

Ocular manifestations of mucopolysaccharidosi s



Ocular manifestations of mucopolysacchridosis

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Mucopolysaccharidoses (MPS) are a group of disorders caused by the inherited deficiency of lysosomal enzymes involved in the metabolism of glycosaminoglycan (GAG), resulting in the widespread intracellular and extracellular accumulation of GAG. >

Type	Gene	Deficient enzyme	GAG deposit ed	Inheritance pattern
Hurler syndrome (MPS I-H)	IDUA (4p16.3)	Alpha-L-iduronidase	Dermatan sulfate, heparan sulfate	AR
Hurler-Scheie syndrome (MPS I-H/S)	IDUA (4p16.3)	Alpha-L-iduronidase	Dermatan sulfate, heparan sulfate	AR
Scheie syndrome	IDUA (4p16.3)	Alpha-L-iduronidase	Dermatan	AR

(MPS I-S)	3)		sulfate, hepara n sulfate
Hunter syndrome, severe (MPS II-A)	IDS (Xq28)	Iduronate sulfatase	Derma t an sulfate, hepara n sulfate
Hunter syndrome, mild (MPS II- B)	IDS (Xq28)	Iduronate sulfatase	Derma t an sulfate, hepara n sulfate
Sanfilippo syndrome A (MPS III-A)	SGSH (17q25. 3)	Heparan <i>M</i> -sulfatase	Hepara n sulfate
Sanfilippo syndrome B (MPS III-B)	NAGLU (17q21)	Alpha-N- acetylglucosaminidase	Hepara n sulfate
Sanfilippo	HGSNAT	Heparan-alpha-	Hepara AR

syndrome C (MPS III-C)	(8p11.1)	glucosaminide N - acetyltransferase	n sulfate	
Sanfilippo syndrome D (MPS III-D)	GNS (12q14)	N-acetyl alpha- glucosamine-6-sulfatase	Hepara n sulfate	AR
Morquio syndrome A (MPS IV-A)	GALNS (16q24.3)	N-acetylgalactosamine 6- sulfatase	Keratan sulfate	AR
Morquio syndrome B (MPS IV-B)	GLB1 (3p21.33)	Beta-galactosidase	Keratan sulfate	AR
Maroteaux- Lamy syndrome (MPS VI)	ARSB (5q14.1)	Arylsulfatase B	Dermat an sulfate	AR
Sly syndrome (MPS VII)	GUSB (7q21.11)	Beta-glucuronidase	Dermat an sulfate, hepara n sulfate, Chondr oitin	AR

sulfate

Natowicz			
syndrome (M	HYAL1	Hyaluronidase	AR
PS IX)	(3p21)		

Ocular manifestations

1. Ocular adnexa

Eyelid thickening occurs due to the accumulation of GAG. Hypertelorism has been reported in MPS types III, II and VII. Pseudoproptosis due to shallow orbit has been reported in a patient with MPS VI and MPS II.

2. Cornea

The extracellular matrix of corneal stroma contains dermatan sulfate and keratan sulfate in equal proportion. Both dermatan sulfate and keratan sulfate are synthesized by stromal keratocytes. Dermatan sulfate proteoglycans are involved in the control of interfibrillar spacing and in the lamellar adhesion of corneal collagens. Keratan sulfate proteoglycans are involved in the regulation of collagen fibril diameter. Mainly, epithelial cells synthesize heparan sulfate proteoglycans, and they are minor components of cornea.

Since dermatan sulfate and keratan sulfate are the major GAGs in the corneal stroma, corneal involvement is mainly seen in MPS types I, IV, VI and VII. In corneas of patients with MPS, the excessive accumulation of dermatan sulfate or keratan sulfate in the form of vacuoles can be seen in

epithelial cells, keratocytes, histiocytes and extracellular matrix. An increase in the mean fibril diameter of collagen and an increase in fibril spacing are noted in the corneal stroma of patients with MPS I. These structural alterations in collagen fibrils may contribute to light scattering. But the corneal clouding is mainly due to the accumulation of GAGs in all the layers of cornea with enlarged stromal keratocytes.

