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 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. 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, 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 μmol substrate cleaved/mg protein/h at 37°C (normal

**FIG 1** The proband at 22 months of age. Note coarse facies, gibbus deformity, and joint contractures.
mean = 178 μmol). The father and mother exhibited intermediate values of 42 and 79 μmol, respectively. β-glucuronidase was assayed fluorometrically according to standard methods by measuring the 4-methyl umbelliferone released from the β-glucuronidic derivative.

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. The remaining three presented in the second decade of life and have few clinical similarities among one another. The clinical features of the infantile form of MPS VII are summarised in the table.

With respect to postnatal growth deficiency, height and weight were below the 3rd centile in two patients, and in two growth delay was mild (10th centile). With regard to macrocephaly, onset of accelerated head growth was variable, occurring in the first year in TM and CR and in the third year in KB. 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, has been non-pro-
progressive 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 develop-
mental delay which we feel goes beyond the effect of
β-glucuronidase deficiency. 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
months to 8 years.

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 vari-
able. 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.4–6 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
child1 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.3
Hip dysplasia has been noted in two patients1 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 de-
scribed in all patients.1–3

The variability in urinary acid mucopolysac-
charide 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 preser-
vation 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 con-
tractures 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

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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 displace-
ment of the medial canthi and lacrimal punctae.1 The