Presentation of mucopolysaccharidosis VII (β -glucuronidase deficiency) in infancy

SUMMARY A child is presented with mucopolysaccharidosis VII (β -glucuronidase deficiency), bringing to six the number of reported patients with the infantile onset form of this disorder. This patient exhibited the following features, previously unrecognised as part of this syndrome: presentation in the neonatal period, progressive joint contractures, and hydrocephalus. This child's course and data from published reports indicate that mucopolysaccharidosis VII, unlike the other known mucopolysaccharidoses, is clinically recognisable in the newborn period and is most likely to be associated with moderate mental deficiency which does not progress over time.

Mucopolysaccharidosis VII (MPS VII) was first described by Sly *et al*¹ in an infant with short stature, skeletal deformities, hepatosplenomegaly, and mental retardation. In both leucocyte and fibroblast cultures, a profound deficiency of β -glucuronidase was identified. Subsequently four additional patients with β -glucuronidase deficiency presenting in infancy have been described.²⁻⁴ We have recently evaluated a child with MPS VII who exhibited the following features previously unrecognised as part of this syndrome: presentation in the neonatal period, progressive joint contractures, and hydrocephalus. The purpose of this report is to delineate further the clinical features of this disorder and to support the concept that there exist at least two forms of MPS VII: an early onset type and at least one other form presenting in the second decade of life.

Case report

The patient (fig 1) was born after a 40 week gestation to a gravida 5, para 5, 34-year-old white woman and 36-year-old white man. The parents denied consanguinity. Gestation was remarkable for decreased fetal activity. Birthweight was 4.2 kg. (90th centile) and length was 55 cm (90th centile). He had coarse facies, a muscular torticollis, generalised contractures,

FIG 1 The proband at 22 months of age. Note coarse facies, gibbus deformity, and joint contractures.

bilateral metatarsus adductus, and camptodactyly of the left hand with absent distal interphalangeal creases of the third and fourth fingers.

At 11 weeks of age, he had a height of 62 cm (75th centile), a weight of 5.3 kg (30th centile), and a head circumference of 41.5 cm (50th centile). Over the first 9 months of life, he was admitted to hospital on four occasions for episodes of wheezing and pneumonia. At 9 months, his weight and height were 8.7 kg (30th centile) and 72 cm (30th centile), respectively. His head circumference, which up until 6 months had followed the 50th centile, had increased to 50 cm (>97th centile). In addition, a gibbus deformity of the lumbosacral spine and bilateral inguinal hernias were noted. Development was delayed with a history of first rolling over at 6 months and sitting at 8 to 9 months. He had a poor pincer grasp. A urine screen for acid mucopolysaccharides was normal. Complete skeletal survey revealed findings of dysostosis multiplex (fig 2). Computerised tomogram of the skull showed generalised enlargement of the third, fourth, and lateral ventricles, as well as prominence of the Sylvian fissures. A ventriculoperitoneal shunt was placed at 10 months. A ventricular tap at the time of surgery revealed increased intraventricular pressure.

At 11 months fibroblast culture and enzyme assay demonstrated a specific profound deficiency of β -glucuronidase with a mean value of 0.69 μ mol substrate cleaved/mg protein/h at 37°C (normal

Received for publication 11 July 1980

FIG 2 Roentgenographic findings of dysostosis multiplex. Upper left: note the gibbus deformity and anterior inferior beaking of the lower thoracic and lumbar vertebrae. Upper right: there is proximal pointing of the metacarpals. Lower left: note the abnormal irregular ossification of the humeral head. Lower right: the pelvis is low and broad with a narrow sciatic notch and hypoplastic basilar portions of the ilia. There are irregularities of the femoral heads and acetabular dysplasia.

mean = 178 μ mol). The father and mother exhibited intermediate values of 42 and 79 μ mol, respectively. β -glucuronidase was assayed fluorometrically according to standard methods by measuring the 4-methyl umbelliferone released from the β -glucuronidic derivative.⁵

At 22 months, his height was 82 cm (10th centile), his weight was 12.2 kg (30th centile), and his head circumference was 51.5 cm (98th centile). Physical examination revealed diffuse mild corneal clouding, coarse facies, hepatosplenomegaly, a gibbus deformity, and increased joint stiffness. Development continued to be mildly delayed. Walking began at 18 months, finger feeding began at 19 months, and language was restricted to two single words. Repeat urine screen by the acid albumin turbidity test demonstrated grossly raised acid mucopolysaccharides (one hundred times the normal value).

Discussion

The patient described here represents the ninth report of a patient with β -glucuronidase deficiency. Six of these presented in infancy and manifest a distinct pattern of altered growth, structure, and development.¹⁻⁴ The remaining three presented in the second decade of life and have few clinical similarities among one another.^{3,5,6} The clinical features of the infantile form of MPS VII are summarised in the table.

TABLE Summary of clinical features of mucopolysaccharidosis VII presenting in infancy

	CR ^{1,4}	MB ²	KB ³	JE ⁴	ME ⁴	TM [*]	Total
Postnatal growth deficiency	+	+	+	?	?	+	4/4
Macrocephaly	+	-	+	?	?	+	3/4
Developmental delay	+	+	+	+	+	+	6/6
Coarsened facies	+	+	+	+	+	+	6/6
Corneal clouding	+	+	+	?	?	+	5/5
Inguinal hernia	+	+	+	?	?	+	4/4
Hepatosplenomegaly	+	+	+	?	?	+	4/4
Gibbus deformity	+	+	+	?	?	+	4/4
Joint contractures	-	-	-	?	?	+	1/4
Dysostosis multiplex	+	+	+	?	?	+	4/4

*The patient described here.