Corneal involvement is typically not seen in type III, as the metabolism of heparan sulfate is impaired in type III and heparan sulfate is not synthesized by stromal keratocytes.

Symptoms include gradually progressive painless diminution of visual acuity and light intolerance due to scattering of light. In early cases, fine grey punctuate opacities in anterior stroma are visible. In advanced cases, there is diffuse corneal clouding. Corneal thickness is variable, and it may be increased or normal. Corneal hysteresis is increased. Corneal oedema occurs in cases with increased intra-ocular pressure (IOP).

3. Optic nerve

GAGs are the major components of the extracellular matrix of the optic nerve head. Proteoglycans containing chondroitin sulfate and dermatan sulfate are located in lamina cribrosa, supporting tissues of the optic nerve head like septae, pia. Proteoglycans containing heparan sulfate are located in margins of laminae of lamina cribrosa. The optic nerve involvement can be due to accumulation of GAG in the extracellular matrix of the optic nerve, narrowing of pores in lamina cribrosa, thickening of dura and narrowing of bony optic canal that leads to

disc oedema (pseudopapilloedema). It can also be due to raised intracranial pressure manifesting as true papilloedema. Long-standing axonal compression or papilloedema can lead to secondary optic atrophy. The accumulation of GAG in ganglion cells of retina can lead to axonal degeneration and optic atrophy.

Optic nerve involvement is more commonly seen in types I, II, VI and VII, as the major GAGs in optic nerve and lamina cribrosa are dermatan sulfate and chondritin sulfate.

Optic nerve involvement is less with type III, as heparan sulfate is located in the margins of lamina cribrosa, and in type IV, as keratan sulfate is not present in the optic nerve head in human.

4. Glaucoma

The human trabecular meshwork contains chondroitin sulfate, keratan sulfate, heparan sulfate and dermatan sulfate. The accumulation of GAG in the anterior segment structures can lead to the narrowing of angle resulting in acute angle closure and chronic angle closure glaucoma. Anterior segment optical coherence tomography (OCT) imaging in mucopolysacchridosis suggests crowded anterior segment and increased corneal thickness in type VI than in type I. The accumulation of GAG in trabecular cells can lead to features similar to open-angle glaucoma. The measurement of IOP by Goldmann applanation tonometer may be falsely high due to increased corneal thickness and corneal hysteresis. The visualization of angle by gonioscopy may be compromised due to corneal clouding, thus posing difficulty in differentiating open angle <https://assignbuster.com/ocular-manifestations-of-mucopolysacchridosis/>

from closed angle. The monitoring of progression and severity of glaucomatous optic neuropathy may be compromised by corneal clouding and disc oedema. Anterior segment OCT is a valuable tool in the assessment of angle, particularly in patients with corneal clouding. Ocular response analyser can be used for the accurate measurement of IOP in these cases.

5. Retina

Heparan sulfate, dermatan sulfate, chondroitin sulfate and hyaluronan are present throughout the retina and choroid. Heparan sulfate is particularly located in the basement membrane containing structures, the RNFL and RPE. Keratan sulfate is absent in the retina and choroid. GAGs are integral components of the basement membrane of retinal microvasculature, and heparan sulfate is the predominant variety. Tapetoretinal degeneration has been reported in MPS types I, II, III and IV.

6. Sclera

Scleral thickening may lead to the uveal effusion syndrome.

Suggested Reading

1. Villas-Boas FS, Fernandes Filho DJ, Acosta AX. Ocular findings in patients with mucopolysaccharidosis. *Arq Bras Oftalmol* 2011; 74(6): 430-434.
2. Viestenz A, Shin YS, Viestenz A, Naumann GO. Ocular manifestation of mucopolysaccharidosis I-S (Scheie's syndrome). *Klin Monbl Augenheilkd* 2002; 219(10): 745-748.