Hurler-Scheie Phenotype: A Report of Two Pairs of Inbred Sibs

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Summary. Four cases from two families with dermatan sulfate mucopolysacchariduria who lack α-L-iduronidase in peripheral leukocytes are described. The clinical and roentgenographic features of these cases represent an intermediate phenotype between Hurler’s syndrome and Scheie’s syndrome, and both parents in each family are first cousins. In the presence of parental consanguinity, a phenotypic variation or a third mutant allele at the iduronidase locus seems to be a more reasonable explanation for these cases than a genetic compound.

Introduction

On clinical grounds, Hurler’s syndrome and Scheie’s syndrome are clearly distinct entities, although they have been shown to be caused by a deficiency of the same enzyme, α-L-iduronidase. To account for the impressive clinical difference between Hurler’s syndrome and Scheie’s syndrome, McKusick et al. (1972) suggested that the mutations causing these syndromes are not identical but allelic. They also postulated that since the genes responsible for Hurler’s and Scheie’s syndrome might be allelic, a genetic compound of the two syndromes might occur, i.e., a Hurler-Scheie genetic compound showing some phenotypic expression of both mutant genes. This hypothesis of a recessive genetic compound is based primarily on their intermediate clinical features, the absence of parental consanguinity, and is in keeping with the hypothesis that the Hurler’s and Scheie’s genes are allelic. An intermediate Hurler-Scheie phenotype has been reported in 18 patients with α-L-iduronidase deficiency (Danes, 1977; Elliott and Dorst, 1974; Horton and Schimke, 1970; Jensen et al., 1978; Kajii et al., 1974; Leisti et al., 1976; McKusick et al., 1972; Paragariya et al., 1975; Thompson et al., 1975; Tondeur et al., 1976; Winters et al., 1976). Although some cases may represent a Hurler-Scheie genetic compound, there may exist a phenotypic variation or a third mutant allele at the Hurler-Scheie cistron.

This report describes four patients showing phenotypic expression intermediate between Hurler’s syndrome and Scheie’s syndrome, with parental consanguinity. Similar inbred sibship has been reported by Jensen et al. (1978).

Case Reports

Family 1

Case 1. S.D., a 35-year-old Japanese female, was referred to the University Hospital for evaluation of her physical deformities. The parents were healthy and were first cousins. Two younger brothers and one younger sister were normal. One younger brother had the same condition (case 2).

Except for frequent respiratory infections, the patient’s early physical development was considered normal. When she was 6 years old, increasingly coarse facial features, small stature, and restricted joint mobility were noted. During the following years night blindness developed. She was graduated from junior high school with average marks. When she was 20 years old, she underwent an operation to repair an umbilical hernia. At 23 years of age she married, and a pregnancy ended in an artificial abortion during the third month.

Physical examination when the patient was 35 years old revealed the mild “gargoyle-like” features seen in Fig. 1. Her head circumference was 54 cm, her height was 130.5 cm, and her weight was 39 kg. Her coarse facial features, depressed nasal bridge, anteverted nostrils, thick lips, and widely spaced teeth contributed to the typical appearance of a patient with a mucopolysaccharide disorder. The corneas showed gross clouding. Irregular retinal pigmentation was noted in the equatorial areas of the fundi. A systolic murmur was heard at the lower
Fig. 1a–d. Frontal view in (a) Case 1, age 35 years; (b) Case 2, age 28 years; (c) Case 3, age 33 years; (d) Case 4, age 30 years.

Fig. 2. Roentgenograms of case 1. The carpal bones are small and irregular (top left). The end-plates of lumbar spine show varying degree of irregularities (top right). The acetabula appear shallow and coxa valga is present bilaterally (bottom).

Fig. 3. Roentgenograms of case 2. Findings are almost identical to those in case 1.