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PROGRESSION OF CONGENITAL KYPHOSIS IN ISHIBASHI RATS

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The development of congenital kyphosis was studied radiographically and histologically in 32 female and 34 male Ishibashi rats between the fourth and thirty-sixth week after birth. The major congenital spinal anomalies were defects of segmentation in the lumbar area. The malformation was classified into four groups according to the state of non-segmentation seen in radiographs. The progression of kyphosis was closely related to various changes at intervertebral spaces. The spinal deformity resulting from narrowing of the intervertebral spaces without bony fusion did not progress with growth, and the epiphyseal plates remained relatively intact unrelated to the existence of disc tissue. The deformity resulting from ventral bony fusion without radiographic bony anomalies showed histologically dysplastic epiphyseal plates on the ventral side. Progression of the kyphosis occurred in this type of deformity. The kyphosis resulting from bony fusion and ventral wedge-vertebrae progressed in the males. Progressive kyphosis appeared to be due to a difference in growth potential between the ventral and dorsal epiphyseal plates.

Key words: congenital kyphosis; development; growth; Ishibashi rat; spinal deformity

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Several studies have clarified that congenital deformity progresses with growth of the spine (Kuhns 1934, Ullich 1956, Winter et al. 1968), as seen in idiopathic cases, especially during the adolescent growth spurt. Spinal deformities due to congenital anomalies appear to progress in two ways: in the primary type, the curvature progresses with the development of the malformed spine; in the secondary type, malformed segments only trigger progression of the deformity at the neighbouring normal segments. Therefore, it is essential to understand how the vertebra itself becomes malformed.

We have attempted to clarify the development of kyphosis due to defects of segmentation in the Ishibashi (1979) rat which has the hereditary characteristic of spinal deformity, developing mainly in the lumbar area.

MATERIALS AND METHODS

To observe the development of kyphosis with growth, 32 female and 34 male Ishibashi rats (ISR) with kyphotic angles of 20 degrees or more at the beginning of the fifth week of life were used.

Soft radiographs in lateral and A-P projections were taken sequentially, weekly up to 8 weeks, and biweekly after 10 weeks. During the roentgenography, animals were kept under ether anesthesia with the lumbar spine held in the extended position in a styrol-foam frame which conformed to the body shape.

Defective segmentation in ISR occurs most frequently in the intervertebral spaces L3 and L4 or L4 and L5. Multiple defects are also frequent (Yamada et al. 1982). As the kyphosis is usually associated with only one segmental defect, the kyphotic curvature was defined as the angle of intersection of lines joining the cephalic and the caudal points on the dorsal aspects of the vertebral bodies adjacent to the critical vertebral disc space (Figures 5, 9 and 10).

Routine histological examination was made of sagittal sections of the lumbar spine in order to examine the condition of the growth plates of the vertebral bodies.

RESULTS

Of the 309 ISR (150 females, 159 males) used for the experiment, nine had a butterfly vertebra. Hemivertebrae or diastematomyelia-like anomalies were never seen on the roentgenograms. The pattern of the kyphotic curvature consisted only of the malformed segments; the normal segments were not involved in the congenital curve. The incidence of kyphosis measured on radiograms after 8 weeks of life was similar in both sexes with 56% of 20 degrees or more, 27% under 20 degrees, and 17% normal.

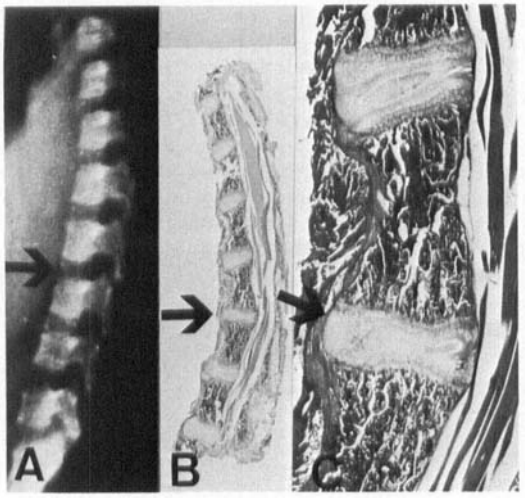

Figure 1. In Group 1, there was disc narrowing only. The microscopic illustrations (Figures 1–5c, 8d, 9d) were stained with hematoxylin and eosin, ×10.

