and Minauchi (1976)</td>
<td>M16</td>
<td>Present/larynx</td>
<td>Nystagmus</td>
<td>Ataxic limbs, dysarthria, Ataxic trunk and limbs</td>
<td>Areflexia, distal atrophy Autonomic failure, dementia, Babinski Pseudobulbar palsy, bilateral Babinski, aphthous stomatitis Pseudobulbar palsy, spastic paraplegia</td>
<td>OPCA **</td>
<td></td>
</tr>
<tr>
<td>6 Ohsumi et al. (1982)</td>
<td>M33</td>
<td>2.6–3 Hz/larynx</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CSF and EEG normal *</td>
</tr>
<tr>
<td>8 Nagaoka and Narabayashi (1984) Patient 2</td>
<td>F45</td>
<td>9</td>
<td>Present/nil reported</td>
<td>Horizontal pendular nystagmus</td>
<td>Dysarthria, ataxia</td>
<td></td>
<td>CT: atrophy pons, midbrain and cerebellum. SCD+</td>
</tr>
<tr>
<td>9 Gomi et al. (1985)</td>
<td>M41</td>
<td>Present/larynx</td>
<td>See-saw nystagmus, alternating deviation</td>
<td></td>
<td>Dysarthria, ataxia</td>
<td></td>
<td>CSF and EEG normal *</td>
</tr>
<tr>
<td>10 Sperling and Herrmann (1985) Patient 1</td>
<td>F40</td>
<td>8</td>
<td>1.3 Hz/buccal area</td>
<td>Normal</td>
<td>Dysarthria, ataxia gait &gt; limbs</td>
<td>Emotional lability, hyperactive reflexes, treated hypertension</td>
<td>CT cerebellar atrophy, white matter lucency</td>
</tr>
<tr>
<td>11 Sperling and Herrmann (1985) Patient 2</td>
<td>F60</td>
<td>3</td>
<td>1.2 Hz/lower eyelid, chin, larynx, diaphragm</td>
<td>Upbeat and torsional nystagmus</td>
<td>Dysarthria, ataxic limbs</td>
<td>Ear clicks, SHL since childhood</td>
<td>MRI* olivary hypertrophy and ↑ olivary signal Cerebellar degeneration+</td>
</tr>
<tr>
<td>12 Jankovic and Pardo (1986)</td>
<td>68F</td>
<td>Present/diaphragm and abdomen</td>
<td></td>
<td></td>
<td>‘Cerebellar degeneration’</td>
<td>Emotional lability, dysphagia, amyotrophy, fasciculations, hyper-reflexia, Babinski</td>
<td>Normal CT and EEG</td>
</tr>
<tr>
<td>13 Leger et al. (1986)</td>
<td>M51</td>
<td>1</td>
<td>2 Hz/nil</td>
<td>Normal</td>
<td>Dysarthria, ataxic limbs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 Schmidley (1986)</td>
<td>M44</td>
<td>4</td>
<td>2.2 Hz/pharynx</td>
<td>Normal</td>
<td>Dysarthria, ataxic limbs</td>
<td></td>
<td>CT: choroid plexus calcified. MRI: enlarged 4th ventricle and white matter changes</td>
</tr>
<tr>
<td>Reference</td>
<td>Sex/agea (years)</td>
<td>Duration (years)</td>
<td>Frequency of palatal tremor (Hz)/other cranial movements</td>
<td>Ocular disorders</td>
<td>Cerebellar disorder</td>
<td>Other disorders</td>
<td>Investigations and authors’ conclusions</td>
</tr>
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</tr>
<tr>
<td>15 Sasaki et al. (1987) Patient 1</td>
<td>M42 9</td>
<td>3 Hz/tongue, diaphragm shoulders, arms, legs</td>
<td>Saccadic pursuit, horizontal gaze-evoked nystagmus,</td>
<td>Dysarthria, ataxic limbs</td>
<td>Rigidity, hypokinesia, autonomic failure, hyper-reflexia, Babinski</td>
<td>CT: atrophy of brainstem and cerebellum. “Likely OPCA”</td>
<td></td>
</tr>
<tr>
<td>16 Yokota et al. (1989b) Patient 4</td>
<td>F38 5–6</td>
<td>Present/pharynx, larynx, diaphragm</td>
<td>Nystagmus</td>
<td>Dysarthria, ataxia</td>
<td>Bilateral pyramidal signs, urinary incontinence</td>
<td>MRI brainstem and cerebellar atrophy</td>
<td></td>
</tr>
<tr>
<td>17 Elble (1991)</td>
<td>F66 8</td>
<td>Present/postural tremor</td>
<td>Slow saccades</td>
<td>Dysarthria, limb and trunk ataxia</td>
<td>MRI olivary hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 Deuschl et al. (1994) Patient 5</td>
<td>M73 &gt;3</td>
<td>Present/nil reported</td>
<td>Vertical binocular pendular nystagmus</td>
<td>Dysarthria, ataxic limbs</td>
<td>MRI cerebellar and medulla atrophy. Increased T2 medullary signal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>19 Davenport et al. (1995) Patient 1</td>
<td>41</td>
<td>Present/orbicularis oculi, larynx, pharynx, platysma</td>
<td>Nystagmus</td>
<td>Dysarthria, ataxia</td>
<td>5th, 7th, 9th, 10th nerve palsies, dysphagia</td>
<td>MRI olivary signal and ventricular dilatation</td>
<td></td>
</tr>
<tr>
<td>20 Davenport et al. (1995) Patient 2</td>
<td>45</td>
<td>Present/orbicularis oculi, larynx, pharynx, platysma</td>
<td>Nystagmus</td>
<td>Dysarthria, ataxia</td>
<td>MRI olivary signal and hypertrophy, cerebellar atrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>21 Kulkarni et al. (1999)</td>
<td>M40 8</td>
<td>Present/head tremor</td>
<td>Horizontal and upbeat nystagmus, bilateral 6th nerve palsies, left 3rd nerve palsy</td>
<td>Dysarthria, trunk &gt; limb ataxia, intention tremor</td>
<td>MRI olivary signal and hypertrophy, cerebellar atrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22 Phanthumchinda (1999)</td>
<td>M46 5</td>
<td>Present/tongue</td>
<td>Ataxic limbs and trunk</td>
<td>Spasticity of the legs</td>
<td>MRI olivary signal and hypertrophy, cerebellar atrophy</td>
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**Table 4 Continued**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex/agea (years)</th>
<th>Duration (years)</th>
<th>Frequency of palatal tremor (Hz)/other cranial movements</th>
<th>Ocular disorders</th>
<th>Cerebellar disorder</th>
<th>Other disorders</th>
<th>Investigations and authors’ conclusions</th>
</tr>
</thead>
</table>

