Atlantoaxial instability in Dyggve-Melchior-Clausen syndrome

Case report and review of the literature

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Dyggve-Melchior-Clausen (DMC) syndrome is a very rare disease. Only 58 cases have been reported in the literature. The syndrome is probably an autosomal recessively inherited disorder, one that is characterized by mental retardation, the short-spine type of dwarfism, and skeletal abnormalities, especially of the spine, hands, and pelvis. Atlantoaxial instability–induced spinal cord compression is a serious and preventable complication. The purpose of this report is to describe the first case of DMC syndrome in which anterior transarticular atlantoaxial screw fixation was used to treat atlantoaxial instability. The authors report on a 17-year-old man with DMC syndrome and concomitant severe atlantoaxial instability. Computerized tomography scanning and magnetic resonance angiography demonstrated an irregular course of the vertebral artery (VA) at C-2, which made a posterior fixation procedure impossible. Additionally, transoral fusion was impossible because the patient was unable to open his mouth sufficiently. Therefore, the patient underwent anterior transarticular screw fixation. Follow-up examination 36 weeks after surgery showed solid fusion without implant failure. In conclusion, treatment of atlantoaxial instability in DMC syndrome must be considered. Specific care must be taken to determine the course of the VA. If posterior and transoral fusion are impossible, anterior transarticular atlantoaxial screw fixation might be the only alternative.

**KEY WORDS** • Dyggve-Melchior-Clausen syndrome • cervical spine • atlantoaxial stabilization • anterocervical fusion • vertebral artery • screw fixation

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**Case Report**

**History.** At birth the patient weighed 3500 g; his mother's pregnancy was uneventful. The parents are healthy first cousins from Georgia with four children. Two daughters are healthy with normal development. A 19-year-old brother, who still lives in Georgia, seems to be similarly affected. He is said to look like a twin brother of our patient.

The birth and early developmental growth of our patient were normal. Psychomotor development was delayed. He started to speak his first words at the age of 4 years. He walked independently at the age of 7 years.

**Examination.** Physical examination at the age of 17 years (Fig. 1) revealed short trunk, severely delayed short stature (height 105.5 cm, weight 18.4 kg), and relative microcephaly (head circumference 48 cm). He had a coarse face, long chin, short neck, sternal protrusion, barrel chest, abdominal distension, lumbar hyperlordosis, mild scoliosis, valgus deformity of the knee, limitation of knee move-
ment, and broad feet. The upper extremities were characterized by limited elbow extension, broad hands, and clawed fingers.

The patient was still prepubertal in his development. External genitalia were prepubertal. He was mentally retarded and exhibited a happy compliant disposition. He spoke in whole sentences and was able to articulate his thoughts, but he had poor comprehension and was not able to write.

Biochemical studies of urine and skin fibroblast samples revealed no evidence of a mucopolysaccharidosis.

Fig. 2. Upper: Radiograph demonstrating a typical abnormality of DMC syndrome: small ilia with broad lacelike borders of the thickened iliac crest (crest sign) found on radiographic examination. Lower: Radiograph demonstrating the typical double-hump endplates with central constriction of the flat VBs (generalized platyspondyly) typical of DMC syndrome.
Examination of blood chemistry and the patient’s hemogram demonstrated normal findings. Chromosome analysis demonstrated a normal karyotype 46, XY.

Radiography revealed a lacelike appearance of the iliac crest (Fig. 2 upper), generalized platyspondyly (Fig. 2 lower), and accessory ossification centers of the first metacarpals.

The patient was sent to our department with a 3-year history of severe neck pain. Clinical examination of the cervical spine revealed a reduced range of motion with hardening of the splenius capitis muscle on both sides. Neurological and neurophysiological examinations, including investigation of somatosensory evoked potentials, showed no signs of cervical myelopathy or radiculopathy. Os odontoideum was demonstrated on MR imaging (Fig. 3). Flexion–extension radiography revealed severe atlantoaxial instability. The anterior and posterior atlantoaxial interval in flexion was 7 and 10 mm, respectively (Fig. 4). Computerized tomography scans of the upper cervical spine revealed a broad foramen of the VA at C-2, extending deep into both pedicles (Fig. 5). Evaluation with MR angiography confirmed the irregular course of the VA at C-2.

Operation. The patient underwent anterior transarticular atlantoaxial screw fixation. Patient positioning, setup in the operating room, and anterior exposure were identical to those used when performing anterior odontoid screw fixation. The atlantoaxial joints were decorticated bilaterally by using curved curettes. The screws were inserted at the groove between the junction of the C-2 VB and the superior articular facet of C-2. Open-mouth and lateral C-arm images were obtained simultaneously to guide precise screw placement. In this case, a far-lateral trajectory for screw positioning was chosen to avoid interference with the barrel chest and sternal protrusion. Two 3.5-mm-diameter and 22-mm-long screws were inserted.

Postoperative Course. The postoperative course was uneventful and the patient was discharged 5 days after surgery wearing a Philadelphia collar for 8 weeks.

Follow-up examination at 2, 4, 12, 24, and 36 weeks postoperatively demonstrated evidence of solid fusion without implant failure (Fig. 6). The patient had no complaints of any pain.

Discussion

In a review of published cases, we found that 74 patients with DMC syndrome and SMD have been reported. Fifty-eight patients were mentally retarded (those with DMC syndrome) and 16 patients were not (those with SMD). This report adds a further patient to medical literature.

