probably do not contribute as our clinical test of saccular and otolithic function was normal.

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doi: 10.1136/jnnp.2006.106179

Competing interests: None.

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The syndrome of (predominantly cervical) dystonia and cerebellar ataxia: new cases indicate a distinct but heterogeneous entity

Patients displaying a slowly progressive syndrome combining dystonia and cerebellar ataxia are relatively rare and can cause considerable diagnostic uncertainty. The main differentials in these cases are the genetic spinocerebellar ataxias (SCAs), in which dystonia can be observed and can even be the presenting feature.¹ We recently reported five patients with mainly cervical dystonia (torticollis) and cerebellar ataxia in whom common SCA mutations were excluded and no definite cause was established.² Here, we report six further patients.

Case histories

Case 1

This 58-year-old man of Indian ethnicity presented with gait unsteadiness at age 54 years. Family history was negative. Symptoms were slowly progressive, but after 3 years (without neuroleptic exposure) blepharospasm developed and after 1 year involuntary movements of the jaw, lower face and neck developed. Examination at age 58 years showed blepharospasm, gaze-evoked nystagmus, hypermetric saccades, dystonic facial grimacing and tongue protrusion, cerebellar dysarthria, torticollis to the right, gait and

appendicular ataxia, hyper-reflexia and extensor plantar responses.

Cases 2 and 3

At age 24 years, this now 50-year-old woman developed posturing and jerky movements of her right shoulder. She subsequently developed unsteadiness of gait, episodic dizziness and slurred speech. Currently, examination reveals mild limitation of upgaze, jerky pursuit, hypometric saccades, slow tongue movements, marked cerebellar dysarthria, mild limb ataxia, ataxic gait and increased tone in all limbs but no pyramidal signs. She also has left torticollis with right laterocollis and dystonic posturing of the right shoulder/arm and leg.

Her 29-year-old son presented with a head tremor and tremulous speech at age 21 years. At age 29 years, he displayed mild gaze-evoked nystagmus to the left, hypermetric saccades, slow tongue movements, equivocal slurred speech, torticollis to the right with a high-frequency side-to-side tremor, mild dysidiadochokinesis on the left and hyper-reflexia. His gait was normal.

Further family history was negative.

Case 4

This 44-year-old woman developed balancing difficulties 5 years ago, followed by some falls. A cerebellar syndrome and laryngeal dystonia were noted, and the latter was treated with botulinum toxin injections. Family history was negative. Two years after onset, she had jerky pursuit, cerebellar dysarthria, torticollis to the right with left laterocollis, anteroposition of the left shoulder, mild dystonic posturing of the hands, gait and limb ataxia, mildly increased tone in all extremities, hyper-reflexia and extensor plantar responses.

Case 5

A 23-year-old man noticed the gradual onset of head turning at age 21 years. Family history was negative. He had recently developed balancing difficulties, loss of dexterity and slurred speech. A trial of levodopa proved ineffective. Examination revealed normal eye movements, a right torticollis, mild posturing of the right arm, cerebellar dysarthria, and mild gait and limb ataxia.

Case 6

This 58-year-old Ashkenazi Jewish woman, with a negative family history, first developed symptoms of writer's cramp and balance problems at age 8 years. Over the years, symptoms have been slowly progressive. A recent examination revealed jerky pursuit, gaze-evoked nystagmus, dysmetric saccades, cerebellar dysarthria, left torticollis with a side-to-side tremor, gait and limb ataxia, some choreo-athetoid movements of the hands, normal tendon reflexes and flexor plantar responses.

Auxiliary investigations

All patients tested negative for SCA1/2/3/6/7 mutations. In addition, negative investigations in most of the patients included acanthocytes, thyroid function, vitamin E, coeliac screen, copper studies and white cell enzymes. Additional negative investigations were the torsion dystonia gene DYT1, dentatorubropallidolusian atrophy and SCA12 genes (cases 2 and 3), SCA17 (cases 1 and 2), mitochondrial mutations 3243/8344/8993 (case 2),

Figure 1 T2-weighted craniocervical MRI of case 2 showing marked midline cerebellar atrophy with preserved brainstem structures (video supplement is available at <http://jnnp.bmj.com/supplemental>).

Huntington's disease gene (case 3), α -feto-protein (case 3), antineuronal antibodies (cases 1 and 6), bone marrow biopsy (case 2), and nerve conduction studies and electromyography (case 3).

Discussion

We have reported six new patients displaying a combination of dystonia and cerebellar ataxia, with age at onset varying from 8 to 54 years (table 1). Family history was negative in four cases, but indicated autosomal dominant or possibly mitochondrially inherited disease in two patients (cases 2 and 3). These six new cases resemble the five cases we reported previously.² Similar to these earlier reported cases, the dystonia mainly affected the cervical region. However, laryngeal adductor dystonia was the presenting feature in one patient, who only later developed neck and arm dystonia. In addition, severe cranial dystonia was observed in another patient, and in one, the dystonia was more generalised (case 2). Again, the cerebellar ataxia in these cases was relatively mild and always slowly progressive, particularly in the young-onset cases. In most patients, the dystonia was more prominent than the cerebellar ataxia.

Many diseases can cause a clinical picture of dystonia and cerebellar ataxia. However, except for the genetic ataxias, this particular combination as a pure mix seems to be rare in other sporadic/degenerative diseases, most of which can be distinguished by typical clinical, imaging or laboratory characteristics.

