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Sean O'Riordan
Timothy Lynch
Michael Hutchinson

Familial adolescent-onset scoliosis and later segmental dystonia in an Irish family

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S. O'Riordan · Prof. M. Hutchinson (✉)
Dept. of Neurology
St Vincent's University Hospital
Elm Park
Dublin 4, Ireland
Tel.: +353-1/269-5033
Fax: +353-1/269-7949
E-Mail: mhutchin@iol.ie

T. Lynch
Mater Misericordiae Hospital
Dublin, Ireland

Abstract Adolescent-onset scoliosis occurs more frequently than expected in primary adult-onset cervical dystonia and a genetic association between the conditions has been postulated. The authors report a family in which four members have adult-onset cervical and/or brachial dystonia, two of whom have coexistent scoliosis. Four other individuals have isolated childhood- or adolescent-onset scoliosis. Adolescent-onset scoliosis may represent part of the dystonia phenotype in this family.

Key words primary torsion dystonia · scoliosis

Introduction

Scoliosis may occur as part of the phenotype of dopa-responsive dystonia (DRD) [8, 14, 15] and DYT1 dystonia [1] but the relationship between scoliosis and adult-onset focal or segmental dystonia is uncertain. Scoliosis in adult-onset cervical dystonia may be a compensatory spinal adaptation to a longstanding laterocollis. It has been suggested that early-onset scoliosis may induce central cortical and subcortical reorganisation by altering sensory input from the trunk, leading to cervical dystonia [4]. There is evidence that childhood- and adolescent-onset scoliosis is more frequent than expected in primary adult-onset cervical dystonia, possibly due to a common genetic mechanism [4]. A family of German/Scottish-Irish ancestry has been described in which four members had adult-onset cervical dystonia while scoliosis was noted in three other individuals [6]. We report an Irish family in which four members have adult-onset cervical and/or brachial dystonia; two of these affected individuals also have adolescent-onset or asymptomatic scoliosis and four others have isolated childhood- and adolescent-onset scoliosis.

Family and methods

This family was seen as part of a study of familial dystonia in Ireland. The study was approved by the Research Ethics Committee of St. Vincent's University Hospital (SVUH), Dublin. The proband attended the dystonia clinic at SVUH. Following informed consent the other family members were assessed by one of the authors (SOR). Consenting family members underwent standardised videotaped neurological examination. Videotapes were reviewed by two neurologists (TL, MH) and rated for affected status and distribution of dystonia.

Radiological confirmation of scoliosis was obtained in the index case. In others, the diagnosis of scoliosis was based on clinical examination using the Adam's forward bend test and, in one individual, on surgical records of treatment of scoliosis. The Adam's forward bend test is a commonly used, non-invasive, clinical screening test for scoliosis. Estimates of its sensitivity and specificity vary but values as high as 92 % and 93.4 % respectively have been reported [3, 12] and therefore we did not think that x-ray examination of relatives of the index case was warranted.

Results

We assessed eleven family members over three generations of this family (Family Tree, Fig. 1). There was no history of consanguinity. The pattern of inheritance suggests an autosomal dominant trait. The DYT1 GAG deletion was excluded in the index case. Four family