*At presentation. F = female; M = male; empty cells = information not available; OKN = optokinetic nystagmus; SHL = sensorineural hearing loss; SCD = spinocerebellar degeneration; “possible OPCA without pathological verification. *Japanese abstracts as quoted in Sasaki et al. (1987).*
<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex/age (years)</th>
<th>Duration (years)</th>
<th>Palatal tremor (Hz)/other cranial findings</th>
<th>Ocular disorders</th>
<th>Cerebellar disorder</th>
<th>Other disorders</th>
<th>Investigations</th>
<th>Authors' diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Pogacar et al. (1978)</td>
<td>F18</td>
<td>7</td>
<td>Present/nil</td>
<td>Anisocoria, gaze-evoked nystagmus with torsional component, alternating exotropia</td>
<td>Dysmetria, ataxic limbs</td>
<td>Dementia, optic atrophy, facial diplegia, hyper-reflexia</td>
<td>EEG, CSF, brain scan normal.</td>
<td></td>
</tr>
<tr>
<td>2 Masucci et al. (1984)</td>
<td>M22</td>
<td>19</td>
<td>Present/head</td>
<td>'Eye movement'</td>
<td>Dysphagia, ataxic limbs and trunk</td>
<td>Right hemibody myorhythmia</td>
<td>Atrophy of olives, dentate, pons, cerebellar peduncles MRI: medullary, cerebellar and cervical cord atrophy</td>
<td>Autopsy-proven OPCA in mother</td>
</tr>
<tr>
<td>3 de Yebenes et al. (1988)</td>
<td>F46</td>
<td>Present/bulbar palsy</td>
<td>Gaze-evoked horizontal rotatory nystagmus</td>
<td>Dysarthria, dysphagia ataxic gait</td>
<td>Dysarthria, vertigo</td>
<td>Dysphonia, deafness, spastic paraparesis, hyper-reflexia, Babinski</td>
<td>MRI: cervical cord, medullar, callosal and cerebellar atrophy. Putamen high signal, Ventricular dilatation.</td>
<td>'Elusive'</td>
</tr>
<tr>
<td>4 de Yebenes et al. (1988)</td>
<td>M37</td>
<td>5</td>
<td>2 Hz/tongue, face, pharynx, neck</td>
<td>Gaze-evoked horizontal rotatory nystagmus</td>
<td>Dysarthria, vertigo</td>
<td>Dysphonia, deafness, spastic paraparesis, hyper-reflexia, Babinski</td>
<td>MRI: cervical cord, medullar, callosal and cerebellar atrophy. Putamen high signal, Ventricular dilatation.</td>
<td>'Elusive'</td>
</tr>
<tr>
<td>5 Howard et al. (1993)</td>
<td>F25</td>
<td>2-3</td>
<td>Present</td>
<td>Bilateral internuclear ophthalmoplegia, saccadic pursuit, horizontal and rebound nystagmus</td>
<td>Dysarthria, ataxic limbs and gait</td>
<td>Dysphonia, dysphagia, tongue fasciculation, tetraparesis, incontinence</td>
<td>MRI: pontine high signal, spinal cord atrophy, Rosenhau fibres on muscle biopsy</td>
<td>'Alexander’s disease seems inappropriate'</td>
</tr>
<tr>
<td>6 Howard et al. (1993)</td>
<td>M27</td>
<td></td>
<td>Present/tongue, sternocleidomastoid</td>
<td>Horizontal nystagmus</td>
<td>Dysarthria, ataxic limbs</td>
<td>Dysphonia, dysphagia, tongue fasciculation, tetraparesis, incontinence</td>
<td>CT: brainstem atrophy, myelogram- cervical cord atrophy</td>
<td>'Alexander’s disease seems inappropriate’</td>
</tr>
<tr>
<td>7 Schwankhaus et al. (1995)</td>
<td>F43</td>
<td>6.5</td>
<td>2.2 Hz/nil</td>
<td>Saccadic pursuit, slow saccades, gaze-evoked nystagmus</td>
<td>Dysarthria, ataxic limbs</td>
<td>Spastic tetraparesis, incontinence</td>
<td>MRI: atrophic brainstem, cervical cord, cerebellum</td>
<td>Adult-onset Alexander’s disease</td>
</tr>
<tr>
<td>9 Schwankhaus et al. (1995)</td>
<td>F47</td>
<td>2</td>
<td>Present/nil</td>
<td>Saccadic pursuit, slow saccades, gaze-evoked nystagmus</td>
<td>Dysarthria, ataxic gait, intention tremor</td>
<td>Ear clicks, spastic speech, weak deltoid, Babinski, hyper-reflexia</td>
<td>Autopsy: mild cortical atrophy, cervical cord atrophy, cell loss in cerebellum, pontine gliosis</td>
<td>Adult-onset Alexander’s disease</td>
</tr>
</tbody>
</table>
Table 5 Continued

