

SHORT REPORT

Clinical features and natural history of axial predominant adult onset primary dystonia

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Abstract

The clinical features and natural history of 18 patients with adult onset axial predominant severe truncal primary dystonia are presented. The mean age of onset was 41 (42 for men, 39 for women) and there was a higher proportion of men (10:8). Analysis of their clinical features and follow up over three to five years or more showed that these patients generally conform to the characteristics of other types of adult onset primary dystonias. They tended to remain focal although there could be an initial contiguous spread, sometimes beginning in the craniocervical region and spreading axially or, rarely, vice versa. If spread occurred, involvement of the head, neck, and arms was mild in comparison with the severe dystonia of the trunk. However, in none of the patients with craniocervical or truncal onset did the dystonia spread to involve the legs. More than a third (seven of 18) of the patients had a prior history of injury at the site subsequently affected by dystonia. Treatment response to various drugs overall was poor but a third of the patients improved on treatment either with triple therapy (a combination of tetrabenazine, pimozide, and an anticholinergic drug) or high dose anticholinergic drugs alone. Severe depression occurred in 33% of patients, mainly due to the negative personal image arising from their disfiguring dystonia. None of the patients had a family history of dystonia and at the moment it is unclear whether these patients with sporadic axial dystonia are non-genetic phenocopies or are a manifestation of one or more of the genes that cause generalised dystonia or torticollis.

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Dystonia is classified according to aetiology (primary or secondary), by age of onset (childhood or adult), and by site of onset.¹ Among the primary dystonias, site of onset is a good indicator of prognosis.^{2,3} Childhood onset

primary dystonia usually begins in the limbs and tends to generalise.³ On the other hand adult onset focal dystonias tend to remain focal or spread only contiguously to a segmental distribution.^{2,3} Craniocervical dystonia is the commonest of the adult onset focal dystonias, with torticollis being the most frequent manifestation, then blepharospasm and spasmodic dysphonia.^{4,5} Axial dystonia is considerably less frequent, accounting for probably less than 10% of the patients with segmental dystonia (less than 6% of those with cranial segmental, and 4% of those with segmental axial/limb), in a recent epidemiological survey of primary dystonia in the north of England.⁵ Focal axial dystonia is even less common.

Other than reports on single patients⁶ or brief mentions in review articles,² there has been no report of the clinical features, treatment response, and long term follow up of patients presenting with primary adult onset predominantly axial dystonia. Here we describe 18 such patients.

Patients

The patients included were those with adult (or late adolescent) onset of a dystonic syndrome which was predominantly axial and affecting the trunk when first seen by us. These patients were selected from the database maintained in the Department of Clinical Neurology at the Institute of Neurology and had been followed up at the National Hospital of Neurology and Neurosurgery, Queen Square or King's College Hospital. Cases of axial dystonia due to tardive syndromes or those with exposure to neuroleptic drugs before onset of the dystonic syndrome were excluded, as well as those with a diagnosis of secondary dystonia.

Results (table)

There were 18 patients (10 men, eight women) with predominantly axial truncal dystonia. The mean age of onset was 41 (42 for men, 39 for women).

In all 18 patients truncal dystonia was the major disability. Five had severe axial dystonia alone on examination and at onset; six had mild cervical dystonia in addition to severe axial dystonia, with onset of the axial and neck problems simultaneously in five patients, whereas in one the axial dystonia developed

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one year after the onset of torticollis. Two patients had mild craniocervical dystonia at onset with axial dystonia developing within two years of onset. Four patients had mild segmental dystonia (two orofacial plus arm and two craniocervical plus arm) before developing axial dystonia within three years in three patients and five years in one. In one patient there was mild inturning of the left foot three years before the onset of axial dystonia. After the initial onset (and spread), no further spread occurred on further follow up of three to five (or more) years which was possible in 16 patients; two patients had only one year of follow up and the subsequent course in one patient was unknown.

The predominant direction of truncal dystonia in a large proportion (10/18) of patients was forward with flexion spasms; only four patients had predominant extensor (backwards) axial dystonia whereas three had a combination of extensor (lordotic) and lateral (scoliotic) deviation; one patient only had lateral bending spasms. The large majority had worsening of the axial dystonia on action—namely, standing or walking.

