Neurol Sci (2003) 24:134–137
DOI 10.1007/s10072-003-0099-x

CASE REPORT

V. Etus • S. Ceylan • S. Ceylan

Association of spondylocostal dysostosis and type I split cord malformation

Received: 19 November 2002 / Accepted in revised form: 29 April 2003

Abstract In reports on children with congenital segmental costovertebral malformations who showed neural tube defects, cases with type I split cord malformation are quite rare. Up to now such association has been reported only in two cases with Jarcho-Levin syndrome. Here, a 7-year-old girl presenting with spondylocostal dysostosis and type I split cord malformation is reported. To the best of our knowledge, this is the first case documented in the literature. The association of segmental costovertebral malformations and neural tube defects is discussed. Genetic and embryological studies are also briefly reviewed.

Key words Neural tube defects • Segmental costovertebral malformations • Split cord malformations • Spondylocostal dysostosis

V. Etus (✉) • S. Ceylan
Department of Neurosurgery
Kocaeli University School of Medicine
Sopaliçiftligi 41900 Derince
Kocaeli, Turkey

S. Ceylan
Department of Histology and Embryology
Kocaeli University School of Medicine
Kocaeli, Turkey

Introduction

Spondylocostal dysostosis (SCD) is a congenital segmental costovertebral malformation with multiple vertebral and numerical or structural rib abnormalities resulting in thoracic asymmetry. The association of segmental costovertebral malformations and neural tube defects has been reported several times, and it has been proposed that this association is not coincidental [1]. In reports on children with segmental costovertebral malformations who showed some rare form of neural tube defects, presence of type I split cord malformation was reported only in two cases with Jarcho-Levin syndrome [1, 2]. Here we describe a patient with SCD, who also had type I split cord malformation with an accompanying spinal lipoma. To the best of our knowledge, there is no previously reported association of SCD and type I split cord malformation.

Case report

A 7-year-old girl was admitted to hospital with asymmetry of her ribcage, thoracic scoliosis, a midline mass on the lumbar region, fatigue of her legs and intermittent urinary incontinence. She had not undergone any neurosurgical evaluation previously. The child's parents were nonconsanguineous.

On admission, physical examination revealed a thoracic asymmetry with the left hemithorax being salient and deformed. A fully skin-covered, soft and nontender lumbar mass was noticed in the midline. An area with hypertrichosis and a small hairless region with hypopigmentation and Port-wine spot were neighboring the mass.

Neurological examination revealed muscle weakness of the lower extremities. Hip flexors, quadriceps femoris, thigh adductors and lateral thigh flexors were minimally affected. Anal sphincter tonus was normal.

Thoracic X-ray showed irregular fusion of the ribs (fourth through ninth) on the left side, T3 hemivertebra, fusion of the sixth and the seventh thoracic vertebral bodies and rotoscoliosis of the thoracic vertebrae. A midline dense

area at the level of L2 and L3 vertebral bodies was also noted (Fig. 1a). Lumbar X-ray demonstrated that this density was consistent with a midline bony spur (Fig. 1b).

Complete spinal magnetic resonance imaging (MRI) showed vertebral abnormalities with T3 hemivertebra and fusion of the sixth and the seventh thoracic vertebral bodies (Fig. 2). Midsaggital lumbar MRI sections revealed segmentation anomalies in L2 and L3 vertebral bodies and a low-lying conus medullaris, which ended at the level of L4-L5 intervertebral disc space (Fig. 2a). A bony spur originating from segmented lumbar vertebrae was found to divide the spinal cord. Two hemicords were shown to course within two separate dural sleeves for a segment of approximately 4 centimeters in length (Fig. 2b, c). A small