<table>
<thead>
<tr>
<th>Reference</th>
<th>Sex/age (years)</th>
<th>Duration (years)</th>
<th>Palatal tremor (Hz)/other cranial findings</th>
<th>Ocular disorders</th>
<th>Cerebellar disorder</th>
<th>Other disorders</th>
<th>Investigations</th>
<th>Authors’ diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 Okamoto et al. (2002), Patient 2</td>
<td>F27</td>
<td>10</td>
<td>Present/nil</td>
<td>Gaze-evoked nystagmus</td>
<td>Ataxic limbs and gait</td>
<td>Dysphonia, hyper-reflexia, weak legs, Babinski</td>
<td>MRI: white matter lesions, atrophic pons, medulla, cervical cord, cerebellum, corpus callosum</td>
<td>“Familial palatal myoclonus and cord atrophy”. V87G GFAP mutation</td>
</tr>
</tbody>
</table>

*At presentation; OPCA = olivopontocerebellar atrophy; GFAP = glial fibrillary acidic protein; SCA = spinocerebellar ataxia; PP = proprioception.
and increase in severity of cerebellar dysfunction with time (Table 2). Accepting that our work is retrospective, it is limited by incomplete documentation in some instances, dating back several years. Additionally, patients who attend a family physician or neurologist with cerebellar symptoms may not always be examined for palatal tremor unless the examining physician is aware of this sign. Hence, our retrospective analysis may not have documented accurately the precise timing of onset of palatal tremor in the course of the illness, especially because palatal tremor in PAPT is not associated with ear clicks (which can sometimes be used to date the onset of palatal tremor in EPT).

