THE ODONTOID PROCESS IN MORQUIO-BRAILSFORD'S DISEASE

THE EFFECTS OF OCCIPITOCERVICAL FUSION

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High definition computed cervical myelograms have been made in flexion and extension in 13 patients with Morquio–Brailsford's disease. We observed that: 1) odontoid dysplasia was present in every case, with a hypoplastic dens and a detached distal portion which was not always ossified; 2) atlanto-axial instability was mild, and anterior atlanto-axial subluxation was absent in most cases; 3) severe spinal cord compression, when present, was due to anterior extradural soft-tissue thickening; 4) this compression was not relieved by flexing or extending the neck and was manifested early in life; 5) posterior occipitocervical fusion resulted in disappearance of the soft-tissue thickening and normalisation of subsequent development of the dens.

We conclude that the severity of neurological involvement at the craniovertebral junction was determined by soft-tissue changes, not by the type of odontoid dysplasia nor by subluxation. Posterior occipitocervical fusion proved to be an effective treatment.

Morquio–Brailsford's disease (MPS IV) is a congenital connective tissue disorder caused by reduced activity of one of two lysosomal hydrolases: N-acetyl-galactosamine-6-sulphatase (MPS IV type A) and B-galactosidase (MPS IV type B) (Lake 1984). The phenotype is a dysplastic dwarf, but less severe forms occur (Nelson, Broadhead and Mossman 1988). Patients often die in late childhood or early adult life from neurological disability or valvular and myocardial dysfunction, but survival into the fourth and fifth decades is reported (Langer and Carey 1966; Lake 1984; Nelson et al 1988).

Neurological disability arises from spinal cord compression either in the thoracic region or more commonly at the craniovertebral junction (Blaw and Langer 1969; Kopits et al 1972; Lipson 1977). Dysplasia of the odontoid process has been found in all adequately documented cases (Lipson 1977; Nelson and Thomas 1988), and is considered to be the major factor predispos-

Table I. Some features of 13 patients with Morquio–Brailsford's disease

Case	Age at time of first CTM (yr)	Sex	Enzyme deficiency (per cent of normal activity)	Neurological deficit*
1	0.9	M	Galactosidase (0)	+
2	3.1	M	Galactosidase (0)	+
3	3.2	M	–	+++
4	3.4	M	–	+++
5	3.6	M	–	+++
6	4.8	F	Galactosamine sulphatase (< 5)	+++
7	6.2	M	Galactosamine sulphatase (> 5)	+++
8	9.5	F	–	+++
9	9.5	F	–	++
10	9.8	F	–	+
11	21.0	M	–	+++
12	23.0	F	–	+++
13	28.2	M	Galactosamine sulphatase (< 5)	+/-

* neurological deficit: + mild, ++ moderate, +++ severe

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ing to subluxation. Anterior atlanto-axial subluxation is thought to be the main cause of spinal cord compression. Additional factors have been present in some cases, namely, thickening of the posterior longitudinal ligament, invagination of the posterior arch of the atlas into the foramen magnum (Kopits et al 1972; Goldberg 1976; Kopits 1976; Edwards et al 1982), and stenosis of the foramen magnum (Naidich, McLone and Harwood-Nash 1983).

We have performed 16 high definition computed myelograms on 13 affected patients, and some of our findings are inconsistent with these concepts. The aims of this paper are to redefine the abnormalities and to formulate firmer therapeutic guidelines than are currently available.

MATERIALS AND METHODS

Some features of the patients are shown in Table I. Keratan-sulphaturia was demonstrated in all cases. The results of specific enzyme studies were available in only five; three were MPS IV type A, and two were type B.

All patients had been referred because atlanto-axial subluxation was diagnosed on plain radiographs, and because some neurological disability was considered to be present, varying from minimal functional disturbance in the lower limbs (five cases), to spastic paraparesis or quadriplegia (nine cases). Neurological signs were present only in the nine paretic patients.