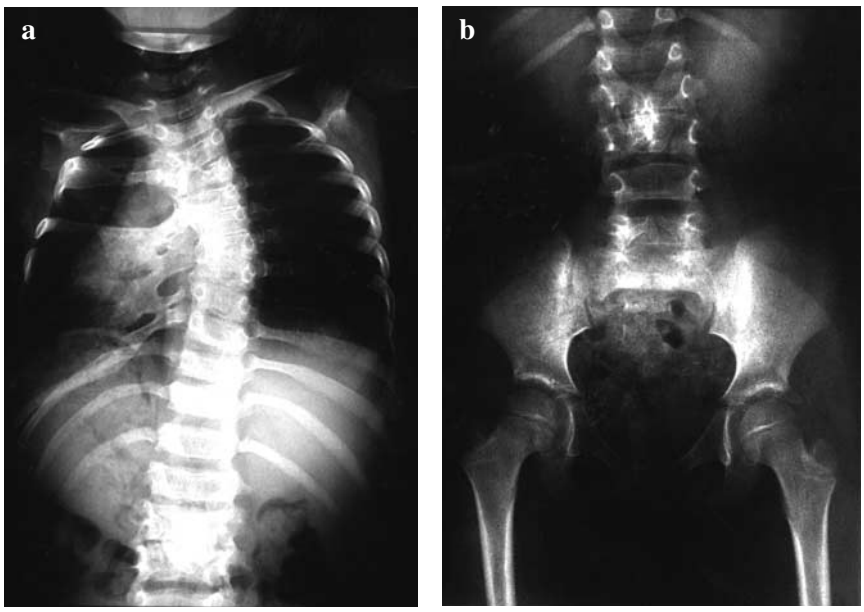

Fig. 1a,b *Radiographs of the spinal area in a 7-year-old girl*. **a** Chest radiograph shows irregular fusion of the ribs (4–9) on the left side, T3 hemivertebra and rotoscoliosis of the thoracic vertebrae. A dense area is seen at L2-L3 level. **b** Lumbar radiograph shows the median dense area at the level of L2 and L3 vertebral bodies to correspond to the bony spur

