Tripolitana Medical Journal; 2017, Vol. 6, No. 1, pp. 26 - 29

tmj

Short Communication

ISSN 2077-5628

Mucopolysacchardosis Type I in Western Libya Experience of Tripoli Children Hospital

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Received 3 April 2017/Accepted 27 May 2017

ABSTRACT

Mucoplosacchardosis type 1 is a genetic metabolic disease caused by deficiency in alphaidournidase enzyme, it manifested mainly in 3 forms, Hurler, Hurler-Scheie, and Scheie types according to the degree of enzyme deficiency.

In Libya the actual incidence of type 1 is not known exactly. The aim of this study is to describe the clinical profile of type 1 Mucopolysacchardosis and to discuss the problems encountered in identifying and diagnosing these patients. 13 patients were seen at Metabolic Clinic diagnosed as type 1 Mucopolysacchardosis were included in this study and data were taken from their medical files.

13 patients confirmed type 1, 85% of them have normal IQ, 61% have history of developmental delay and all have repeated respiratory problems, hepatosplenomegaly and umbilical hernia, joint involvement is an early finding. Corneal opacity was seen in96% of the patientsand 75% have heart problems mainly in Mitral and Aortic valves.

Mucopolysacchardosis Scheie type is the most common in our patients, delay in diagnosis mainly due to absence of facial coarseness and lack of awareness among Pediatrician and unavailability of laboratory investigations.

Key words- *Mucopolysacchadosis type 1; MPS 1; Scheie type.*

INTRODUCTION

Mucopolysacchardosis (MPSs) are group of inherited diseases known as lysosomal storage disorders (LSD).[1] Type 1 caused by deficiency in alpha idournidase enzyme which leads to accumulation of dermatan and heparn sulphate in urine of these patients.[2]

Estimated incidence of Mucopolysacchardosis is 1/25000, For MPS1 is 1/100000, for the attenuated forms 1/500000 births.[3]

3 types of mucopolysacchardosis type 1: Type 1H(Hurler syndrome) constitute 57% of the cases, for H-S (Hurler Scheie) 23% and Scheie type 20%, in USA the incidence about 1/200000 patients, attenuated forms of the disease are less common 1/500000 people.[3]

Mucopolysacchardosis is caused by mutation in IDUA gene and is divided into 3 sub types according to disease severity;

a. Severe form characterized by coarse facial features with progressive physical problems

b. Intermediate form patients have near normal or normal facial features, mild physical problems and mental retardation.

c. While patients with Mild or attenuated form have normal intelligence with mild less progressive disease and normal life span.[4] Enzyme replacement therapy with laronidase may provide clinically important benefits such as improved pulmonary function and walking ability and reduction of excess carbohydrates stored in organ.[6,7] Gene therapy may cure such patients in future.[8]

The study aimed to identify clinical presentation of type 1 Mucopolysachardosis, prevalence of the disease and to discuss the problems encountered in diagnosis and management of this disorder.

MATERIALS AND METHODS

Review of medical files of 13 patients (8 females and 5 males) diagnosed as MPS type 1 who are currently receiving ERT (enzyme replacement therapy) at Metabolic department, Tripoli Children Hospital .

Diagnosis of Type 1 Mucopolysacchardosis was based on urine Aminoglycans (high dermatan and heparan sulphate) and enzyme assay which was very low or undetectable in all patients.

Data including sex, age, age at diagnosis (Table 1) region coming from, history including family history, clinical presentation and physical examination with review of laboratory and radiological investigations like skeletal X rays, MRI brain, urinary GAGs (glycosaminoglycan), enzyme assay, Genetic testing's, IQ assessment, echocardiography, ENT examination and hearing

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tests, ophthalmological and orthopedic consultations.

RESULTS

13 patients diagnosed as MPS 1 from the period from 2010 to 2015. Female to male ratio 8:5, 11 patients have a mild or attenuated form with normal IQ, 2 patients had a severe form with low IQ.

13 patients belong to 9 families, 7 families have one affected child, one family has 2 affected children and one family has 4 affected patients.

Parents of 6 families are first degree cousin, 2 families their parents are 2nd degree cousin, and in 2 families there is double cousin consanguinity. Age at presentation range from 7 months to 4 years mean age 2 years +8months

Table 1: Shows patients'age and sex and age at diagnosis.

Sex	Age	Age at diagnosis
M	6y	2y,8m
M	7y,6m	4y,11m
F	8y	5y,1m
F	3y	2y
F	3y	1y,6m
F(died)	3y6m	2y
F(died)	9m	7m
M	1y	1y
F	18m	1y
M	8y	2y6m
F	14y	8y
M	7y	4y
F	7y	5y

IQ assessment: 2 female patients have IQ less than 25, other 11 have normal IQ from 75-110, one of them male has poor school performance due to hearing difficulty and 8 out of 13 (61%) have history of gross motor developmental delay (Figure 1, 2).

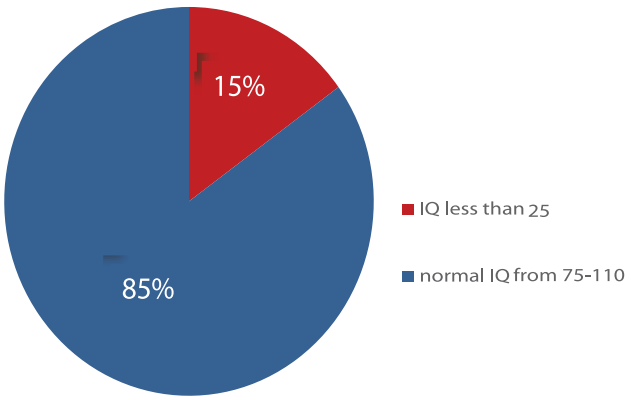

Figure 1: Shows intelligence quotient.