In future, it could be possible to document clinical milestones in patients in whom a diagnosis of PAPT is made. From our experience, the features which are most problematic in PAPT include the developments of: (i) visual disturbance, e.g. oscillopsia, diplopia; (ii) dysarthria; (iii) dysphagia; (iv) arm ataxia; (v) difficulty in walking; (vi) difficulty in standing; (vii) use of a wheelchair; and (viii) other neurological system failures, sometimes associated with cerebellar syndromes but not directly due to cerebellar failure (e.g. incontinence, peripheral neuropathy). Other features which can be objectively measured may, however, be less symptomatic (e.g. nystagmus, loss of VOR, MRI evidence of cerebellar atrophy) and these findings could also be used as milestones. However, not all institutions may have facilities to document these objectively and a pragmatic clinical set of milestones may be more useful. In SPT, 77% of cases of the early review (Deuschl et al., 1990) and 79% of our reviewed cases over the last 13 years (Table 3) followed a unique cerebral insult with a generally monophasic and non-progressive course (stroke, trauma, tumour, encephalitis). In contrast to both SPT and to cases of ‘tardive ataxia’ associated with palatal tremor (Eggenberger et al., 2001), the presumed degenerative forms of PAPT have no identifiable insult, but cerebellar ataxia and atrophy progress over years (e.g. Table 2 and Fig. 1F–H). This is the most symptomatic feature of the disorder.

In our cases and from the literature review of 22 cases of presumed sporadic degenerative PAPT, the aetiology is typically unidentified (Table 4). Only four cases may have had an identified aetiology (treated hypertension, alcohol-related, Behcet’s disease and anti-gliadin antibodies). Three of our cases had treated hypertension and one had previous high alcohol consumption, although he had been abstinent for 3 years before symptom onset. Some of the other reported cases of sporadic PAPT (cases 8, 15, 16, 19 and 20 from Table 4) had brainstem and cerebellar atrophy on structural imaging (without other more specific findings), compatible with a diagnosis of ‘olivopontocerebellar atrophy’ (OPCA). It is possible that cases 2, 5 and 12 in Table 4 also represent OPCA. The true incidence of palatal tremor in OPCA is, however, unknown. Noda et al. (1993) reported only one case of palatal tremor from 139 cases diagnosed as having OPCA (Japanese literature). Typical OPCA is not associated with palatal tremor or MRI olivary changes, but limited clinical, neuroimaging and pathological studies are available. Complicating this issue is the heterogeneous nature of the disorders grouped together under the umbrella term OPCA. ‘Sporadic OPCA’ excludes cases now referred to as hereditary spinocerebellar atrophy (SCAs) but includes cases of the cerebellar form of ‘multiple system atrophy’ (MSA-c) (Gilman et al., 1999). To our knowledge, no case of pathologically proven OPCA or MSA-c has been associated with palatal tremor. Given these limitations, a single theory unifying the aetiologies of sporadic PAPT seems unlikely.

**Ocular motility findings.** Palatal tremor is often associated with synchronous eye movements which have been termed oculopalatal tremor (OPT) (oculopalatal myoclonus is an older term). From our cases (case 2) and Table 4, four patients had features consistent with typical OPT [case 3 (Herrmann and Brown, 1967), case 11 (Averbuch-Heller et al., 1995) and case 18 (Deuschl et al., 1994); the case of Averbuch-Heller is also described as case 2 of Sperling and Herrmann (1985)].