Complete conventional myelography was performed on all patients by injecting Iohexol (240 mg/ml) by lumbar puncture. Each patient was then transferred to a GE 8800 CT scanner and contiguous 1.5 mm sections were made from the level of the lower border of the external auditory meatus to at least the third cervical vertebra, with the head flexed and then with it extended.

One patient (case 12) was scanned ten years after an occipitocervical fusion. Three patients were scanned on two separate occasions, the second being six months (case 7), 18 months (case 8) and two years (case 6) after fusion. The fusions were occipitocervical (occiput to C1, and C1 to C2) in eight cases and atlanto-axial in one. Seven patients were treated by posterior fusion alone, and these had internal fixation using tibial and femoral strut grafts from the occiput to the axis. In case 5 we performed transoral excision of the anterior soft-tissue mass, since in this case it was the only definable cause of the severe cord compression. Under the same anaesthetic, a posterior fusion was also performed.

The one case of atlanto-axial fusion was not performed at our institution, nor was one of the occipitocervical fusions.

RESULTS

General features. The well known skeletal abnormalities of osteochondrodystrophy were present in all patients. Retrodisplacement of a vertebra between T9 and L2 was seen in seven and in one case C7 was also retrodisplaced. In nine patients there was diffuse constriction of the theca over two to four adjacent levels in the thoracolumbar region but in all cases the spinal cord compression was less severe than at the craniovertebral junction. There was mild paramedian basilar impression in case 7 with basilar clefts and a persistent hypochordal bow of the pro-atlas. Mild bilateral condylar hypoplasia was

present in case 13. The cerebellar tonsils protruded 4 mm below the lower margin of the foramen magnum in case 1.

Craniovertebral junction

Atlas. The anterior arch of the atlas was unossified in the midline in five cases (Fig. 1). In three of these, all aged less than seven years, there was an ossification centre within the defect indicating that fusion was likely to occur. There was a midline ossification defect in the posterior arch of the atlas in 11 cases, which included two of the three patients aged 20 years or more. The neurocentral synchondroses of the atlas showed a normal fusion pattern.

The internal sagittal diameter of the atlas ring was small in relation to the foramen magnum and to the rest of the cervical spine in ten cases, including eight of the 11 patients aged over four years. The unossified part of the posterior arch contributed significantly to spinal cord compression in eight cases. In cases 7 and 13 the arch invaginated slightly into the foramen magnum.

Fig. 1

Case 8. Axial image from a computed myelogram through the atlas, showing ossification defects in both the anterior and the posterior arches and an anterior soft-tissue mass indenting the theca and compressing the spinal cord.

Axis. The basal part of the dens was ossified in all cases (Fig. 2). In case 1, aged 11 months (see Fig. 3a) and case 3 aged three years, this part of the dens remained bipartite. The subdental synchondrosis showed a normal fusion pattern. Case 12, in whom there had been a craniovertebral fusion ten years previously, had a fully developed odontoid process (see Fig. 4c).

An os odontoideum was present in five patients; cases 11 and 13 were aged 20 years and over, and cases 4, 6 and 7 were aged three, four and six years respectively. The os was a large well corticated structure in the skeletally mature patients (see Fig. 3b); in cases six and seven it was a small nodule located posteriorly close to the basal part of the dens, but in case 4 it was more distal

Fig. 2

Tracings of three reformatted images from the computed myelograms of each of the 13 patients. The numbers correspond to the case numbers in Table I. For each patient, the left trace is from a mid-sagittal image made in flexion, the centre trace is from a mid-sagittal image made in extension, and the right trace is from a coronal image in the plane of the longitudinal axis of the body of the axis. (Various scales.) The arrows in the left traces of cases 1 and 2 indicate the subdental synchondrosis.

Figure 3a - Case 1. Coronally reformatted image through the axis to show the ossification pattern. The ossification centres for the dens are un-united and abnormally truncated. Figure 3b - Case 13. Coronally reformatted image through C2 showing an os odontoideum.