With respect to postnatal growth deficiency, height and weight were below the 3rd centile in two patients,^{1,3} and in two growth delay was mild (10th centile).² With regard to macrocephaly, onset of accelerated head growth was variable, occurring in the first year in TM and CR^{1,4} and in the third year in KB.³ TM, the subject of this report, is the only patient in whom increased intracranial pressure requiring ventriculoperitoneal shunting has been described.

Developmental delay, mild to moderate in four of the six affected children,^{1,2,4} has been non-pro-

gressive in the two children followed up for some time, one for 8 years and one for 22 months. Two patients, KB and ME, showed marked developmental delay which we feel goes beyond the effect of β -glucuronidase deficiency.^{2,4} Both of these patients had neonatal hyperbilirubinaemia. KB developed a giant cell hepatitis and a downhill clinical course with death at 2 years 9 months and ME developed neurological signs of kernicterus.

Onset of corneal opacification varied from 7 months³ to 8 years.⁴

Progressive joint contractures, first manifest in the newborn period, have been seen in one patient, the subject of this report.

Findings of dysostosis multiplex have been variable. Consistent findings have included a 'J-shaped' sella and characteristic pelvic abnormalities with acetabular dysplasia, narrow sciatic notches, and hypoplastic basilar portions of the ilia.¹⁻⁴ Widening of the ribs has been noted in three patients,^{1,3} and pointed proximal metacarpals have been described in two.¹ Vertebral abnormalities have differed: a hypoplastic odontoid and shortening and anterior irregularities of the vertebral bodies occurred in one child^{1,4}; wedge deformities of the lumbar vertebrae were described in another.³ Anterior inferior beaking of the lower thoracic and lumbar vertebrae was noted in the subject of this report. In one additional patient the spine was reportedly normal, although a mild gibbus deformity was apparent.² Hip dysplasia has been noted in two patients^{1,4} and has been severe and progressive in one child.⁴ Other abnormalities have included medullary expansion of the proximal humeri¹ and abnormal irregular ossification of the humeral heads.

Frequent respiratory infections have been described in all patients.¹⁻³

The variability in urinary acid mucopolysaccharide excretion exhibited by this child merits comment. The two screens were carried out in the same laboratory using the same procedure. Although we cannot rule out a problem with faulty preservation of the first urine sample, variable urinary acid mucopolysaccharide excretion in other patients at various points in time has previously been encountered (Sly, 1980, personal communication).

In summary, this patient's course and data from published reports indicate that MPS VII, unlike the other known mucopolysaccharidoses, is a distinct clinical entity recognisable in the newborn period. Hydrocephalus and progressive joint contractures are occasional features. With respect to developmental prognosis, this disorder is most likely to be associated with moderate mental deficiency which does not progress over time.⁴

We appreciate the secretarial assistance of Ms Betty Grenier in the preparation of this manuscript.

H EUGENE HOYME,*† KENNETH LYONS JONES,*
MARILYN C HIGGINBOTTOM*,
AND JOHN S O'BRIEN†

*Department of Pediatrics and †the Department
of Neurosciences, University of California,
San Diego School of Medicine, La Jolla,
California, and Children's Hospital and Health
Center, San Diego, California, USA

†Supported by March of Dimes Birth Defects Foundation

References

- Sly WS, Quinton BA, McAlister WH, Rimoin DL. Beta glucuronidase deficiency. Report of clinical, radiologic, and biochemical features of a new mucopolysaccharidosis. *J Pediatr* 1973;**82**:249-57.
- Gehler J, Cantz M, Tolksdorf M, Spranger J, Gilbert E, Drube H. Mucopolysaccharidosis VII: beta glucuronidase deficiency. *Humangenetik* 1974;**23**:149-58.
- Beaudet AL, DiFerrante NM, Ferry GD, Nichols BL, Mullins CE. Variation in the phenotypic expression of beta glucuronidase deficiency. *J Pediatr* 1975;**86**:388-94.
- Sly WS. The mucopolysaccharidoses. In: Bondy PK, Rosenberg LE, eds. *Metabolic control and disease*. 8th ed. Philadelphia: Saunders, 1980: 545-81.
- Leroy JG, Ho MW, MacBrinn MC, et al. I-cell disease: biochemical studies. *Pediatr Res* 1972;**6**:752-7.
- Danes BS, Degnan M. Different clinical and biochemical phenotypes associated with beta glucuronidase deficiency. In: Bergsma D, ed. *Skeletal dysplasias*. New York: National Foundation—March of Dimes, 1974:251-7.
- Pfeiffer RA, Kresse H, Baumer N, Sattinger E. Beta glucuronidase deficiency in a girl with unusual clinical features. *Eur J Pediatr* 1977;**126**:155-61.

Requests for reprints to Dr Kenneth L Jones, Department of Pediatrics, University Hospital H-814-B, 225 West Dickinson Street, San Diego, California 92103, USA.

Anal atresia and the Klein-Waardenburg syndrome

SUMMARY A 3-month-old male infant with type I Klein-Waardenburg syndrome with an imperforated anus and a perineal fistula is reported. The possible association of this gastrointestinal malformation with the KW syndrome is discussed.

The most common form of the Klein-Waardenburg (KW) syndrome is characterised by lateral displacement of the medial canthi and lacrimal punctae.¹ The

Received for publication 1 July 1980