Dyggve-Melchior-Clausen syndrome is an inherited disorder. In a formal segregation analysis of 23 reported siblings, Toledo, et al., showed autosomal inheritance in DMC syndrome and SMD. Genetic heterogeneity can be suggested by the presence of mental retardation in DMC syndrome and its absence in SMD. The fact that the family of our patient has two affected and two unaffected children, together with the presence of parental consanguinity, provides further evidence for autosomal recessive inheritance. The localization of the faulty gene has not yet been determined.

The pathogenesis of DMC syndrome is unclear. Several authors have discussed a disturbance in the proteoglycan metabolism including: a deficiency of a specific sulfatase and/or protease involved in proteoglycan degradation, an error in glycoprotein–adenosine monophosphate metabolism, or an endoplasmatic storage disorder resulting in a defect of enchondral ossification. Analysis of biopsy samples of iliac crest obtained in patients with SMD or DMC syndrome have con...
firmed the disturbance of enchondral ossification. In these biopsy specimens bone tissue was deposited in a wavy pattern at the osteochondral junction. The growth plate showed abnormal enchondral ossification with no columnarization of the chondrocytes. Electron microscopy had demonstrated chondrocytes with dilated cisternae of rough endoplasmic reticulum containing fine granular or amorphous material. These criteria may be helpful to establish diagnosis of DMC syndrome.

The earliest clinical signs of DMC syndrome as thoracic deformities may be visible in the 1st months of life. After the 1st year short trunk dwarfism develops and is severe in the fully grown patient. The mean height in an adult male patients is approximately 128 cm.

In addition to dwarfism and mental retardation, DMC is characterized especially by skeletal abnormalities of the pelvis, hands, and spine. A typical abnormality are the small ilia in which there are broad, lacelike borders of the thickened iliac crest (crest sign) demonstrated on radiographic examination. Changes in the iliac crest seem to be unique and increase with advancing age. Characteristic radiographic changes in the hands are accessory ossification centers of the first metacarpals and the proximal and middle phalanges. Reports of radiographic changes of the spine in early childhood are sparse. In the case of a 5-month-old girl, the VBs were flat, there was minimal notching of some vertebrae, but not all vertebrae pointed anteriorly. In the case of an 18-month-old girl the VBs were flat with mild anterior wedging; minimal notches of some thoracic VBs were present. The typical double-hump endplates with central constrictions of the flat VBs (generalized platyspondyly) is usually present at age of 4 years and becomes more distinct in late childhood. These radiographic abnormalities are pathognomonic and distinctive for DMC syndrome.

Dwarfism and clawing of the digits somewhat resemble those in mucopolysaccharidosis. Initial reports of mucopolysaccharidosis could not be confirmed. Morquio disease and spondyloepiphysial dysplasia share the short-spine type of dwarfism with platyspondyly. The radiographic features permit differentiation, in particular the lacy configuration of the iliac crest.

In terms of survival the prognosis in DMC syndrome is not bad. The oldest patient described in the literature was 51 years of age. Our patient has not suffered from infections. He experienced no further medical problems other than those related to the disturbed growth of bone.

Atlantoaxial instability—induced spinal cord compression is a severe and preventable complication of both disorders. Including our patient, odontoid hypoplasia or os- sicleum terminale persists of the odontoid process has been described in nine patients with DMC syndrome (11% of all patients with DMC). Therefore, this feature seems to be associated with DMC syndrome. Three patients exhibited no neurological symptoms, including our patient and two brothers, age 5 and 6 years, respectively. Five patients were symptomatic. In a 15-year-old boy and his 13-year-old sister, as well as in a 12-year-old boy mild hyperreflexia has been observed. In a 34-year-old man with SMD spinal cord compression was present. In a 17-year-old woman with DMC syndrome quadriparesis was observed. This girl had severe atlantoaxial instability and underwent occipitocervical fusion (occiput–C3). In a follow-up period of 3 years, she exhibited no further deterioration. The affected brother of this girl developed a spastic paraparesis and became unable to walk.

With these potential complications in mind, we suggest that manifest atlantoaxial instability in DMC syndrome requires early stabilization. Several fixation methods to achieve this have been described in the literature: wire fixa-
tion techniques, posterior transarticular screw fixation, occipitocervical fusion (occiput–C2), long-term external fixation, transoral plate fixation, and anterior atlantoaxial plating combined with posterior wire fixation.

Because of the irregular course of the VA at C-2, our patient’s inability to open his mouth sufficiently, the short spine type of dwarfism, the barrel chest, and his questionable ability to comply, anterior transarticular atlantoaxial screw fixation was chosen. Usually, this procedure is reserved as a salvage technique in complex cases, such as the one presented here, in which posterior or transoral fixation devices cannot be applied. The screws provide rigid internal fixation. Bone grafts, however, cannot be inserted easily. In the present case decortication of the atlantoaxial joints was performed and solid fusion was achieved 9 months postoperatively in an anatomically reduced position of C-1 and C-2.

In conclusion, atlantoaxial instability in DMC syndrome must be considered even in asymptomatic patients. Specific care must be taken concerning the course of the VA. If posterior or transoral fixation is impossible, anterior or transarticular atlantoaxial screw fixation might represent an alternative procedure.

References

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