The flexion spasms could be severe enough to pull the patients head to the level of the knees (patient 1). The extensor spasms could be strong enough to prevent walking and to remove the hair from the back of the head due

to friction with the headrest. Some had a sensory trick in the form of a particular attitude—for example, pressing the back into the corner of a chair or using a pillow placed at a particular area of the back in another.

A history of injury (trauma or surgical procedure) at the site subsequently affected by dystonia was present in more than a third (seven of 18; 39%) of the patients within three months of the onset of the dystonia (table). In none of the patients was there a history of neuroleptic drug intake before the onset of the dystonic syndrome. All patients had normal basic investigations ruling out secondary causes of dystonia (brain CT/MRI and copper studies in those under the age of 50 years). In none was there a family history of dystonia or any other neurological disorder.

Response to various drug treatments overall was poor (table); only seven patients showed improvement, which was pronounced in four and moderate in the other three. All four patients who had a pronounced response were on triple combination therapy with tetrabenazine, pimozone, and an anticholinergic drug (usually benzhexol (trihexiphenidyl) in three patients; orphenadrine in one patient). Two of the three remaining patients had moderate benefit on high dose anticholinergic therapy, whereas one improved on a combination of tetrabenazine, pimozone, and dexamphetamine.

Summary of the clinical features of patients with adult onset predominant axial dystonia

Patient	Age/sex	Onset age	Onset site	Predominant axial movements	Prior trauma	Drug regimen /response	Follow up (duration; remarks)
1	52/M	49	Torticollis, back,	Axial flexion spasms	laminectomy	D, AC, NP-nil	> 5 y; suicidal, ECT, dystonia unchanged
2	43/M	39	L arm, torticollis,	Lordotic and scoliotic	No	TT, NP -good, but SE	> 5 y; unchanged, died -no postmortem
3	59/F	53	Back and shoulder	Action lateral flexion	Back sprain	Not known	> 3 y; unchanged
4	49/M	44	Back and neck	Extensor spasms	No	Lith- good, Triple-good	> 4y; remission on treatment
5	28/F	21	Torticollis, writing craniocervical	Lateral axial and hyperlordotic	RTA, neck injury whiplash	TT-good but SE, AC-good	3 y; partial response to treatment
6	39/F	18	Back and neck	Flexion spasms	No	Lith, AC, D-nil	> 5y; suicidal, depression, dystonia unchanged
7	58/F	54	Torticollis and back	Flexion spasms	No	Triple-good	> 5y; greatly improved on treatment
8	63/M	57	Cranio-cervical	Axial extension spasms	RTA	D, dopa, TT-nil	5 year history of dystonia unchanged
9	60/M	50	Arm, orofacial	Lordotic axial jerks, kyphosis	No	Triple-benefit	> 5 y; suicidal, dystonia unchanged
10	72/M	30	Orofacial, neck	Flexion stoop	No	AC-SE	> 3 y; unchanged
11	61/F	30	Orofacial, arm	Flexion jerks	Mandible fracture	AC, NL-nil	> 5y; depressed, recluse, dystonia unchanged
12	55/M	42	Foot mild	Action flexion spasms	No	BC, AC-nil	> 5 y; dystonia unchanged
13	63/F	38	Back	Action flexion spasms	No	Dopa-nil, TT, Ac and Dex-good	> 20y; improved on treatment
14	51/M	40	Back	Flexion extension jerks	Laminectomy	Not known	Not known
15	57/M	56	Back	Flexion spasms	No	TT, NP, dopa-nil, AC -good	1 y; remitted on AC
16	62/F	60	Back, neck	Flexion spasms	No	Triple-good	1 y; pronounced improvement on treatment
17	40/F	39	Back	Extensor spasms	No	NP and AC-nil, triple -good	> 5y; remission on triple, partial relapse later
18	22/M	17	Neck	Extensor spasms	Neck injury	AC, D, dopa -nil, BT-nil	> 5y; unchanged

Exam=examination; D=diazepam; AC=anticholinergic drugs; NP=neuroleptic drugs; TT=tetrabenazine; lith=lithium; dex=dexamphetamine
Triple=combination of tetrabenazine; artane, and pimozone; BT=botulinum toxin; SE=side effects; RTA=road traffic accident.

Where tried (n=4), levodopa did not produce benefit in any patient. Over the follow up period the dystonia remained more or less unchanged in the remainder with no response to various drug treatments tried alone or in combination.

