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CASE REPORT

Reversed papilledema in an MPS VI patient with galsulfase (Naglazyme®) therapy

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Abstract MPS VI (mucopolysaccharidosis VI, known as Maroteaux–Lamy syndrome) is a multi-systemic inherited disease, resulting from a deficiency of *N*-acetylgalactosamine-4-sulfatase, causing accumulation of the glycosaminoglycan (GAG) dermatan sulfate in all tissues. It is one of almost 50 lysosomal storage disorders. Ocular pathology is common in patients with MPS VI, with complications including ocular hypertension, progressive corneal clouding, optic nerve swelling (or papilledema) often associated with communicating hydrocephalus (Ashworth et al., Eye 20(5), 553–563, 2006; Goldberg et al., AJO 69(6), 969–975), and raised intracranial pressure (ICP) progressing to atrophy with loss of vision (Goodrich et al., Loss of vision in MPS VI is a consequence of increased intracranial pressure, 2002). This is the first case report of reversed papilledema and improved visual acuity in an 11-year-old MPS VI patient receiving galsulfase (Naglazyme®), an enzyme-replacement therapy (ERT) of recombinant human arylsulfatase B (rhASB) (Harmatz et al., J Pediatr 148(4), 533–539, 2006).

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Keywords Galsulfase · Glycosominoglycans · Mucopolysaccharidosis VI · *N*-Acetylgalactosamine-4-sulfatase · Papilledema

Abbreviations

ERT	Enzyme replacement therapy
MPS VI	Mucopolysaccharidosis VI, known as Maroteaux–Lamy syndrome
RhASB	Recombinant human arylsulfatase B

MPS VI (Maroteaux–Lamy syndrome) is a multi-systemic inherited disease, resulting from a deficiency of *N*-acetylgalactosamine-4-sulfatase (arylsulfatase B), causing accumulation of glycosaminoglycan (GAG) dermatan sulfate in all tissues. Ocular pathology is common in patients with MPS VI, with complications including ocular hypertension, progressive corneal clouding, optic nerve swelling and atrophy, papilledema secondary to hydrocephalus, glaucoma, and blindness.

The objective of this case report is to describe the first report of a patient with MPS VI disease with resolution of papilledema and improved vision subsequent to enzyme-replacement therapy with recombinant human arylsulfatase B (rhASB), galsulfase.

The patient, an 11-year-old Hispanic female, was treated with rhASB in an open-label extension of a 24-week randomized double-blind study evaluating the safety and efficacy of rhASB. At baseline, the patient presented with characteristic features of MPS

VI: short stature, coarse facies, large tongue, hepatosplenomegaly, joint contractures, and mitral and aortic regurgitation. Leukocyte pellet and fibroblast cell analyses showed no detectable *N*-acetylgalactosamine-4-sulfatase activity. The patient received placebo during the double-blind portion of the trial and began rhASB during the open-label extension study. She was followed for two years.

During baseline screening for a phase-three clinical trial, the MPS VI patient presented with a urinary glycosaminoglycan (GAG) level of 243 μg/mg creatinine [1]. Ocular pathology included optic atrophy, and moderate corneal clouding in both eyes, with decreased visual acuity: right eye 20/60, left eye 20/400 (Table 1). Her ophthalmic condition worsened and included papilledema while on placebo concomitant with urinary GAG level increasing to 358 μg/mg creatinine, but both parameters rapidly improved after switching to open-label extension and commencing active drug at 1 mg/kg delivered by weekly IV infusion from week 25. Papilledema had largely resolved in both eyes, associated with a recorded decrease of urinary GAG levels to 77 μg/mg creatinine when monitored at week 36 of trial. Resolution of papilledema was maintained with weekly galsulfase treatment for two and a half years. Visual acuity improved from 20/60 to 20/40 in her right eye with best correction. Both corneas remained moderately cloudy during the study. The left optic nerve continued to be atrophic and vision got worse, likely due to the severity of the damage, counting fingers only at one meter. A second MPS VI patient in the trial developed papilledema while on placebo, and had to be treated for underlying hydrocephalus with an emergency shunt procedure.

Discussion

Although galsulfase may not adequately cross the blood–brain barrier [2], possible beneficial mechanisms include relief of pressure around the optic nerve by reducing dural thickening along the optic canal or reducing scleral thickening at the disc. It is possible that galsulfase ERT reduced ICP by working intravascularly or relieving pressure around the brainstem. This case study suggests that earlier galsulfase ERT may prevent or decrease optic nerve swelling, atrophy, and blindness in MPS VI patients, in the absence of increased ICP. These findings suggest that MPS VI patients who show acute vision changes or optic nerve swelling, as evaluated by specialists in ophthalmology, radiology, and neurosurgery, might benefit from ERT with galsulfase, but further studies are necessary to confirm this hypothesis. Galsulfase has been found to have an adequate safety profile in clinical trials and is approved by the FDA and EMEA.

This is the first case of papilledema resolution with improved vision associated with rhASB therapy of MPS VI. Early enzyme-replacement therapy may prevent or decrease optic nerve atrophy resulting in blindness in MPS VI patients.

Table 1 Ocular examination findings

Exam date	VAR[b]	VAL[c]	CR[d]	CL[e]	Alignment	ONPR[f]	ONPL[g]
8/27/2003[a]	20/60	20/400	Cloudy	Cloudy	Extropia	Negative	Negative
2/5/2004	20/60	CF[h] @ 1 m	Cloudy	Cloudy	Extropia	Positive	Positive
3/4/2004	20/60	CF @ 1 m	Cloudy	Cloudy	Extropia	Negative	Negative
6/21/2005	20/50	CF @ 1 m	Cloudy	Cloudy	Extropia	Negative	Negative
9/27/2006	20/40	CF @ 1 m	Cloudy	Cloudy	Extropia	Negative	Negative

[a] 8/27/2003 was date of baseline reading

[b] VAR = visual acuity right

[c] VAL = visual acuity left

[d] CR = cornea right

[e] CL = cornea left

[f] ONPR = optical nerve papilledema right

[g] ONPL = optical nerve papilledema left

[h] CF @ 1 m = counting fingers at a distance of 1 m

Note to editor: The procedures followed in this clinical case were in accordance with the Institutional Review Board (IRB) subjected to the United States FDA's IRB regulations, and the ethical standards of the Declaration of Helsinki (1964) of the World Medical Association (amended in 1975 and 1983).

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References

1. Swiedler SJ, Beck M, Bajbouj M et al (2005) Threshold effect of urinary glycosaminoglycans and the walk test as indicators of disease progression in a survey of subjects with mucopolysaccharidosis VI (Maroteaux–Lamy syndrome). Am J Med Genet A 134(2):144–150
2. Byers S, Crawley AC, Brumfield LK, Nuttall JD, Hopwood JJ (2000) Enzyme-replacement therapy in a feline model of MPS VI: modification of enzyme structure and dose frequency. Pediatr Res 47(6):743–749