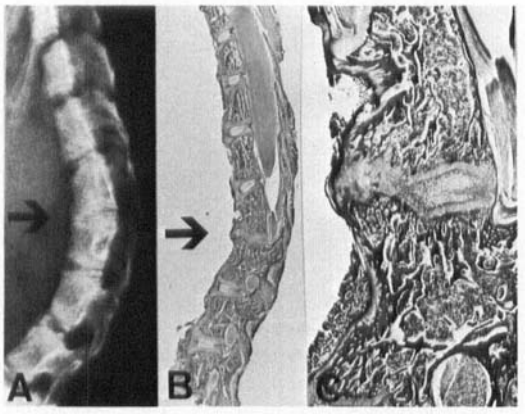

Figure 2. In Group 2, there was disc narrowing and irregularity of the ends of the vertebral bodies adjacent to defect of segmentation.

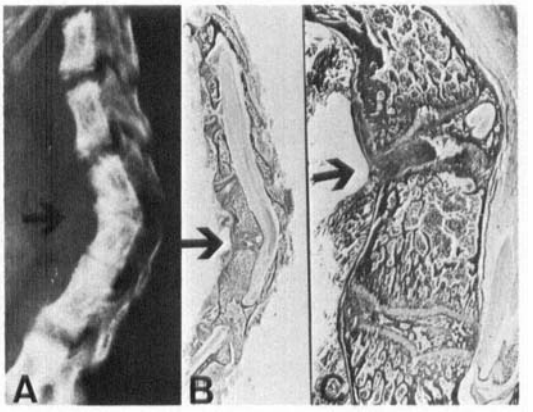

Figure 3. In Group 3, there was a rudimentary linear space, sometimes with a radiolucent mass dorsally.

Segmental defects as assessed radiographically at 4 weeks of life were classified into four groups according to the degree of non-segmentation, and the progression of kyphosis was followed in each group.

In *Group 1* (Figure 1), there was only disc narrowing. In histological specimens, the nucleus pulposus was found to be displaced dorsally in the narrowed disc. Ventrally, the annulus fibrosus was diminished and replaced by cartilage tissue. Localized calcification was also detected. The growth plates adjacent to the narrowed disc were intact.

In *Group 2* (Figure 2), there was narrowing of the intervertebral spaces and irregularity of the adjacent ends of the vertebral bodies. In histological specimens, the disc tissue was not distinguishable. The intervertebral space was occupied ventrally by partially calcified fibrous connective tissue and dorsally by cartilage-like cells. The growth plates were most often intact, but some had a ventral narrowing.

In *Group 3* (Figure 3), there were rudimentary linear spaces at the disc level, sometimes accompanied by a wedge-shaped dorsal radiolucent

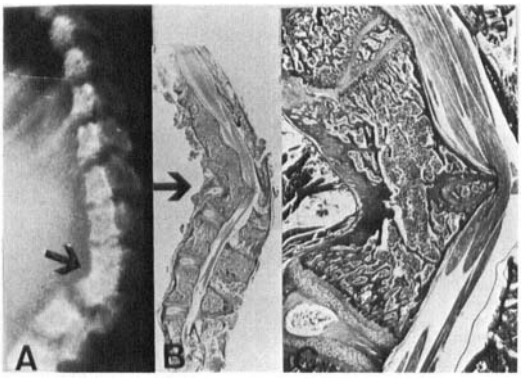

Figure 4. In Group 4, the vertebrae were fused.

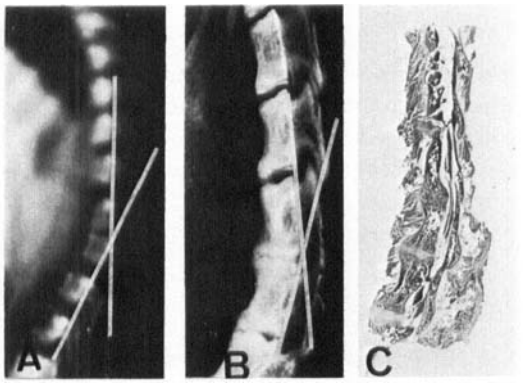

Figure 5. Progress of curvature was nil in Group 2. A: At 3 weeks, the angle of kyphosis was 23 degrees. B: At 10 weeks, it was 20 degrees.

mass. In histological specimens, the disc tissue was completely replaced by cartilage cells. In some specimens there was a dorsal rudimentary nucleus pulposus. Growth cartilage was virtually intact dorsally, but thin or absent ventrally.