Depression requiring psychiatric intervention occurred in six of 18 (33%) patients, three of whom had attempted suicide mainly due to the negative personal image arising from their disfiguring dystonia.

Discussion

This group of patients falls into the classification of adult onset focal (or segmental) primary dystonia manifesting as predominantly severe axial dystonia. Of all the adult onset focal dystonias axial dystonia is the least common and to our knowledge this is the first report of the clinical features and follow up of a large group of such patients.

Analysis of their clinical features and outcome shows that they generally conform to the characteristics of other types of adult onset dystonia. They tended to remain focal although there could be an initial contiguous spread, sometimes beginning in the craniocervical region and spreading axially or, rarely, vice versa. However, in none of the patients with craniocervical or truncal onset did the dystonia spread to involve the legs (although in patient 12 the onset was from the foot and spread axially). If spread occurred, involvement of the head, neck, and arms was mild in comparison with the severe dystonia of the trunk.

There were some differences when compared with other adult onset focal dystonias. There was a higher preponderance of men to women (10:8) when compared with adult onset craniocervical dystonia, which is commoner in woman (nearly 2:1).⁴ Another difference was the absence of family history of dystonia in all these patients (although this cannot be completely excluded in the absence of examining relatives). A family history of dystonia is present in up to 13% of patients of adult onset torticollis, although it is less for blepharospasm (3%).³ However in another study in which relatives were examined a family history of dystonia was present in 23% of patients with idiopathic focal dystonia.⁷

Trauma precipitating focal dystonia has been described and is estimated to occur in 10% of patients with adult onset torticollis.⁸ More than a third of our patients reported a history of trauma (either an operation or injury) at the site of the onset of the dystonia occurring within three months before the onset of their symptoms. Thus there seems to be a higher incidence of trauma in patients with axial dystonia when compared with those with torticollis alone.

Overall, the response to treatment was poor. However, a third of patients showed benefit, either with triple therapy (tetrabenazine, pimozide, and benzhexol), or high dose anticholinergic drugs alone. However, due to the poor response to available treatments as well as the negative personal image a high proportion of patients had severe depression.

Occasionally, primary focal dystonias can remit spontaneously or while on drug treatment. The remission rate in patients with torticollis is about 20% according to one study;⁹ in another study 9% of patients with torticollis went into partial or complete remission but all of them eventually relapsed after two months to 40 years.³ The remission rate for our patients with axial dystonia was low and only three of 18 patients (two on triple therapy, one on anticholinergic drugs) reported a near total remission; however, in two of the three patients the symptoms returned after two years.

Previously it was thought that adult onset focal dystonias may be an incomplete form of primary childhood onset limb dystonia (ITD), which usually begins in the legs and becomes generalised. However, there is growing evidence that this is not the case. The common autosomal dominant gene for ITD (labelled DYT1) on chromosome 9q34 is almost always present in Ashkenazi Jewish families, but also in the large proportion of non-Jewish patients with young onset primary dystonia.¹⁰ Virtually all manifesting carriers of the DYT1 gene present before the age of 28 years. The DYT1 gene is not responsible for the vast majority of adult onset primary dystonias. One large family with adult onset torticollis was found not to be linked to the DYT1 locus.¹¹ Haplotype analysis of patients of Ashkenazi Jewish descent with adult onset torticollis disclosed that the large majority did not carry the mutant DYT1 gene.¹² It is now becoming clear that adult onset focal dystonias are a genetically heterogeneous group. Recently a family with torticollis has been linked to chromosome 18.¹³ In none of our patients was there a family history of dystonia and at the moment it is not clear whether these patients with sporadic axial dystonia are non-genetic phenocopies or a manifestation of one or more genes which cause generalised primary dystonia or torticollis. The picture will be clearer once further genes for dystonia have been identified.

In conclusion, as with other forms of adult onset dystonia, patients with predominantly axial primary dystonia can be reassured that the condition will not significantly progress or worsen and will probably not involve the legs. Treatment may be helpful in a third of patients and we recommend that a trial of high dose anticholinergic drugs be tried first and, if not found beneficial, tetrabenazine and pimozide or haloperidol should be added. Overall, these patients of axial dystonia present a difficult management problem. This disfiguring condition often results in severe depression leading to attempted suicide in some patients.

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