In OPT, the ocular movements can be vertical and pendular or horizontal and torsional (Yap et al., 1968; Chokroverty and Barron, 1969; Tahmoush et al., 1972; Nakada and Kwee, 1986; Yokota et al., 1989a, 1999; Chang et al., 1990; Massry and Chung, 1994; Talks and Elston, 1997; Wu et al., 2000; Cackett et al., 2002). OPT has been subdivided into midline and lateral forms (Nakada and Kwee, 1986). The midline form is characterized by vertical, primarily pendular, oscillations and symmetrical bilateral palatal tremor. The lateralized form has jerk nystagmus with oblique and rotatory components and unilateral palatal tremor. Unlike our case 2, patients with lateralized OPT have not had clinically progressive cerebellar degeneration (Nakada and Kwee, 1986). However, from these small numbers, it is unclear whether ocular motor abnormalities can be used to subclassify PAPT, and PAPT cannot be differentiated from other causes of palatal tremor on the basis of these without progressive cerebellar degeneration.

Two non-specific ocular movement abnormalities common to our patients were hypermetric saccades (Fig. 2C) and saccadic pursuit. Two of our patients also had INO (Fig. 2D), implicating a lesion of the medial longitudinal fasciculus of the brainstem. We believe it unlikely that these patients had additional aetiologies for these lesions and we suggest that the ocular motility abnormalities of PAPT extend beyond the cerebellum, to include the brainstem.

The specific role of the dentate nucleus (part of ‘Mollaret’s triangle’ implicated in SPT) and its relationship in OPT is unclear. Dentate neurons send axons to the contralateral inferior olive via the descending branch of the superior cerebellar peduncle. Olivary climbing fibres return to all parts of the cerebellar cortex in a topographical manner (Blanks, 1988). These pathways may provide a route by which dentate dysfunction may be hypothesized to lead to olivary and cerebellar cortical dysfunction, ultimately leading to ocular motor abnormalities.
Progressive ataxia–palatal tremor–eye movement

Hearing. Four of our patients had hearing-related findings: patients 1 and 2 had tinnitus, patient 6 had a family history of early-onset deafness, and patient 3 had sensorineural hearing loss and a history of noise exposure. One patient from our review of sporadic cases had sensorineural deafness. We are unaware of a relationship between progressive ataxia, palatal tremor and hearing loss, though this combination could suggest a mitochondrial or a complex brainstem disorder. In support of this is the finding of abnormal auditory evoked potentials despite normal pure tone audiometry in SPT (Kurauchi et al., 1996). At the time of presentation of our patients, it was only possible partially to investigate mitochondrial disorders. We would now consider investigations of mitochondrial cytopathies for patients with this combination of signs.

Neuroradiology. Our patients with PAPT all showed increased signal intensity on proton density- or T2-weighted MRI, and five out of six showed olivary hypertrophy. These findings are typical of SPT. This contrasts with seven out of 11 cases from the reported literature on sporadic PAPT (Table 4) who had MRI. Why the other four cases from the literature did not have the typical MRI changes is unclear. This may have been due to the MRI sequences used or the experience of the radiologists. Olivary signal abnormalities are present for a fraction of time during the course of the illness (Goyal et al., 2000) and so MRI outside this time frame may not detect the typical changes. Finally, as in EPT and familial PAPT, palatal tremor occurs in the presence of normally appearing olives, and so functional (as opposed to structural) mechanisms may be part of the PAPT syndrome.

Familial PAPT

We are unaware of palatal tremor having been associated previously with a mitochondrial cytopathy or a defined recessively or dominantly inherited cerebellar ataxia including all the established SCAs. At the time of presentation, we were able to exclude known dominant, recessive and mitochondrial mutations in our cases 1, 4 and 6, in which we felt it appropriate to undertake these investigations.

Review of the literature revealed full reports on 11 patients in six publications in whom familial PAPT was described (Table 5). Clinically, nine of these patients had brainstem atrophy (medulla more than pons), nine had atrophy of the cervical cord, eight had cerebellar atrophy and seven had signs of corticospinal tract dysfunction. Unlike SPT and sporadic PAPT, no patient with familial PAPT had olivary hypertrophy. The mechanisms underlying palatal tremor in the familial PAPT syndromes currently remain unknown.