Fig. 3a

Fig. 3b

and anterior. The os was mobile in four cases, but not apparently so in case 11. Ossification in the distal part of the dens progressed rapidly after occipitocervical fusion in cases 6 and 7, suggesting normalisation of odontoid development (Fig. 4). In case 8, no ossification was visible in the distal part of the dens 18 months after atlanto-axial fusion.

Joints. Anterior atlanto-axial subluxation was defined as widening of the atlanto-dental interval of more than 4 mm. However, where no distal dens was visible,

separation of the upper anterior cortex of the remnant of the dens from the anterior arch of the atlas in a plane transverse to the spinal canal was measured. Where there was defective ossification in the anterior arch of the atlas the position of the dens remnant relative to the clival line was used, subluxation being present when the dens remnant lay posterior to this line. The clival line is drawn along the posterior surface of the clivus and projected down across the upper cervical region. Normally it just touches the apex of the dens. Posterior atlanto-axial

Fig. 4a

Fig. 4b

Case 7. Sagittal (left) and coronal (right) reformatted images from computed myelograms. The upper images are pre-operative and the lower images six months after cranio-cervical fusion.

Case 6. Sagittal (left) and coronal (right) reformatted images from computed myelograms. The upper images are pre-operative and the lower images two years after fusion.

Fig. 4c

Case 12. Sagittal and coronal images at ten years after craniocervical fusion.

Fig. 5

Sagittal reformatted image (below) of a computed myelogram showing the plane, indicated by the dotted double line, from which the axial image (above) was generated. The reformatted axial image of the axis shows a posterior concavity (arrow) adjacent to part of the extradural soft-tissue thickening.

subluxation was regarded as present when any part of the anterior arch of the atlas overrode the body of the axis. Using these criteria, posterior atlanto-axial subluxation was shown in 11 cases, and anterior atlanto-axial subluxation in three (cases 8, 9 and 13). The sagittal diameter of the spinal canal was reduced only minimally by the subluxation in each case and ranged from 12 to 14 mm.

The joint spaces between the lateral masses of the atlas and axis and between the occipital condyles and the atlas were abnormally wide in 12 cases, the exception being case 12 where the joint spaces were narrow.

Diminution of the abnormally wide joint spaces was observed in cases 6 and 7 after occipitocervical fusion (Fig. 4).

Soft tissues. The anterior extradural soft tissues were thickened in all except case 12. The soft-tissue thickening indented the thecal sac giving it a concave anterior contour on axial as well as sagittal images and was maximal at the level of the basal or distal part of the dens (see Fig. 1). In seven cases it also extended over the body of the axis, in three it included C3, and in one also C4. The posterior aspects of the basal part of the dens and the vertebral bodies adjacent to this soft-tissue thickening showed concavities which were not present in vertebrae immediately below it (Fig. 5). Two years after occipitocervical fusion in case 6, an ossification centre became visible within the concavity in the base of the dens and concavities in the bodies of the axis and C3 had disappeared. Also the soft-tissue thickening had greatly diminished, resulting in widening of the available subarachnoid space in cases 6, 7 and 8 (Fig. 4). The meninges were not thickened in any case.

A transoral odontoidectomy was performed on case 5, and firm tissue with a glistening cut surface that looked like cartilage was removed. Histological examination of this fragment of material revealed non-specific immature fibrous and fibrocartilaginous tissue.

Spinal cord. Severe compression of the spinal cord, defined as a reduction in the mid-sagittal diameter of greater than 50%, was present in eight patients. The site of maximal compression was opposite the basal part of the dens and the compressing agents were soft-tissue thickening anteriorly and unossified parts of the neural arch of the atlas posteriorly. The severity of compression of the subarachnoid space and spinal cord was similar in both flexion and extension.

In three patients spinal cord compression was only moderate, defined as definite overall reduction in the mid-sagittal diameter of the spinal cord of less than 50%. Compression was maximal at the base of the dens, but was relieved by extending the neck. In a further patient

there was slight flattening of the anterior surface of the spinal cord in flexion but not in extension.