Dystonia, with occasional cervical predominance, has been observed in many of the dominant and recessive ataxias.¹ Although many of the recessive ataxias have not formally been excluded in the patients reported here, we consider that the known recessive ataxia genes are less likely to be the cause in these cases as they are usually characterised by additional distinctive features (such as oculomotor apraxia, overt peripheral neuropathy or spastic ataxia, which were all absent) and a more progressive disease course.

With new cases and families reported, new gene mutations will eventually be identified and may be more likely in the clearly dominant cases. In the "non-familial" young-onset cases, both recessive and dominant genes with incomplete penetrance are possible. Although most of the known SCA genes are thought to be fully penetrant, dystonia genes—for example, the torsion dystonia gene—can have low

Table 1 Disease characteristics of the six patients

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sex/age (years)	M/58	F/50	M/29	F/44	M/23	F/58
Age at onset (years)	54	24	21	39	21	8
Family history	—	AD	AD	—	—	—
Presentation	CA	Dystonia	Dystonia	CA	Dystonia	CA/dystonia
Dystonia						
Cranial	+	—	—	+	—	—
Cervical	+	+	+	+	+	+
Axial	—	+	—	—	—	—
Brachial	—	+	—	+/-	—	+
Crural	—	+	—	—	—	—
Cerebellar signs						
Eyes	+	+	+	+	—	+
Speech	+	+	+/-	+	+	+
Gait	+	+	—	+	+/-	+
Arms	+	+	+	+	+	+
Legs	+	+	—	+	+	+
Ataxia disease stage	1	1	1	1	1	1
MRI of the brain						
Cerebellar atrophy	Mild/global	Severe/global (fig 1)	Severe/global	Normal	Moderate/global	Moderate/global
Brainstem	Mild atrophy	Normal	Normal	Normal	Normal	Normal
Basal ganglia	Normal	Normal	Normal	Normal	Normal	Normal
White matter	Normal	Normal	Normal	Normal	Normal	Normal

AD, autosomal dominant; CA, cerebellar ataxia; F, female; M, male; +, positive or present; —, negative or absent; +/- subtle or equivocal.

Ataxia disease stages includes scores 0 (no ataxia), 1 (ataxia, but walking independently), 2 (permanently dependent on walking aids), 3 (permanently dependent on wheelchair) and 4 (death).³

penetrance.⁴ Patients with sporadic late-onset disease, such as case 1, might represent variants of idiopathic late-onset cerebellar ataxias or late-onset primary dystonias.

In conclusion, we present six new patients with a combination of slowly progressive cerebellar ataxia and dystonia, which clinically seems to represent a separate entity, not explained by the known ataxia genes. The wide range in age at onset and variable family history suggest a heterogeneous background, probably including yet unidentified genetic conditions. However, a single causative gene mutation with variable penetrance and expression cannot be excluded.

Acknowledgements

BPCvdW was supported by grants from the Niels Stensen Foundation and the Dr Jan Meerwaldt Foundation and SAS was supported by the Brain Research Trust. We also thank the NHNN diagnostic DNA laboratory. PG and NWW acknowledge the support of EUROSCA.

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Informed consent was obtained for publication of the patients' details in this report.

doi: 10.1136/jnnp.2006.105841

Competing interests: None declared.

Supplementary video is available at <http://jnnp.bmj.com/supplemental>

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Paraneoplastic cerebellar degeneration and anti-Yo antibodies in a man with prostatic adenocarcinoma

Paraneoplastic cerebellar degeneration (PCD) is a heterogeneous group of disorders characterised by the subacute onset of a cerebellar syndrome in patients with cancer. Although PCD may occur in patients with a variety of cancers with or without autoantibodies, it is most commonly associated with ovarian or

breast tumours in women seropositive for anti-Yo antibodies. Anti-Yo antibodies bind to protein antigens of 34 and 62 kDa, respectively, found exclusively in the cytoplasm of Purkinje cells. Morphological studies have revealed loss of Purkinje cells accompanied by relatively few or absent inflammatory changes.¹ We present a case of a man with a subacute cerebellar syndrome in whom further diagnostic workup disclosed prostatic adenocarcinoma (PA) and anti-Yo antibodies. Furthermore, the PA showed expression of Yo antigen. Therefore, this case represents simultaneously the first case of PCD associated with PA as well as the fifth case of anti-Yo positive PCD in a male patient.

Case report

A 79-year-old, previously healthy man presented with a 6 month history of disequilibrium that had aggravated in the past 10 days. Neurological examination revealed a cerebellar syndrome with unsteadiness of stance and gait, scanning dysarthria, nystagmus and saccadic dysmetria, and dysidiadochokinesis. Both MRI and CT of the brain were unremarkable. Apart from oligoclonal bands, examination of CSF was normal. Routine laboratory analysis revealed elevated serum levels of prostate specific antigen (174 µg/l; normal <4.2 µg/l). In core biopsies of the prostatic gland, the diagnosis of adenocarcinoma was made. Further laboratory studies detected anti-Yo-antibodies both in the patient's serum and in CSF (fig 1A) by western blot analysis using recombinant Yo transferred to nitrocellulose and blotted against the patient's serum (standard dilution 1:100) and CSF (standard dilution 1:1). Anti-Hu and anti-Ri antibodies were not detected. The clinical status of the patient deteriorated rapidly over the following days and he died a week after admission of acute heart failure. Autopsy revealed prostatic neoplasm, metastasised to the regional lymph nodes and the osseous system. No concurrent secondary tumour was identified after