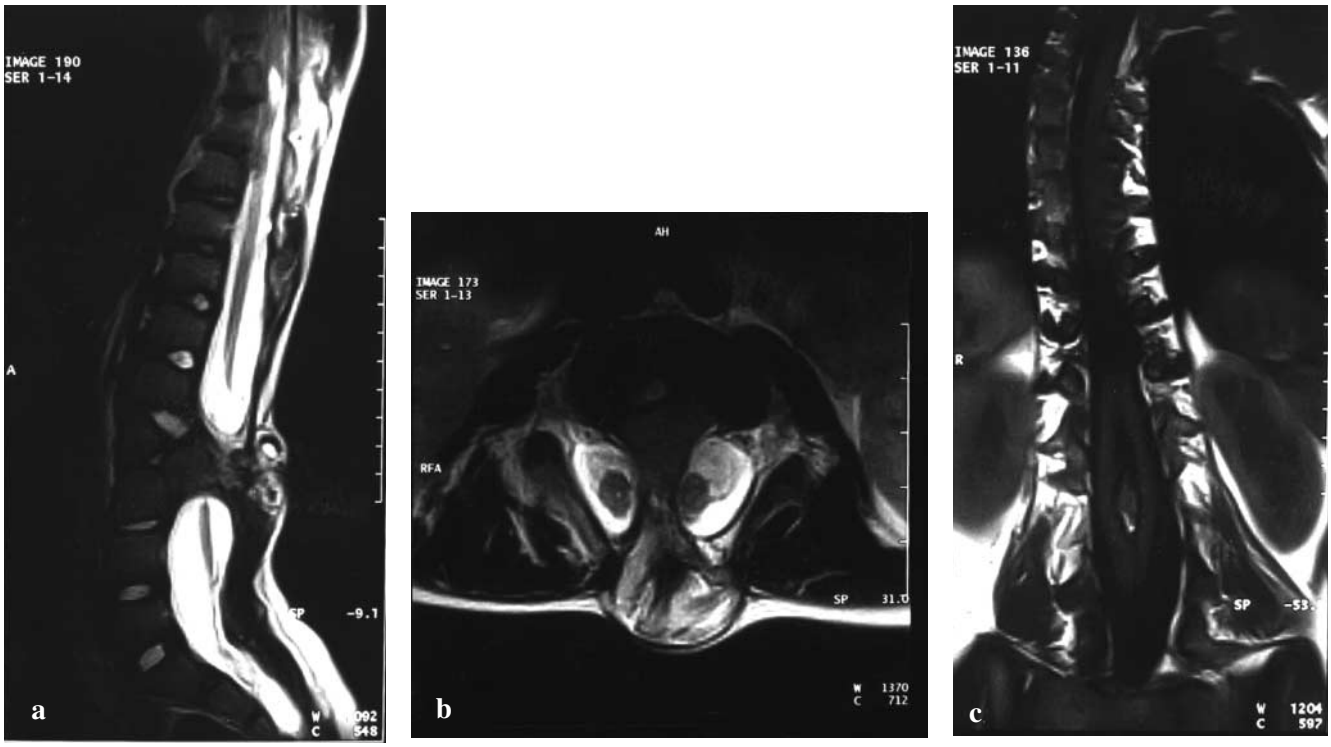

Fig. 2 *Spinal MR images showing vertebral anomalies.* **a** Sagittal T2-weighted image reveals segmentation anomalies in L2 and L3 vertebral bodies and a low-lying conus medullaris, which ends at the level of L4-L5 intervertebral disc space. **b** Axial T2-weighted scan at the level of L2-L3 shows the bony spur originating from segmented lumbar vertebrae to divide the spinal cord. Two hemicords stay within two separate dural sleeves. **c** Coronal T1-weighted image reveals a lumbar bony spur, which divides the spinal cord. Two hemicords course within two separate dural sleeves for a segment of approximately 4 centimeters in length. Scoliosis of the thoracic vertebrae is also noticed

cord cavitation was also noticed at the level of T7 vertebral body.

She was operated. The spinal cord was untethered and decompressed by removal of the median septum. A mass of lipoma, which was originated from the bony spur, was observed to extend into the subcutaneous fat presenting as a lumbar mass posteriorly. Also the filum tethering the cord was divided.

The diagnosis was established as spondylocostal dysostosis and coexisting type I split cord malformation with an accompanying spinal lipoma.

Discussion

Segmental costovertebral malformations include Jarcho-Levin syndrome (JLS), spondylothoracic dysostosis (STD) and spondylocostal dysostosis (SCD), which are rare and distinct entities and share similar clinical phenotypes [3]. JLS, which is transmitted in an autosomal recessive way, is a severe form with involvement of the whole vertebral column. [1, 3]. STD is transmitted in an autosomal recessive way; it involves the spine and leads to a fanlike chest, but there are no intrinsic rib malformations reported [3]. SCD is characterized by vertebral abnormalities such as hemivertebrae, fused, hypoplastic, "butterfly" vertebrae, and characteristic rib anomalies such as rib fusions and deletions with a non-progressive kyphoscoliosis [3].

Malformations of the spinal cord with a separation into two hemicords have been termed "diastematomyelia". The term "diplomyelia" is reserved to a true duplication of the spinal cord which is, however, difficult to demonstrate. In 1992, Pang et al. [4] recommended the term "split cord malformation" for all double spinal cords. Split cord malformations are grouped in the complex closed (skin-covered) spinal dysraphism category in the classification suggested by Tortori-Donati et al. [5]. A type I split cord malformation consists of two hemicords, each contained within its own dural tube and separated by a dura-sheathed rigid osseocartilaginous median septum. A type II split cord malformation consists of two hemicords housed in a single dural tube separated by a nonrigid, fibrous median septum [4].

In their report on the embryogenesis of complex dysraphic malformations, Dias and Walker [6] explained the embryogenesis of split cord malformations and related malformations through a failure of midline axial integration during gastrulation. According to their theory, the primitive streak is abnormally wide and the prospective notochordal cells in primitive node begin ingressing more laterally than normal. These notochordal precursors remain separate and develop independently over a variable portion of their length, and similarly, bilaterally paired prospective neuroepithelial cells remain separate and differentiate independently to produce two hemicords. Laterally displaced somitic tissue would form an abnormally widened spinal canal with numerous associated vertebral segmentation anomalies, including butterfly vertebrae and hemivertebrae (as is seen in our case). The intervening space between the paired hemicords is composed of pluripotent primitive streak cells and could give rise to a variety of tissue types from any of the three primary germ layers. Finally, secondary problems with subsequent primary neurulation of each or both of the hemicords could produce associated neural tube defects through a failure of segmental neurulation (producing myelomeningoceles if both hemicords are involved or hemimyelomeningoceles if only one hemicord is involved); secondary neurulation defects include skin-covered variants of spina bifida, such as lipomas (as is seen in our case), lipomyelomeningoceles or dermal sinus tracts due to an abnormality of cutaneous ectodermal separation.

