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Case report

EARLY OCULAR FINDINGS IN A PATIENT OF MAROTEAUX-LAMY SYNDROME

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ABSTRACT

The Maroteaux-Lamy disease or mucopolysaccharidosis type VI is an inherited severe metabolic disorder which is very rare. It is caused by a deficiency of the enzyme Arylsulfatase B and characterized by a heterogeneous clinical, radiological and genetic presentation. We report a case of Maroteaux-Lamy syndrome in a child aged 9 years whose diagnosis was suspected clinically by the combination of a dysmorphic syndrome, prominent ophthalmological signs, hepatomegaly and normal intelligence.

Keywords: Maroteaux- Lamy, cloudy cornea, retinopathy

INTRODUCTION

The mucopolysaccharidoses (MPSs) are a group of disorders caused by inherited defects in lysosomal enzymes resulting in widespread intra- and extra-cellular accumulation of glycosaminoglycans (GAG). Mucopolysaccharidoses are caused by a reduction in the activity of specific lysosomal enzymes involved in the breakdown of GAG, which results in a wide spectrum of clinical manifestations. They may present as a mild type which is compatible with a normal lifespan or may be fatal in the first few months of life.¹ They have been subdivided according to the enzyme defect and systemic manifestations. They include MPS IH (Hurler), MPS IS (Scheie), MPS IH/S (Hurler/Scheie), MPS II (Hunter), MPS III (Sanfilippo), MPS IV (Morquio), MPS VI (Maroteaux-Lamy), MPS VII (Sly) and MPS IX (Natowicz). The Mucopolysaccharidoses have a spectrum of systemic manifestations, including airway and respiratory distress, skeletal deformities, ophthalmological, intellectual and neurological impairment, cardiac abnormalities, and gastrointestinal problems¹. Ocular findings are common in mucopolysaccharidosis and occasionally can manifest with significant visual

impairment. Corneal opacification of varying severity is frequently seen which prompts the paediatrician to refer a patient to the ophthalmologist. Other ocular findings may include retinopathy, optic nerve swelling and optic atrophy, ocular hypertension, and glaucoma.²

CASE

A 9 year old male child presented to our out-patient department (OPD) with complaints of diminution of vision in the eyes, stunted growth and coarse facial features (Fig 1). His father had noticed the stunted growth and coarse facial feature since two years. On inquiry, the child had mild bone aches, joint pain and restricted joint movements in the region of wrists and neck. He gave complaints of diminution of vision for the past two years for both distance and near. The patient's father also noticed whitening of both corneas which prompted him to bring the child to the ophthalmology OPD. The parents of the boy had a second degree consanguineous marriage. He had an elder male sibling with no similar complaints and no positive family history suggestive of a metabolic

disorder. The boy had previously visited more than one general practitioner for stunted growth but was misdiagnosed as malnutrition.

We did a complete ophthalmological and systemic examination of the child along with blood investigations which revealed the diagnosis of mucopolysaccharidosis type VI (Maroteaux-Lamy).³ On ophthalmological examination we found the vision to be 6/36 and 6/60 in the right and the left eye respectively. Best corrected vision was 6/9 in both eyes with a refractive error of +0.75/-1.00 X 55°, +1.00/-1.50 X 105° in right (RE) and left (LE) eye respectively. On external examination with slit lamp biomicroscopy, patient had bilateral diffuse epithelial haze (Fig 2) with reduced central convexity of the corneas. Corneal topography with Allegro Oculyzer (Wavelight AG, Germany) showed central corneal flattening (Fig. 3) with a keratometry values as follows: RE -K1: 39.6D K2: 40.2D, LE -K1: 39.3D K2: 40.4D. Intraocular pressure (IOP) with an applanation tonometer was 16 and 18mm Hg in the right and left eyes respectively. Central corneal thickness noted was 555µm and 520µm respectively. On electrophysiological testing, the electroretinogram (ERG) showed a bilateral reduced sensitivity of photoreceptors especially cones. Optical coherence tomography (OCT) of the retinal nerve fibre layer and macula was within normal level.

On systemic evaluation the child showed the most signs of MPS, namely stunted growth, skeletal deformity with skeletal dystosis multiplex demonstrated on X-ray (Fig 4), and cardiac involvement with non-rheumatic affection of the cardiac valves which was confirmed by 2D echography. Urine was positive for mucopolysaccharidosis and a confirmatory diagnosis was done by assessing the arylsulphatase B enzyme levels in the blood³. Spectrophotometric assay using para nitro catchecol sulphate and fluorimetric assay using 4-methyl umbelliferone showed a low level of aryl sulphatase B 12.6 nmol/hr/mg (normal-115-226).



