Article *NIMHANS Journal*

Mucopolysaccharidoses - A Clinical, Radiological and Biochemical Study .

This paper won the Bombay Psychiatry society Silver Jubilee Award at the 38th Annual Conference of I.P.S. at Jaipur

Volume: 04 Issue: 02 July 1986 Page: 85-90

H S Narayanan, K S Mohan &, - *Department of Psychiatry, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

B S Sreedhara Rama Rao, - *Department of Neurochemistry, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Abstract

72 cases of mucopolysaccharidoses were seen in the M. R. Clinic of NIMHANS and of these 58 cases were studied clinically and radiologically. Biochemical investigations were done in each case. Out of the 58 cases, 40 were Hurlers, 14 Hunters' and the remaining 4 were Morquio's. They had all the clinical findings of these categories. A surprising finding was the large number of Hurler's cases as compared to Hunter's which was explained as due to the high consanguinity rate. This study is one of the largest series in the world and should serve to identify cases early so as to help in reducing morbidity with appropriate measures.

Key words -

Mucopolysaccharidoses,
Gargoylosm,
Hepatosplenomegaly,
Mental retardation

The mucopolysaccharidoses are lysosomal storage diseases resulting from deficiency of specific lysosomal enzymes involved in the degradation of dermatan sulfate, heparan sulfate, or keratan sulfate, singly or in combination. These monogenically determined diseases have a progressive course and a common pathological hallmark viz., the accumulation mainly of acid mucopolysaccharidoses in various tissues and their excessive excretion in the urine [1].

The common features of the mucopolysaccharidoses are mental retardation, gargoylosm, characteristic roentgenographic findings, hepatosplenomegaly and evidence of mucopolysaccharide accumulation in tissues with their excretion in the urine.

McKusick [2] has classified the mucopolysaccharidoses as shown in Table 1.

Table I - Tabulation of mucopolysaccharidoses and corresponding primary enzymatic defects

Table I - Tabulation of mucopolysaccharidoses and corresponding primary enzymatic defects

All cases of mucopolysaccharidoses which were initially suspected at the mental retardation clinic of NIMHANS were studied from the time of their detection till their death over the last 17 years. All the cases were studied clinically, radiologically and biochemically. Some of the findings are given in Tables 2 and 3 and Fig.1

Table IIa - Age and sex distribution of MPSs cases

Table IIa - Age and sex distribution of MPSs cases

Table IIb - Age and sex distribution of MPSs cases

Table IIb - Age and sex distribution of MPSs cases

Table III - Age range of index and affected sibs (Hunter's)

Table III - Age range of index and affected sibs (Hunter's)

Age distribution of cases of mucopolysaccharidoses

Majority of the cases were between the cases of 4 and 6 years. All the patients (index, affected sib and dead sib) were males, since it is an X-linked disorder.

The number of different types of MPSs cases detected were :

Hurler's disease (MPS-I) is a classic MPSs [3] inherited as an autosomal recessive condition and the enzyme defect is of a-linduronidase. The prevalence is 1/100,000 and mental retardation can be severe. Clinically severe manifestations with early clouding of cornea and CVS defects can occur with early onset and early death of the patients. Behaviourly the patients are mild and calm and friendly (Table 4 and Fig. 2). Hunter's disease (MPS-II) is a sexlinked disorder with a prevalence of 1/150,000 and the enzyme defect is of L-iduronosulfhate sulphatase. The manifestation apparently is at 2-3 years and the disease is slowly progressive with mental retardation which is not as severe as in MPS-I. There is absence of corneal clouding with marked skeletal deformities. The children live longer [4]; cases living till the age of 7 have been reported. The patients are stubborn, aggressive and destructive (Table 5 and Fig 3).

Table IV - Clinical features of Hurler's syndrome

Table IV - Clinical features of Hurler's syndrome

Hurler's syndrome

Table V - Clinical features of Hunter's syndrome

Table V - Clinical features of Hunter's syndrome

Hunter's Syndrome

Morquio's syndrome (MPS-IV) is an autosomal recessive condition with a prevalence of 1/100,000 and the enzymatic defect is of N-acetyl galuctosamine-6-sulphate-sulfhatase. Clinically severe distinctive bony changes, cloudy cornea and aortic regurgitation can occur by the age of 1 to 2 years. Skeletal abnormalities like thoraco lumber kyphosis, scoliosis, sternal deformities, short neck, swelling with limited articulation of joints of long bones and hyperlaxity can occur. The mental retardation is milder (Table 6 and Fig 4). The cases were studied radiologically and the findings are shown in Tables 7-9 and Figs. 5-7.