In the patient studied ten years after occipitocervical fusion, the upper spinal cord was flattened in a capacious subarachnoid space. This suggested that the cord had been severely compressed in the past and irreversibly damaged.

There was a close correlation between clinical disability and severe spinal cord compression at the craniocervical junction, but not with atlanto-axial subluxation nor with size of the spinal canal. Only the eight patients with severe spinal cord compression had objective neurological signs; three were quadriparetic and five paraparetic. Case 12 had an atrophic spinal cord with a cross-sectional area of 33 mm at the level of C1, and she was quadriparetic.

The eight patients operated on tolerated their surgery well. However, only limited improvement in clinical status was achieved, which was the reason for re-investigating two of them, a third refused further investigation.

The two cases operated on elsewhere also experienced little improvement. Case 12 remained severely disabled after the operation. Case 8 continued to deteriorate neurologically, but this was perhaps due to worsening spinal cord compression in the lower thoracic region as shown by myelography. Further surgery on the craniocervical junction is not planned in the immediate future.

DISCUSSION

Patients with Morquio-Brailsford's disease often appear more or less normal until the age of two or three years, although characteristic skeletal abnormalities are usually apparent radiologically by the age of one year (Langer and Carey 1966). Clinical and radiological abnormalities progress most rapidly between the ages of two and six years, and thereafter relatively little skeletal growth and remodelling occurs. Nevertheless, there is considerable clinical heterogeneity, which does not correlate with the severity of the enzyme defect (Nelson et al 1988). The main effects of the disease are seen in cartilaginous and ligamentous tissues which become mechanically defective, and do not mature normally. In certain sites endochondral ossification remains incomplete, particularly in the vertebral bodies of the more mobile parts of the spine, and there is a generalised failure to remodel after ossification (Spranger, Langer and Weidemann 1974).

In the normal population, clefts in the anterior arch of the atlas occur in about 0.1% to 2%, and clefts in the posterior arch in 4% (Naidich et al 1983; Calvy et al 1987). In our patients, defects in the anterior arch were found in 24% and in the posterior arch in 72%, interpreted as persistence of unossified cartilage in these locations. In normal children the internal diameter of the atlas ring

is often narrow compared to the rest of the cervical canal up to the age of about two years (Calvy et al 1987), whereas in all our patients this diameter remained small, and the neural arch abnormally thick. Mild invagination of this neural arch into the foramen magnum, seen in two patients, was explained by the presence of paramedian basilar invagination in one and symmetrical condylar hypoplasia in the other.

Dysplasia of the dens of one type or another has been a feature of all cases in which the craniovertebral junction was examined. It has become conventional to classify the dysplasias as (a) hypoplasia, (b) aplasia, (c) aplasia of the basal portion, and (d) os odontoideum (Beighton and Craig 1973; Kennedy, Swash and Dean 1973; Bethem et al 1981). Nelson and Thomas (1988) suggested two categories, major and minor, only the major being associated with atlanto-axial instability. However, interpretation of plain radiographs of the craniovertebral junction is not easy in these patients, and computed myelography is more reliable (Edwards et al 1982). MRI is also effective (Kulkarni et al 1987), but may not show the early appearance of ossification.

The odontoid abnormality shown in this study was strikingly uniform. Only the portion of the odontoid contained within the body of the axis was ossified by birth, and all skeletally mature patients had an os odontoideum. Although adult patients without an os odontoideum have been reported (Langer and Carey 1966; Lipson 1977; Nelson and Thomas 1988) illustrations have been either inadequate, or indicate additional segmental fusions which sometimes are associated with an abnormally short dens. Other anomalies at the craniovertebral junction have also been described (Jenkins, Davies and Harper 1973), and among our patients case 7 displayed remnants of the pro-atlas.