The case reported here is a patient with type I split cord malformation and accompanying spinal lipoma, occurring in association with findings characteristic of SCD. There was no other congenital malformation in our case. Her family reported no other previous members having anomalies.

Spina bifida occulta appears to be a common finding in reported SCD cases [2], but to the best of our knowledge the association with type I split cord malformation has not been reported.

Currently, in reports on children with segmental costovertebral malformations, only two cases were presented with type I split cord malformation. Both of those children had JLS. Reyes et al. [2] reported a case of JLS associated with type I split cord malformation. Giacoia and Say [1] reported a patient with JLS who also had spina bifida and type I split cord malformation.

However, some authors [1, 7] do not make a clear distinction among JLS, STD and SCD. It is possible that cases observed by a neuroradiologist rather than a general pediatric radiologist had emphasis thrown on the split cord and vertebral abnormalities while the associated costal abnormalities were overlooked.

SCD cases may be sporadic or familial, with both autosomal dominant and autosomal recessive modes of inheritance reported [8]. Autosomal recessive SCD maps to a 7.8-cM interval on chromosome 19q13.1-q13.3 that is homologous with a mouse region containing a gene encoding the Notch ligand delta-like 3 (DLL3). In 2000 Bulman et al. [8] cloned and sequenced human DLL3 to evaluate it as a candidate gene for SCD and identified mutations in three autosomal recessive SCD families. As Bulman et al. [8] reported in their study, several studies in fish, chick and mouse embryos have indicated that segmentation of the body relies on a molecular oscillator, called the segmentation clock, which requires Notch signaling for its proper functioning. DLL3 seems to be another gene required for oscillation and the fact that its mutation in humans results in abnormal segmentation of the vertebral column suggests that the segmentation clock also acts during human embryonic development [8].

The association of segmental costovertebral anomalies and neural tube defects can be explained with an early gastrulation genomic defect or with a genomic defect occurring just after gastrulation, when two independent somitic columns exist. The interaction of different genes may result in this complex phenotype.

In our case, the association of type I split cord malformation and spinal lipoma with SCD points to a possible gastrulation defect, which progressed to involve secondary neurulation. This seems to support the theory of Dias and Walker [6]. The hypothesis that spondylocostal dysplasia and neural tube defects are etiologically related still needs to be proven. Further genetic and detailed embryological studies will provide evidence of an etiological relationship between segmental costovertebral anomalies and neural tube defects.

Acknowledgement We gratefully thank Mehmet Eryurek for his help in photography.

References

1. Giacoia GP, Say B (1991) Spondylocostal dysplasia and neural tube defects. J Med Genet 28:51–53
2. Reyes MG, Morales A, Harris V, Barreta TM, Goldbarg H (1989) Neural defects in Jarcho-Levin syndrome. J Child Neurol 4:51–54
3. McCall CP, Hudgins L, Cloutier M, Greenstein RM, Cassidy SB (1994) Jarcho-Levin syndrome: unusual survival in a classical case. Am J Med Genet 49:328–332
4. Pang D, Dias MS, Ahab-Barmada M (1992) Split cord malformation: Part I: a unified theory of embryogenesis for double spinal cord malformations. Neurosurgery 31:451–480
5. Tortori-Donati P, Rossi A, Cama A (2000) Spinal dysraphism: a review of neuroradiological features with embryological correlations and proposal for a new classification. Neuroradiology 42:471–491
6. Dias MS, Walker ML (1992) The embryogenesis of complex dysraphic malformations: a disorder of gastrulation? Pediatr Neurosurg 18:229–253
7. Lawson ME, Share J, Benacerraf B, Krauss CM (1997) Jarcho-Levin syndrome: prenatal diagnosis, perinatal care, and follow-up of siblings. J Perinatol 17:407–409
8. Bulman MP, Kusumi K, Frayling TM, McKeown C, Garrett C, Lander ES, Krumlauf R, Hattersley AT, Ellard S, Turnpenny PD (2000) Mutations in the human Delta homologue, DLL3, cause axial skeletal defects in spondylocostal dysostosis. Nat Genet 24:438–441