Table VI - Clinical features of Morquio's Syndrome

Table VI - Clinical features of Morquio's Syndrome

Morquio's syndrome

Table VII - Roentgenographic changes in Hurler's Syndrome

Table VII - Roentgenographic changes in Hurler's Syndrome

Table VIII - Roentgenographic changes in Hunter's Syndrome

Table VIII - Roentgenographic changes in Hunter's Syndrome

Table IX - Roentgenographic changes in Morquio's Syndrome

Table IX - Roentgenographic changes in Morquio's Syndrome

- ***MPSs case showing breaking of vertebral body***
- ***MPSs case showing short stubby metacarpals and lower end of radius and ulna shows metaphyses spreading***
- ***MPSs case showing skull hyperosteosis with boot shaped sella turcica***

Radiologically, distortion of skull, hyperosteosis, root shaped sella turcica with abnormalities of facial bones, with beaking, hook-like or wedge-shaped appearance of vertebral bodies are common findings in the MPSs. In addition in MPS-IV the osseous changes are more severe with kyphosis, scoliosis, sternal deformities, dysplasia of long bones and platyspondyly of vertebrae.

The biochemical abnormalities are as follows:

In all cases spot tests (toluidine blue) and turbidity tests (acid albumin) were positive. Cellulose acetate electrophoresis of concentrated urine showed the nature of MPS excreted.

The consanguinity rates are :

Psychological assessment : (As per the percentile for the age)

Discussion

The need for accurate diagnosis for genetic counselling in general and more particularly to permit parental diagnosis in subsequent pregnancies is highlighted herein [4].

The essentially differentiating features of Hurler's syndrome from that of Hunter's is corneal clouding, early onset of symptoms with early death and behaviour being calm and friendly in Hurler's cases while Hunter's cases have no corneal clouding, show later onset of symptoms with slow progression and patients are stubborn and restless [5]. Morquio's syndrome is largely characterised by skeletal abnormalities and when associated with corneal clouding the patient is described as suffering from Morquio-Ullrich's disease [6].

Genetic counselling for prevention remains the main intervention available for these diseases [3]. Fetal monitoring by enzyme assay in cultured amniotic fluid cells is an important practical element in the prevention of the MPS. Because early diagnosis of this type of disease in the propositus is an element

of paramount importance in its future prevention, much attention should be paid to clinical features.

General practitioners and paediatricians not conversant with the MPS should not always consider noisy breathing and congested upper airways as respiratory infections but the possibility of MPS should be kept in mind. Inguinal herniae should be repaired early with the anaesthesiologist warned early against increased cardiovascular pathology leading to mortality [7]. In MPS-IV orthopaedic surgery has a place [8]. For breathing and hearing defects myringotomy and bilateral insertion of plastic tubes through the drumheads have been used.

Cardiac evaluation is appropriate at regular intervals. Recurrent diarrhoea have to be controlled by dietary measures and by antidiarrhoeals. Hyperactivity, agitation, unmanageable behaviour and sleeplessness at night seen in MPS-II have to be controlled with minimal drugs. The more peaceful the environment the better the chances of controlling the patient's behaviour. Punishment has only a worsening effect.

Supportive management of the patients cannot be very effective without simultaneous and long term guidance and counselling to the parents and to the healthy siblings [9]. The principle of management of the MPSs should have as the central theme the principle of prevention with earlier diagnosis in index cases, genetic counselling and prenatal diagnosis as practical strategies [1].

Conclusion

This is one of the largest series in this part of the world. Taking into account the dead sibs we have a series of 72 patients. Different types of MPSs have been observed at one centre and their complete clinical, biochemical and radiological examinations have been done in each group and the characteristic findings have been demonstrated.

1.Leroy J G, Management of the mucopolysaccharidoses and allied disorders
In The Management of Genetic Disorders Page: 133-155 Allan R Liss. Inc. 150, Fifth Avenue New York, 1979

2.Mckusick V A, Neufeld E F & Kelly T E, The mucopolysaccharide storage diseases
In : Stanbury J B, Wyngaarden J B & Frederickson D S (Eds.) : The Metabolic Basis of Inherited Dise Page: 1282, 1978

3.Horwitz A L, The mucopolysaccharidoses : clinical and biochemical correlations
American Journal of Mental Deficiency Page: 84: 113-123, 1979

4.Dorfman A & Metalon R, The mucopolysaccharidoses
*In Stanbury J B, Wyngaarden J B & Frederickson D S (Eds.) The Metabolic Basis of Inherited Disease 3rd edn. New York, McGraw-Hill*1972

5.McKusick V A, Heritable disorders of Connective Tissue
*4th edn. St. Louis, C V Mosby Company*1972

6.Kumar Y V, Narayanan H S, Rao B S S R & Devi K V, A report of two cases of Morquio's syndrome associated with mental retardation
Australian Journal of Mental Retardation Page: 5: 319-321, 1979

7.Coran A G & Eraklis A J, Inguinal hernia in the Hurler-Hunter syndrome
Surgery Page: 61:302, 1967

8.Elliot D E, Kopitz S E & Ozer F L, The Morquio syndrome (MPS IV)
Birth Defects Page: 10: 458, 1974

9.Crocker A C & Cullinane M M, Families under stress. The diagnosis of Hurler's syndrome *Pract. Radiat.* Page: 51: 223, 1972