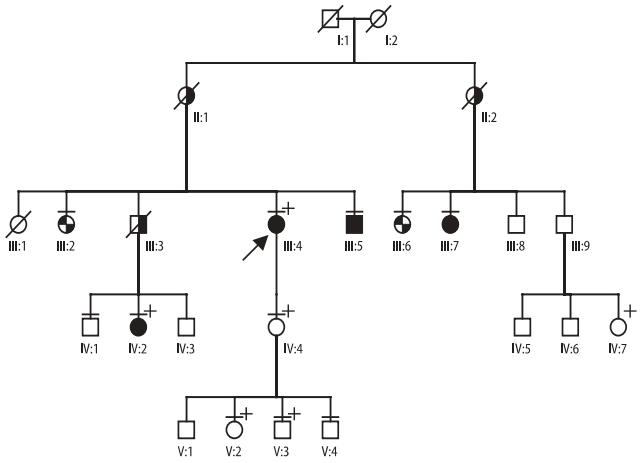

Fig. 1 Abbreviated pedigree showing five generations of the reported family. Square symbols = males; circles = females. Horizontal line above symbol = clinically assessed; a black arrow denotes the index case; clear symbol = unaffected by dystonia, tremor or scoliosis; filled black symbol = affected by dystonia; adjacent cross = affected by scoliosis; filled opposing quadrants = affected by postural arm tremor; vertically half-filled symbol = reportedly affected by tremor; diagonal line through symbol = deceased

members (III:4, III:5, III:7 and IV:2) had cervical and/or brachial dystonia. This was preceded by adolescent-onset scoliosis in two individuals (III:4 and IV:2). Four members (IV:4, IV:7, V:2 and V:3) had childhood- or adolescent-onset scoliosis without dystonia and three deceased family members (II:1, II:2 and III:3) had a history of tremor and may have had dystonia. Two family members (IV:1 and V:4) were found to be unaffected by scoliosis, dystonia or tremor.

Clinical features of affected individuals (Table1)

Index Case (III:4): A 73-year-old woman developed mild scoliosis at age 15 years. At 50 years of age she developed spasmodic involuntary movements of arms and head. On examination, segmental cervical and bibrachial dystonia with disabling dystonic arm tremor was noted. Cervical dystonia manifested as tremulous retrocollis. There was no evidence of laryngeal dystonia or blepharospasm and there was no myoclonus. There was no diurnal variation in symptoms. Treatment with anticholinergics and with two prolonged trials of levodopa was unsuccessful. Botulinum toxin injections resulted in moderate improvement of the cervical dystonia.

Her brother (III:5), a 70-year-old man, developed bilateral upper-limb action tremor in his late fifties and writing became impossible. On examination he had tremulous cervical dystonia, dystonic writer's cramp and asymmetric, dystonic arm tremor and posturing, but was not affected by scoliosis.

III:7, a 70-year-old woman, developed jerking involuntary movements of head and arms at age 53 years. Examination revealed tremulous cervical dystonia with retrocollis and head turning to the left as well as bilateral dystonic upper limb tremor. There was no scoliosis.

Table 1 Clinical features of affected family members detailing age of onset and affected sites for each of dystonia, scoliosis and tremor

Family member	Age at exam/death (years)	Scoliosis		Dystonia			Tremor		
		Yes/No/unknown	Onset (years)	Yes/No/unknown	Onset (years)	Site	Yes/No/unknown	Onset (years)	Site
II: 1	Died, 80	unknown		unknown			yes	60–70	head and upper limb
II: 2	Died, 85	unknown		unknown			yes	70–75	head and upper limb
III: 2	80	no		no			yes	asymptomatic	postural upper limb
III: 3	Died, 72	unknown		unknown			yes	60–65	head and upper limb
III: 4	73	yes	15	yes	50	cervical, brachial			
III: 5	70	no		yes	55–60	cervical, brachial			
III: 6	71	no		no			yes	asymptomatic	postural upper limb
III: 7	70	no		yes	53	cervical, brachial			
IV: 2	29	yes	asymptomatic	yes	asymptomatic	brachial	yes	19	postural upper limb
IV: 4	48	yes	childhood	no			no		
IV: 7	23	yes	childhood	unknown			unknown		
V: 2	25	yes	13	no			no		
V: 3	24	yes	childhood	no			no		

A niece of the index case (IV:2, aged 29 years) describes onset of an upper limb tremor aged 19 years. On examination there was dystonic posturing of the left upper limb, bilateral postural upper limb tremor and asymptomatic scoliosis.