In five of these families, it is likely that the disorder was autosomal dominant (Pogacar et al., 1978; de Yebenes et al., 1988; Howard et al., 1993; Schwankhaus et al., 1995; Okamoto et al., 2002). In three families, Rosenthal fibres were detected on autopsy or brain biopsy (Howard et al., 1993; Schwankhaus et al., 1995; Okamoto et al., 2002), raising the possibility of adult-onset Alexander’s disease. Palatal tremor has now also been described in two cases of sporadic juvenile and adult-onset disease associated with Rosenthal fibres and demyelination (Table 3). Rosenthal fibres are astrocytic intracytoplasmic inclusions which are characteristic, but not pathognomonic, of Alexander’s disease. They have been described in glial scars adjacent to multiple sclerosis plaques, syrinxes, central pontine myelolysis, pilocytic astrocytomas, ‘parkinsonism’ (not otherwise characterized) and asymptomatic adults (Goldman and Corbin, 1988; Riggs et al., 1988; Friedman and Ambler, 1992; Schwankhaus et al., 1995). They stain positively for glial fibrillary acidic protein (GFAP), a filament protein specific for mature astrocytes. Heterozygous mutations in the GFAP gene have been described in the juvenile form of Alexander’s disease (Brenner et al., 2001) and more recently a novel heterozygous amino acid substitution was detected in the family with adult-onset Alexander’s disease, manifesting as an autosomal dominant disease of palatal tremor, cerebellar signs, pyramidal tract degeneration with medullary and cervical cord atrophy (Okamoto et al., 2002). No pathological specimens were available from this family, but the marked clinical and radiological similarity with the other cases of familial PAPT (Table 5) raises the possibility of Alexander’s disease as the diagnosis in these cases and suggests that similar presentations should be screened for GFAP mutations in future.

Very recently, two other familial syndromes of palatal tremor have been reported. Ten members of an Anglo-Celtic pedigree in Australia were described with autosomal dominant, slowly progressive, almost pure cerebellar ataxia, palatal tremor and dysphonia. Genetic testing for SCA 1–17 mutations was negative. CT scans showed dentate and pallidal calcification. MRI showed cerebellar atrophy and a dark dentate signal, leading the authors to term this syndrome ‘dark dentate disease’ (DDD) (Storey et al., 2002).

Dark dentate signal, presumably due to excessive iron accumulation in the dentate and basal ganglia, was associated with dyskinesia, cognitive decline and palatal tremor in a patient with autosomal dominant neuroferritinopathy due to a mutation in the ferritin light chain gene (Wills et al., 2002). Although this patient had no ataxia or olivary hypertrophy, it is possible that palatal tremor was the result of dentate dysfunction secondary to iron deposition.

Treatment

There is no known effective treatment for the progressive ataxia, which is the most disabling symptoms of PAPT. The palatal tremor is seldom symptomatic, unlike in EPT where bothersome continuous ear clicks often require treatment. In none of our patients was specific treatment for palatal tremor considered necessary.
Conclusion

Sporadic and familial forms of PAPT represent a heterogeneous group of disorders. Features of sporadic PAPT include progression of ataxia, oligivary degeneration, saccadic pursuit, hypermetric saccades, gaze-evoked nystagmus, vertical pendular nystagmus and INO. Sporadic PAPT is a subgroup of SPT, in which the cerebellar syndrome progresses gradually and is not the result of a monophasic illness. Cases of ‘tardive ataxia’ with palatal tremor might be confused with the sporadic PAPT, but have an interval between a monophasic illness and worsening of ataxia or emergence of palatal tremor.

Familial PAPT does not exhibit the MRI abnormalities of olivary hypertrophy which are common to SPT and sporadic PAPT, but is more often associated with brainstem and cervical cord atrophy, and some cases may be related to Alexander’s disease.

The underlying mechanisms of palatal oscillations in EPT, SPT, sporadic PAPT and familial PAPT remain unknown, but these observations suggest that patients with palatal tremor could be classified into four categories. It is likely that some difficulty in classification will remain due to heterogeneity of the disorders (e.g. Bharucha and Sethi, 1996; Jamieson et al., 1996; Cho et al., 2001; Eggenberger et al., 2001; Lang, 2001). This difficulty in classification is likely to persist until new improved pre-mortem diagnostic tools are developed and post-mortem data are available to better define the current categories.

Acknowledgements

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Blanks R. Cerebellum. In: Buttner-Ennever JA, editor. Neuroanatomy of the cerebellum atrophy, and some cases may be related to Alexander’s disease.