In normal development most of the dens has ossified by birth. In two of our youngest cases the ossification centres remained paired and their truncated appearance suggested that functional detachment of the distal part of the cartilaginous anlage had occurred early in development. This interpretation was strengthened by the rapid appearance of ossification in the soft tissues above the odontoid base after occipitocervical fusion in two cases, and it probably also had happened in case 12, which to our knowledge is the only reported biochemically proven case of Morquio-Brailsford's disease with a well developed dens. It is postulated that early detachment of the distal part of the dens, and its delayed ossification, are both the result of abnormal mobility during development.

Severe atlanto-axial subluxation is uncommon. The minimum mid-sagittal diameter of the spinal canal usually has varied between 12 and 16 mm even in cases showing subluxation (Lipson 1977), and subluxation of any degree has been shown in only 42% to 90% of cases overall (Blaw and Langer 1969; Lipson 1977; Nelson and Thomas 1988). Since articular hypermobility is a univer-

sal feature of Morquio-Brailesford's disease it might be expected at the craniovertebral junction in all cases, and failure to show it probably only indicates an unreliable aspect of flexion and extension imaging.

In this study it was clear that the severity of spinal cord compression was determined by the thickness of the anterior extradural soft tissues. In mild cases anterior soft-tissue thickening was contained within concavities in adjacent vertebral bodies and the basal part of the dens. Since this tissue ossified after craniocervical fusion it probably represented unossified cartilage. In severe cases the soft-tissue thickening was greater and rapid regression after fusion suggested that much of it represented reactive ligamentous changes, such as has been reported in other forms of non-inflammatory atlanto-axial instability (Sze et al 1986). The histological appearance of this material from case 5 was not very revealing, and this has been the experience of others (Einhorn, Moore and Rowntree 1946; Lake 1984), but some of it did appear to be cartilage. Thickening of the spinal dura mater may cause spinal cord compression in Hurler-Scheie and Maroteau-Lamy types of mucopolysaccharoidosis, and the histology of this material was reportedly similar to that found extradurally in our case (Kennedy et al 1973; Sostrin et al 1977).

The surgical strategy of establishing an occipitocervical fusion seems a satisfactory solution for most cases. It may be necessary to consider a transoral excision of the anterior soft-tissue mass when this is the only way of achieving an immediate decompression of the spinal cord, and when posterior fusion is judged to be unreasonably hazardous. Cervical laminectomy, such as was performed on one of the cases of Kulkarni et al (1987) is manifestly the wrong approach. One patient treated by atlanto-axial fusion demonstrated less complete radiological resolution than the three in which the occiput was included, which may be significant. The appearance of the spinal cord in case 12 suggests that it had been

irreversibly damaged prior to or possibly during the fusion. This may be the fate of many patients and supports the proposition that the best time for operation may be early in life if the spinal cord is to be protected.

We propose that only patients with marked extradural thickening should be considered for operation. The radiological demonstration of atlanto-axial subluxation is of little value, because many patients with subluxation survive into adult life without major spinal cord compression. The best investigation is high quality magnetic resonance imaging, which will demonstrate both the degree of soft-tissue thickening and of spinal cord compression. It is suggested that the optimal time for elective investigation is between three to eight years of age, since this is when skeletal maldevelopment is usually complete, and little or no axial growth occurs thereafter. It is difficult to say precisely what degree of spinal cord compression constitutes an indication for surgery. Recent clinical and radiological studies of spinal cord compression in cervical spondylosis (Fujiwara et al 1989) and rheumatoid arthritis (Hunter et al 1991) indicate that there is little correlation between reduction in measurable diameters of the spinal cord and clinical status, and that once reductions of about 60% are present, clinical improvement after operation is unlikely. Therefore, we propose, as an indication for operation, reduction in measurable diameters of the spinal cord approaching 50% regardless of the clinical status.

We believe that some aspects of these studies have implications beyond the narrow compass of this rare metabolic disorder.

Since this paper was submitted, we have performed computed myelography on a further two cases and MRI only in one, two of which had a cervicothoracic as well as a thoracolumbar kyphosis. An unossified os odontoides, posterior atlanto-axial subluxation and only minimal spinal cord compression were shown in two and an os odontoides in the third.

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