Fig 1: Stunted growth with coarse facial features (Photograph taken after consent from of the patient's father)

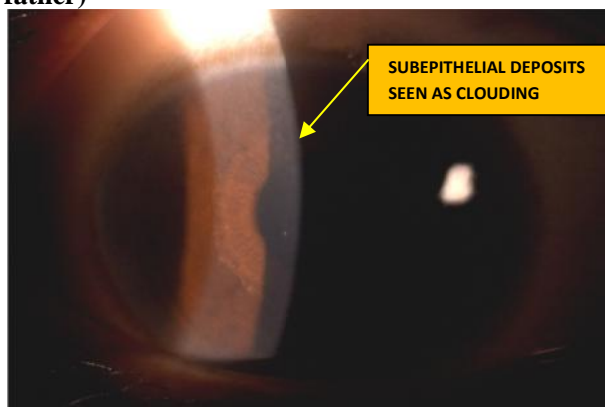


Fig 2: Subepithelial haze seen under slit lamp examination (cloudy cornea)

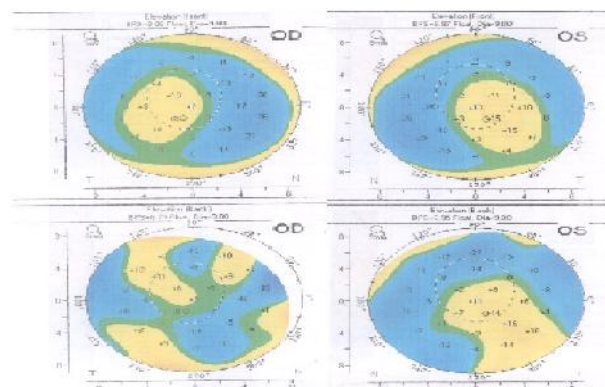


Fig 3: Corneal topography showing central flattening



Fig 4: X-ray showing skeletal dystosis multiplex with short, broad metacarpals and phalanges

DISCUSSION

Maroteaux-Lamy syndrome (mucopolysaccharidosis type VI) is a disorder of lysosomal storage. It is characterised by a defect in the production of the enzyme arylsulphatase B. This causes abnormal deposition of the GAG, dermatan sulphate. The mucopolysaccharidoses are caused by a specific deficiency of lysosomal enzymes which lead to the deposition of glycosaminoglycans in various organs in the body. This may give rise to a wide spectrum of clinical phenotypes.

The deposition of the GAG is seen in many organs and tissues in the body. Patients with the severe form of MPS I, MPS II and MPS VI present early to the clinician, as their respiratory, cardiac and skeletal deformities make the diagnosis straight forward. In case of mild forms of MPS I, MPS III, MPS IV, careful examination may reveal the corneal clouding and thereafter a paediatric reference is often made. The deposition of GAG within the layers of the cornea gives it a cloudy appearance.² Detailed ophthalmological examination often becomes difficult owing to the corneal opacification, thickening and due to the physical and mental capabilities of most patients.

MPS VI may present as a wide spectrum of clinical features, but all the affected children are intellectually normal. This was true in our case which prompted the child to complain about his poor vision. Individuals with Maroteaux-Lamy disease have short stature, coarse facial features, restrictive joint problems and hepatosplenomegaly. Some other features include middle ear disease, sensorineural deafness, upper airway problems and cardiomyopathy.

Ocular findings in MPS VI are progressive increased corneal opacification and corneal thickening. Patients may however present with clear corneas. Raised IOP and both acute and chronic angle closure glaucoma have been reported in MPS VI.⁴ Optic nerve involvement in the form of swelling and optic atrophy has also been seen.^{5, 6} However among the various MPS syndromes, Maroteaux-Lamy disease has a less severe phenotype with mild skeletal deformities and a longer lifespan. Since the ocular findings are progressive in nature, the role of the ophthalmologist becomes paramount. The increased life span of these children due to the advent of the bone marrow transplant and the enzyme replacement therapy has widened the scope for their ocular treatment.⁷

Our case was unique due to isolated ophthalmological symptoms. On examination, we found the other signs suggestive of MPS VI and then further reference was made.⁸ The child had a normal intellect with coarse facial features and skeletal deformities. Cardiac involvement was seen however the respiratory system is unaffected at this time. Ocular involvement with corneal opacification with corneal flattening was seen. On investigation delayed cones response was seen on ERG testing suggesting a retinopathy.⁹ The child needs to be tested on a regular basis for any development of glaucoma⁴, worsening of the corneal clarity or other complications which may reduce his quality of life and require appropriate treatment.

CONCLUSION

Mucopolysaccharidoses are a complex group of diseases which are rare and difficult to diagnose as well as treat. The patient may present to any specialty of medicine due to its varied presentation. It becomes imperative on the clinicians part that a careful and meticulous examination is done which can help diagnose this disease. Ophthalmological involvement, although rare as an initial finding, should definitely be kept in mind when facing a case of mucopolysaccharidosis.

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