β-mannosidosis is an inherited autosomal recessive disorder of glycoprotein catabolism with a deficiency of tissue and plasma β-mannosidase activity and tissue accumulation of oligosaccharide substrates for β-mannosidase. This genetic disorder was identified initially in Nubian goat kids but has since been documented in human patients. The disease has also been recently reported in Salers calves, and the clinical signs and lesions, except for those of the eye and ear, have been described. The objective of this study was to characterize the ocular and otic lesions of bovine β-mannosidosis.

The subjects of this study were 7 newborn affected Salers calves and control calves of other breeds. The diagnosis of β-mannosidosis was confirmed in Salers calves by the measurement of plasma activity of β-mannosidase and by the detection of accumulated tissue oligosaccharides. All affected calves died or were euthanized within 24 hours after birth; 2 of the calves were systemically perfused with formalin. One newborn affected Salers calf and a normal Salers sibling were given a complete clinical examination, including ophthalmic exam and auditory evoked brain stem potential testing. Measurement of palpebral fissures was made shortly after birth on the same affected calf and on 7 normal Salers calves born on the same day. Globes were obtained from 5 affected calves. Globes were injected with either 10% formalin, Davidson’s fixative, or 4% glutaraldehyde, and all globes were submerged in the same fixative. The anterior-posterior axis and vertical axis of each globe, vertical diameter and nasal-temporal diameter of the cornea, and diameter of the optic nerve were recorded. Tissue was processed for routine microscopic examination, except that globes fixed in glutaraldehyde were processed for routine transmission electron microscopy. Both external ears, including pinna, external auditory meatus, and tympanic membrane, and both middle ears from 4 affected calves were examined grossly. Temporal bones were collected and the inner ears were examined from the 2 systemically perfused calves.

The palpebral fissures were vertically narrowed (Fig. 1). One affected calf had palpebral fissures 0.5 x 2.4 cm (OS) and 0.5 x 2.2 cm (OD). The mean palpebral fissure measurements for 7 unaffected calves were 1.0 x 2.3 cm (OS) and 1.0 x 2.4 cm (OD). The globes of affected calves were normal in size and clinically unremarkable. Microscopically, corneal stromal and endothelial cells, outer and inner epithelial cells of the ciliary body (Fig. 2A), cells along the anterior border of the iris, retinal bipolar cells, photoreceptor cells, retinal pigment epithelial cells, glial and vascular cells of the optic nerve, and ocular vascular endothelial cells and fibroblasts throughout the globe were distended with nonstaining spherical intracytoplasmic vacuoles of various sizes. Ultrastructurally, these vacuoles were electron lucent and membrane bound. Axonal spheroids of various sizes were present in the bullar optic nerve.

In affected calves, the pinnae were directed posteriorly (Fig. 1) and the external auditory canals were slightly narrowed. The tympanic bullae were smaller and an auditory evoked brain stem potential recording had normal peaks delayed by 2 msec. Microscopically and ultrastructurally, vacuoles similar to those within ocular cells were present in epithelial and mesenchymal cells of the tympanic membrane, mucosal and mesenchymal cells of the tympanic bullae, epithelial and mesenchymal cells of Reissner’s membrane, mesothelial cells lining the scala tympani, cells of the stria vascularis, numerous supportive cells of the organ of Corti, cochlear hair cells, endothelial cells, perithelial cells, fibroblasts, neurons of the spiral ganglion, and vestibular hair cells (Fig. 2B).

Salers cattle are a beef breed imported from France that are recognized by their dark red, curly hair coat. Newborn Salers calves with β-mannosidosis have been reported in Canada, New Zealand, and the United States. Distinctive clinical features include an inability to stand at birth, head tremors, nystagmus, and opisthotonis. Affected calves have been stillborn, and those liveborn often die from either starvation or secondary septicemia. Phenotypically, affected calves had normal auditory evoked potentials, facial nerve responses, and brain stem auditory evoked responses.

**References**


**The ocular and otic pathology of bovine beta-mannosidosis**

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Figure 1. Narrow palpebral fissures and posteriorly directed pinnae of calf with β-mannosidosis.

Figure 2. A. Numerous electron-lucent intracytoplasmic vacuoles with the inner and outer ciliary epithelial cells and ciliary endothelial cells of calf with β-mannosidosis. Bar = 10 µm. B. Numerous electron-lucent intracytoplasmic vacuoles within the vestibular hair cell of calf with β-mannosidosis. Bar = 1 µm.
bullae are abnormal, but changes are not as severe as in University. The technical assistance of R. Common and C. Ayala is greatly appreciated.

Affected calves also did not have the marked macrophage infiltration and desquamation of cells into the scala media as reported in affected goats. Thus, the more severe lesions in affected goats may be responsible for the complete hearing deficit. In general, the distribution of vacuolation was similar between affected calves and kids, but this is the first report of vacuolation of sensory vestibular hair cells. In contrast to β-mannosidosis, alterations of otic structures have not been reported in bovine α-mannosidosis.

Affected calves1 and goats15 have pupillary reflexes indicating some visual function. However, rigid and thickened eyelids and a hazy vitreous body are clinical findings of caprine β-mannosidosis7 that were not observed in bovine α-mannosidosis. The cytoplasmic vacuolation of many different types of ocular cells observed in bovine β-mannosidosis is similar to that observed in caprine β-mannosidosis7 except that both inner and outer ciliary epithelial cells are vacuolated in bovine β-mannosidosis. The molecular basis for the difference in this specific pattern of vacuolation has not been defined and the relation of the vacuolation to ocular function is not clear because neuronal vacuolation may not alter physiological functions of cells.13 The axonal spheroids in the optic nerve are also present in affected goats, and axonal spheroids have been reported in the central nervous system of cattle affected with α-mannosidosis.7 The optic nerve hypomyelination seen in calves12 and goats15 affected with β-mannosidosis has not been reported in cattle affected with α-mannosidosis, although these cattle have demyelination of the central nervous system.7

The distinctive clinical and phenotypical features of bovine β-mannosidosis are considered helpful in identifying this genetically transmitted disease that may be widespread in full-blood Salers cattle.1 The correlation of clinical and gross findings with microscopic and ultrastructural lesions is important to understand the significance of the morphologic changes and their pathogenesis. Such correlative studies are especially useful for the eye and ear, which are not commonly examined grossly and microscopically even though lesions of these structures may be relevant to the clinical presentation. This study broadens the informational basis for a better understanding of the lesions of bovine β-mannosidosis and extends our understanding of the lesions of glycoprotein catabolic storage diseases in general.

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