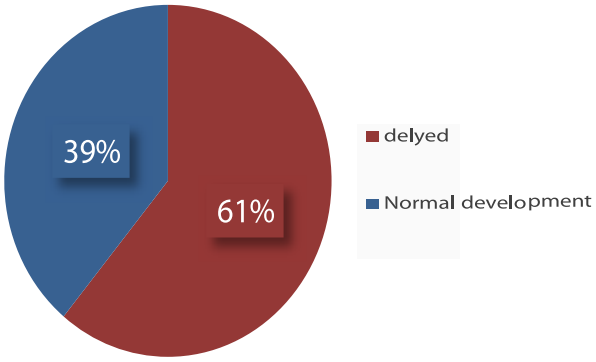

Figure 2: Shows gross motor development.

Heart involvement was observed in 9 patients (69%), 5 patients have mild MR (mitral valve regurgitation), 3 patients have both aortic and mitral valve regurge and one patient has both pulmonary valve stenosis with tricuspid regurge.

All patients have umbilical hernia one patient was operated for inguinal hernia after birth.

All patients have repeated respiratory problems and or adenoid, one female patient diagnosed as severe form (Hurler) died because of sleep apnea.

All patients have hepatosplenomegaly at time of diagnosis and all have dystosis multiplex clinically and radiologically.

Joint disease mainly restriction of abduction of shoulder joint was observed in 12 patients out of 13 (92%). Corneal opacitypresent in 9 out of 13 patients (69%) Table 2.

Table 2: Problems and organ involvement

Problems	No.of patients
Heart disease	9
Umbilical hernia	13
Respiratory problem	13
Hepatosplenomegaly	13
Corneal opacity	9
Joint disease	12

Genetic testing was performed in 4 /9 families 5 patients have C.1598>G.P533R mutation IDUA gene exon 11. One patient has mutation C.502G>TP.G168.

DISCUSSION

Mucopolysachardosis is a genetic disease was first described by Scottish Physician Charles Hurler on 1917 but the discovery of the enzyme was 1971, enzyme replacement therapy is a relatively new started and approved in 2003 in Europe.[4,5]

First report of the mild or attenuated form of type 1 by American Ophthalmologist Harold G. Scheie 1990, initially before discovery of the enzyme the milder form was classified as type V but after discovery of the enzyme responsible for the disease it was found that there is only enzyme (iduronidas) was deficient.[6]

In our hospital which is the main children hospital in western part of Libya we could diagnose 27 patients with various types of Mucopolysachardosis, Type one was most frequent and constitute 50% of the cases, but our patients differ as most of them (85%) are attenuated forms of the disease and not classical form (severe) as mentioned in other countries or in eastern part of Libya (personal communication), and this the main cause of delay in referring these patients as they have a normal intelligence quotient and the disease expression is mild as most of our patients have fast normal facial features also the lack of awareness among the doctors who are dealing with these patients is another reason for delay in referring such patients.

There are no studies in the Arab countries about the attenuated forms those from Tunisia, Algeria describe the severe form (Hurler) and their mutation analysis.[7-9]

We think that we have a high incidence of MPS type one in a small population as the overall population in Libya is 6.25 million according to 2014 census, and the western part from Sirt to Zoltun the border to Tunis and to Jabal Nafosa where the population is much less than in Tripoli, the population in Tripoli area is around 2.2 million.[10] Taking in consideration that this study is only in Children Hospital as there is another hospital where another 4 patients with type 1 on enzyme replacement therapy. More studies is needed to estimate the exact prevalence of this disease in our country.

We think that there are many undiagnosed cases as the diagnosis is a coasty one and many physicians are not aware that there is treatment for this disorder and patients may not be referred to the hospital. Investigations are not available for such patients and need to be sent outside the country on parents cost.

Clinical presentation is also differ as all of them have Visceromegaly, umbilical hernia, frequent upper respiratory tract infection and joint affection mainly that of the shoulder joint, to a lesser degree heart involvement in 75% mainly mild mitral valve regurge which is differ than it was described in the literature (aortic regurge).[11-14]

We do not see any behavior problem in our patients probably this linked to low IQ which is not present in most of our patients.[15]

All of our patients parents are close relatives as first degree cousin was found in 7 families and 2nd degree in 2 families, in general consanguinity is frequent in Libya as well as in other Arab countries and this explains the high prevalence of the disease which is transmitted as an autosomal recessive manner, also the large family size in our Arab countries increase the disease expression.[16]

4/7 families have genetic testing. 5 patients have C.1598>G. P533R mutation in IDUA gene exon 11 and one patient has mutation has C.502G>TP.G168 mutation.

In Caucasian populations homozygosity or compound heterozygosity for W402X and Q70X mutation are most common in severe form of MPS1.[5,17]

In milder forms mutation in R89Q is common,In Japanese Hurler 704 ins 5 mutation is common, while in North Africa p.P533R mutation is common in Hurler syndrome (type1 MPS), these mutations were not described in patients from other Arab countries.[17-19]

CONCLUSION

Mucopolysaccharidosis attenuated form is more frequent among our patients.

Late presentation due to unawareness of physician, unavailability of investigations inside country, high cost, also late arrival of results, delay in treatment and lack of continuity of supply of medication (enzyme replacement therapy) all these factors affect outcome of our patients.

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