In *Group 4* (Figure 4), there were defects involving complete bony fusion of the two vertebral bodies, confirmed histologically. One of the fused bodies was often a ventral wedge-vertebra. Ventrally, the cortex was hypertrophied, while dorsally, oval or wedge-shaped ossification was seen surrounded by growth cartilage.

Kyphosis in Groups 1 and 2 was rarely associated with defects of formation of the vertebral body. The angle of kyphosis in these groups was about 20 degrees, and progression of the curvature with growth was not observed. For example, the angle was 23 degrees at 3 weeks and 20 degrees at 10 weeks in the specimen illustrated in Figure 5.

Animals in Group 3 which lacked defects of formation were divided into two subgroups. In the first, there was a linear space extending across the intervertebral space, and progression was less than 10 degrees (Figure 6 upper). The other showed a bony fusion ventrally, a linear space dorsally, and progression was slight (Figure 6 lower).

In Group 3 with defects of formation and in most of the animals in Group 4, the kyphotic angle reached 40 degrees at 4 weeks. In the

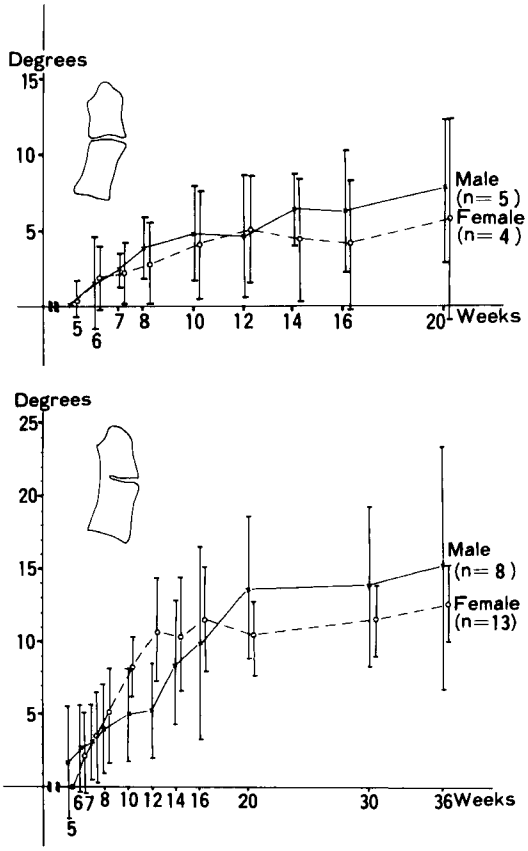

Figure 6. The progress of curvature in Group 3 in the absence of defects of formation. Upper: Cases in which the linear spaces extended across the intervertebral space; no progress was detected in either sex. Lower: Cases in which the intervertebral space was retained only dorsally; slight progress in both sexes.

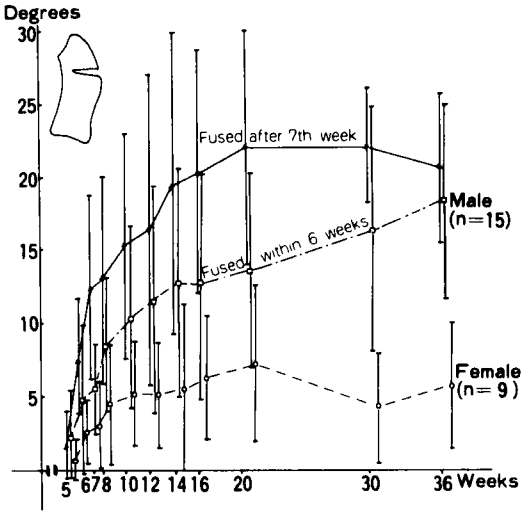

Figure 7. The progress of curvature in animals of Group 3 and 4 with defects of formation. No progression occurred in the females, while in those males which retained a linear space after 7 weeks there was greater progress than in those in which the bony fusion occurred before 6 weeks.

