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Letter to the Editors

XY sex-reversed campomelia - possibly an X-linked disorder?

Key words: Campomelia; gentic heterogeneity, gonadal malignancy; sex reversal; X-linked inheritance.

Sirs,

Hoefnagel et al. (1978) recently recorded two patients with campomelic dwarfism and XY gonadal dysgenesis, bringing the total of such cases with sex-reversal to at least seven (Gardner et al. 1970, Hovmöller et al. 1977, Rochiccioli et al. 1977). Another such patient has recently come to my attention.

The infant, a phenotypic female, was transferred to the University of Kansas Hospital at the age of 6 hours because of respiratory distress. On examination she was found to be 41 cm in length with a head circumference of 36.5 cm and a chest circumference of 30 cm. The occiput was flat, the head appeared large compared to the face, micrognathism was present, the eyes were small but widely set, and there was a cleft extending through the posterior hard and all of the soft palate. The larynx was described as narrow at the time of intubation. There was a left thoracic scoliosis and the clitoris appeared large. Both femurs were bowed anteriorly and there were cutaneous dimples over both tibias. Bilateral equinovarus deformities were present. X-rays showed incomplete development of the right side of the thoracic vertebral bodies. The ribs were slender. Both femurs and both tibias were bowed. There was no craniosynostosis and the upper extremities were normal. A peripheral blood karotype showed a consistent 46,XY pattern in all metaphases. The infant developed progressive respiratory difficulty and expired on the fifth hospital day. At autopsy she was found to have an infantile uterus, vagina, and bilateral fallopian tubes. An ovary was present on the left but no gonad was identified on the right.

Khajavi et al. (1976), in an analysis of 9 personal cases and others from the literature, concluded that the campomelic syndrome was heterogeneous and could be subdivided into three groups. The classic syndrome has all the skeletal features as reported in the present case and is termed the long-limbed type. The others are the short-limbed, normocephalic and the short-limbed, craniosynostotic varieties, respectively. All instances of XY-sex reversal in which sufficient data are available for analysis, have been recorded in patients with the long-limbed type of campomelic syndrome, thereby providing evidence that the condition is even more heterogeneous than originally anticipated. Moreover, the gonadal pathology in the sex-reversed campomelic syndrome has not been consistent, Gardner et al. (1970) describing embryonal testicular tissue, the other reports recording ovarian histology with varying degrees of differentiation. Unfortunately, the single ovary in the present case was inadvertently not sampled at necropsy, so the issue remains unclarified.

It would appear that long-limbed campomelic syndrome is inherited as an auto-

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somal recessive, although the evidence is far from strong. There is a marked preponderance of affected females, some of whom obviously have an XY karyotype. Nothing is known about the genetics of the short-limbed types. All of the patients with XY sex-reversed campomelic syndrome have been sporadic. However, in view of the fact that XY pure gonadal dysgenesis is inherited as an X-linked recessive, one might speculate that XY sex-reversed campomelic dwarfism might follow a similar pattern of inheritance, especially in view of the distorted sex ratio. Although the condition has generally been lethal in infancy, it is possible that some affected infants will eventually survive; conceivably, they could be at-risk for gonadal malignancy. Additional reports of such patients are urgently needed and should include a peripheral blood karyotype and histological examination of the internal genitalia and both gonads. Chromosome studies of the gonads might provide further insight into the basic pathophysiology of the disease process.

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