The daughter of the index case (IV:4, aged 48 years) was advised in late childhood by her doctors to wear a brace for progressive scoliosis. On examination she has scoliosis but no tremor or dystonia. Two of this woman's children (V:2 and V:3) have adolescent-onset scoliosis and otherwise normal examinations. Individual IV:7, aged 23 years, underwent surgery in her mid-teens for scoliosis which developed in late childhood. She lives in Australia and was not examined by the authors.

III:2 (aged 80 years) and III:6 (aged 71 years) have bilateral, postural arm tremor without other abnormalities. III:3 is said to have had onset of head and arm tremor in his sixties. He died aged 72 years from non-Hodgkin's lymphoma. The deceased mother of the index case (II:1) developed head and upper-limb tremor in late adulthood while an aunt of the index case (II:2, died 1985) also had tremor of the upper limbs and head in her seventies.

Discussion

An unusual dystonia phenotype is seen in this family. The index case developed adolescent-onset scoliosis and subsequently segmental cervical and bibrachial dystonia at age 50 years. Another family member (aged 29 years) has upper limb dystonia and asymptomatic scoliosis. Six others are affected by either adult-onset segmental cervico-brachial dystonia or isolated childhood and adolescent-onset scoliosis. Three deceased individuals were reported to have had tremor and may have had dystonia. Postural upper limb tremor alone (as seen in two family members) is well described in relatives of patients with dystonia [10] and may be part of the dystonic syndrome. Isolated scoliosis may also represent part of the phenotypic spectrum of dystonia in this family and the younger members of the family with scoliosis may not have reached the age at which the cervico-brachial dystonia manifests.

Scoliosis was noted in 39 % of 300 patients with cervical dystonia [10], and in another series, adolescent idiopathic scoliosis occurred in 16.5 % of 296 cervical dystonia patients compared to 3 % of 150 controls with back pain [7]. In a recent case-control study [4], childhood or adolescent scoliosis occurred significantly more frequently in a group of 72 patients with cervical dystonia than among 144 control subjects with other neurological conditions. The authors suggest that if a genetic link exists between the conditions then one would expect increased rates of scoliosis in families of patients with CD.

The aetiology of adolescent idiopathic scoliosis is unclear. In a transcranial magnetic stimulation study, children with idiopathic scoliosis had reduced cortico-cortical inhibition when compared with normal subjects and children with congenital scoliosis, suggesting that a dystonic disorder may underlie idiopathic scoliosis [5]. Genetic factors play a significant role. There are numerous reports of families with scoliosis; dominant, recessive and X-linked transmission has been described, while a multifactorial mode of inheritance is likely in other families [13]. A genome-wide linkage survey in two large families with dominantly inherited scoliosis identified suspect loci on chromosome 6p, 10q, and 18q [18] and recently, several genetic loci for idiopathic scoliosis have been assigned [2, 11, 17].

Scoliosis is a common orthopaedic disorder with a prevalence of 2–4 % in children aged between 10 and 16 years [16]. Because of its high prevalence, its occurrence in this dystonia pedigree may be coincidental. Alternatively, it may be an integral part of the family's phenotype with dystonic scoliosis as an early presentation and brachial and cervical PTD as later manifestations. In the index case (III:4), adolescent-onset scoliosis predated the adult development of segmental cervical and bibrachial dystonia by 35 years. IV:2 also has a combination of dystonia and scoliosis but the age of onset of scoliosis is not known in her case and dystonia has not progressed beyond brachial involvement. Several younger family members have adolescent-onset scoliosis and they may be at risk of developing cervical dystonia. If one accepts that scoliosis is a dystonic manifestation then the temporal pattern observed in the index case of adolescent scoliosis followed by cervico-brachial dystonia is consistent with the observation that early-onset limb or trunk dystonia tends to spread whereas late onset cranio-cervical dystonias are less likely to do so [9].

Although scoliosis and dystonia may be two separate genetic disorders segregating in this family, it is more probable that the scoliosis represents part of the dystonic disorder and this has important implications for linkage studies.

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