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Spinal Muscular Atrophy Combined with Congenital Heart Disease: A Report of Two Cases

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Key words

Spinal muscular atrophy – Heart defect – Survival motor neuron gene

Abbreviations

ASD: atrial septal defect
 CHD: congenital heart disease
 NAIP: neuronal apoptosis inhibitor protein
 SMA: spinal muscular atrophy
 SMN: survival motor neuron gene

The spinal muscular atrophies (SMA) are a group of relatively common hereditary neuromuscular disorders, affecting about 1 in every 10,000 children. For all types of SMA, large scale deletions at chromosome 5q13 have been reported (1, 10, 11), and recently two candidate genes have been identified (SMN and NAIP gene), of which the SMN gene is shown to have diagnostic value (8, 13, 14). Variants of SMA, in which the diagnostic features of anterior horn cell degeneration are associated with dysfunction of other organ systems, are infrequently encountered. Co-existing congenital heart disease (CHD) has been reported (2, 4, 7, 12). We report on two children with an association of a congenital cardiac disease and SMA, one with early fatal SMA 1 and atrial septal defect (ASD), the other with a complex cardiac disorder and SMA 3. Both proved to have a homozygous deletion at the SMN gene locus.

Case reports

Case 1

This patient was born after an uncomplicated pregnancy of 39 weeks. Immediate post-partum intubation was warranted because of respiratory failure. Physical examination revealed pectus carinatum, club feet, contractures of knees and hips and fasciculations of the tongue. She was areflexic and extremely hypotonic; no spontaneous bodily movements were observed except in face, fingers and feet. Echocardiography

revealed a large atrial septal defect and electromyography showed fasciculations in several large muscles. The muscle biopsy specimen showed the features of spinal muscular atrophy and a diagnosis of SMA type 1 was made. DNA analysis revealed a homozygous deletion of exon 7 of the SMN gene. The girl died two weeks post-partum.

Case 2

This case involves a girl who was brought to our attention at the age of 2 years and 2 months because of an abnormal gait. Because of a serious cardiac abnormality consisting of an L-transposition of the great vessels, a functional monoventricle, atrial septal defect type II and a small patent ductus arteriosus, she twice had had cardiac surgery. Her motor development had been uneventful until well after the second operation, when it was noted that she had difficulties standing up and walking. She was not able to walk unsupported until 19 months and never gained the ability to run or climb stairs properly. On neurological examination there was marked lumbar lordosis and she walked with a waddling gait, *Gowers'* phenomenon was positive. Muscle power and tone were decreased, most markedly in the lower limbs and proximally more pronounced than distally; patellar taps were decreased. Routine laboratory investigations, including thyroid function tests, were normal, as were EEG and EMG and brain CT scan. Biopsy of the right quadriceps muscle showed all the features of spinal muscular atrophy. A diagnosis of SMA 3 was made on clinical and morphological grounds. DNA analysis revealed a deletion of exon 7 of the SMN gene of both chromosomes 5q.

The association of SMA and CHD is rarely observed, and several authors failed to disclose congenital heart defects in their SMA populations (3, 5, 6, 9, 15). The first cases were reported by *Moller* et al, who described 3 siblings with an atrial septal defect and spinal muscular atrophy (12). Diagnosis was confirmed at autopsy in two children, DNA analysis was not performed. *Bürglen* et al report on six unrelated children with SMA type 1 and CHD, ranging from ASD to complex cyanotic defect with tricuspid atresia and univentricular heart (2). Congenital contractures were present in 4 cases, as in our first patient. Homozygous deletion of SMN exon 7 was found in 4.

Our cases add to a growing list of SMA in association with CHD. The nature of this association is not known, but it may be that it is more than a chance co-occurrence of the two hereditary disorders. At present, any

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Authors	No. cases	Kinship	Case no.	SMA type	CHD type	DNA analysis
Moller et al (1990)	3	sibs	1	1	ASD	not performed
			2	1	ASD	not performed
			3	1	ASD	not performed
Bürglen et al (1995)	6	non-related	1	not reported	ASD	
			2	not reported	ASD, VSD	HD SMN exon 7
			3	not reported	univentricle, TA	HD SMN exon 7
			4	not reported	coarctation, ASD	
			5	not reported	partial AV-canal	HD SMN exon 7
			6	not reported	coarctation	HD SMN exon 7

ASD: Atrial septal defect
VSD: Ventricular septal defect
TA: Tricuspid atresia

AV-canal: Atrioventricular canal
HD SMN exon 7: Homozygous deletion of exon 7 of SMN gene

Table 1 SMA and CHD, summary of published data.

hypothesis about the true cause of this association remains highly speculative.

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