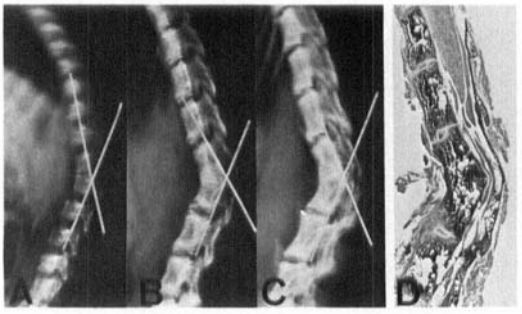

Figure 8. A male rat in which the vertebrae had fused at week 6 with no subsequent progress. A: At 3 weeks, the angle of kyphosis was 32 degrees. B: 6 weeks, it was 40 degrees. C: At 14 weeks, it was 42 degrees.

females, progress was less than 10 degrees, while in the males more rapid progress was observed. In Group 3, bony fusion sometimes developed, and this was characteristic in Group 4 at 6 weeks. When a dorsal linear space at the intervertebral level was visible radiographically at 7 weeks, there was greater progress of kyphosis than when fusion was complete within 6 weeks (Figure 7). For example, when bony fusion occurred before

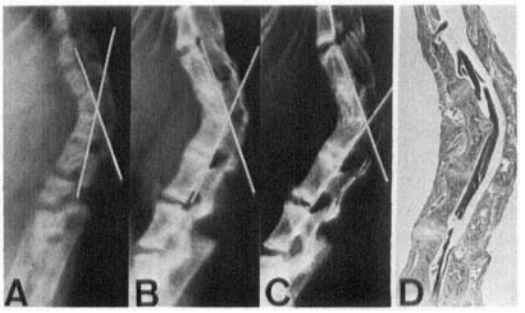

Figure 9, A male rat in which the invertebral space remained dorsally at 12 weeks and which showed rapid continuous progress. A: At 4 weeks, the angle of kyphosis was 31 degrees. B: At 12 weeks, it was 42 degrees. C: At 18 weeks, it was 54 degrees.

the seventh week, the curvature progressed slowly (Figure 8). On the other hand, a spine which retained the dorsal linear space after the seventh week showed more marked progress (Figure 9).

DISCUSSION

Spinal deformity occurs naturally in many species, usually congenitally. Useful models of spinal deformity due to malformed spines include the Taylor (1971) chicken, Ishibashi (1979) rat, and other species with congenital malformations induced by prenatal administration of teratogens have been reported by Nogami & Endo (1970), Theiler (1958) and Watanabe et al. (1979), who reported the development of malformed vertebrae prenatally. However, only two reports have appeared on idiopathic kyphoscoliosis in animals, viz. Reggins chicken (McCarrey et al. 1981) and Japanese quail SQOHM (Hijikata et al. 1979).

According to Ishibashi (1979), a Wistar female rat bred with a wild rat bore agouti-coated offsprings. During selective inbreeding of the agouti-coated rats, abnormal kyphosis was noticed in the sixteenth generation. X-ray examination revealed congenital anomalies of the spine. Further research showed that almost all these rats had spinal malformations, mainly in the lumbar area with defects of segmentation and/or formation. The rats sometimes had spinal cord

compression symptoms or perhaps diastematomyelia (Arima et al. 1976). Most of our rats had mainly a defect of segmentation; the only severe defect of formation noted was ventral wedge-vertebra; about 20% of all these rats were affected.

The mode of inheritance of vertebral anomalies in ISR is still under investigation. Yamada et al. (1982) suggested that the causal gene was a single autosomal recessive one with a penetrance of 50%. Clinico-biological studies disclosed a low level of serum alkaline phosphatase activity in ISR but this appeared unrelated to spinal malformations (Maekawa et al. 1982, Takahashi et al. 1981).

Having examined clinical cases, some authors have postulated that the progress of congenital scoliosis is closely related to the asymmetrical development of malformed vertebrae (MacEwen et al. 1968, Winter 1973). Watanabe (1980) reported that the growth potential and prognosis of each abnormal spine could be predicted early and correctly by the appearance of the bone nucleus for the anlage.

Kyphosis was caused by two factors. One resulted from the dorsal displacement of the nucleus pulposus, which created a curvature of about 20 degrees on the first examination, but no further progress. The other was due to the replacement of the intervertebral disc by cartilage cells, which resulted in hypoplasia or dysplasia of the epiphyseal growth cartilage at its ventral part.

The radiographic classification of the defects proposed here was useful for predicting the prognosis as regards progress of the kyphosis.

In some of the males with ventral wedge-vertebra, neurologic complications were probably caused by a projection of the dorsal prominence into the spinal canal (Figure 4).

Conclusion

Progress of congenital kyphosis is closely related to dysplasia of growth cartilage, which can be predicted radiographically by various changes in the intervertebral spaces. When the growth plates were severely affected, progress of the curvature was more marked in males than in females, presumably due to a difference in growth potential of the spine.

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