

PERSONAL PRACTICE

Management of mucopolysaccharidosis type III

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The mucopolysaccharidoses are a group of inherited metabolic disorders caused by a deficiency of specific lysosomal enzymes. The enzyme deficiency results in interference with cellular function because of excessive accumulation within the cells of partially degraded glycosaminoglycans, which are also excreted to excess in the urine of affected patients.¹ Mucopolysaccharidosis (MPS) type III, or Sanfilippo's syndrome,² is characterised by the accumulation and urinary excretion of partially degraded heparan sulphate. At least four different enzyme deficiencies are known to cause the disorder.¹

Clinically the syndrome is characterised by a mild somatic phenotype combined with a severe neurodegenerative illness with prominent behavioural disturbance. Previous large clinical reviews of this condition have included many patients from small geographical areas and may not be representative of the complete clinical spectrum.^{3,4}

We present the clinical details of the 62 patients attending the special clinic for mucopolysaccharidoses at the Willink Biochemical Genetics Unit highlighting the particular problems associated with the clinical diagnosis and management of the disorder.

Patients

The clinical type and enzyme deficiency of the patients is shown in table 1. In the United Kingdom MPS IIIA is the commonest of the mucopolysaccharidoses, the exact incidence is not known with certainty, but is probably between 1:20-25 000 live births. This may be an underestimate as a number of mildly affected patients will remain undiagnosed. Type B is less common, type C is rare, and no patients with type D attend the clinic. Although the numbers involved are small, we were not able to confirm the previously reported milder clinical course associated with MPS IIIB.⁵ There appeared to be no

significant clinical differences between the different subtypes.

Presenting features

Accurate details about pregnancy and delivery were obtained for 59 of the 62 children. Three pregnancies ended prematurely at 28, 34, and 36 weeks' gestation, the infants having appropriate birth weights for the period of gestation. The other 56 pregnancies resulted in infants of normal birth weight with a mean of 3400 g and a range of 2700-4700 g. Delivery was normal in 46 cases, six followed forceps extraction, and seven were the result of caesarean section. For the majority of infants the neonatal period was uneventful (excluding those born prematurely). One patient required ventilation for meconium aspiration, but made normal progress subsequently. Five other patients were nursed briefly in the special care baby unit because of transient respiratory or feeding difficulties.

The mean age at diagnosis was 4.9 years with a range from 0.8-16 years. In six children a presymptomatic diagnosis was made after establishing the diagnosis in an older sibling. The features present at diagnosis of all the patients are shown in table 2. Most patients had a combination of developmental delay, particularly speech, and recurrent ear, nose, and throat infections. Hearing difficulties were common and a number of patients had failed health visitor screening hearing assessments.

Troublesome diarrhoea was a particular problem in 36 patients. The nature of the bowel disturbance was episodic, severe, watery motions that did not usually lead to dehydration, although many patients were admitted to hospital with a presumptive diagnosis of 'gastroenteritis'. In three patients this symptom was severe enough to lead to investigation to exclude serious bowel pathology, including sweat test and jejunal biopsy. In one patient a diagnosis of 'multiple food allergy'

Table 1 Clinical type and enzyme deficiency of patients studied

MPS III type	Enzyme deficiency	No of patients
A	Heparan <i>N</i> -sulphatase	47
B	α - <i>N</i> -acetylglucosaminidase	12
C	Acetyl-CoA: α -glucosaminide acetyltransferase	3
D	<i>N</i> -acetylglucosamine-6-sulphatase	0

Table 2 Presenting features in 62 patients

Symptom	No of patients
Development delay	58
Speech delay	53
Recurrent ear, nose, and throat infections	49
Diarrhoea	36
Behaviour problems	34
Hearing loss	16

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