The Globe and Orbit in Laron Syndrome

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Patients with LS serve as a unique model for the investigation of the effects of GH/IGF-1 on the eye and orbit. A recent ophthalmologic study reported that in patients with LS, the axial lengths of the eye and anterior chamber are shorter than those in healthy controls. To the best of our knowledge, however, imaging evaluations of these structures have not been performed in patients with LS. The purpose of the present study was to assess, by MR imaging, the size of the eye and the orbit and the relationship between these in LS.

Materials and Methods
A comparative retrospective case series design was used. The study was conducted in a university-affiliated tertiary medical center, and the protocol was approved by the institutional review board, with a waiver of informed consent. The files of the Imaging Department were searched for all patients with LS who underwent MR imaging of the brain from 1999 to 2007. The diagnosis of LS was based on findings of severe short stature, high basal levels of GH with low serum levels of IGF-1, lack of response to exogenous GH administration, and molecular studies of the GH receptor genes. Only patients who had not received replacement therapy with IGF-1 were included. In all cases, the MR imaging examinations had been performed because of clinical symptoms unrelated to the eye or orbit, such as headache and dizziness, and for evaluation of mental retardation.

Owing to the retrospective nature of the study, the MR imaging equipment included both 0.5T and 1.5T systems, depending on the time of examination. The measurements for the present study were made on the axial images, either T1- or T2-weighted, according to the preference of the reviewing radiologist.

We measured the following parameters (Fig 1): axial diameter of the globe (F), interzygomatic distance (A), perpendicular distance from the interzygomatic line to the anterior margin of globe (B), perpendicular distance from the interzygomatic line to the posterior...
margin of the globe (C), medial-to-lateral diameter of the orbit at the anterior orbital rim (G), distance from the anterior orbital rim to the anterior globe (I), maximal distance between the medial walls of the orbits (H), lateral orbital wall angle (D), lateral orbital wall length (E), and mediolateral thickness of the intraorbital fat in the most cranial image of the orbit. We calculated the ratio of the length of the lateral orbital wall to the diameter of the globe and the ratio of the diameter of the orbit at the anterior orbital rim to the diameter of the globe. All measurements were made bilaterally.

The findings were compared with a control group of patients retrieved from the radiology files who underwent MR imaging of the brain for reasons other than investigation of the eyes or orbits. Those with abnormal findings in this region were excluded.

Statistical Analysis
Statistical analysis was performed by using BMDP statistical software (Statistical Solutions, Saugus, Massachusetts). The calculated means and SDs for the left and right eyes were combined because the various measurements were very similar bilaterally. Because the sample was relatively small, we compared the 2 groups by using the Mann-Whitney nonparametric test. A $P$ value of $<.05$ was considered statistically significant.

Results
The study group consisted of 9 patients (5 men, 4 women, 36–68 years of age; mean, 45.5 ± 9.2 years), and the control group consisted of 20 patients (4 men, 16 women; 21–58 years of age; mean, 38.4 ± 13 years). There was no significant difference in age between the groups.

The orbital measurements are shown in the Table. Compared with the control subjects, the patients with LS had a significantly smaller maximal globe diameter, shallower but wider orbits due to a shorter lateral wall, a smaller medial distance between the orbits, and a larger angle of the orbit. There was no significant difference in the most anterior diameter of the orbit. Thus, the ratio between the most anterior orbital diameter and the globe was greater in the study group than in the controls. The ratio between the length of the lateral wall of the orbit and the globe diameter was not significantly different in the LS group, and the position of the globe was more anterior in relation to the interzygomatic line but not in relation to the anterior orbital rim (Fig 2).

Discussion
Patients with LS have a characteristic physiognomy: prominent forehead, decreased vertical dimension of the face, hypoplastic nasal bridge, and small maxilla and mandible. Their appearance reflects the underdevelopment of the facial bones due to lack of IGF-1. The small orbits are part of the impaired facial growth. Earlier studies reported a smaller-than-normal distance between the temporomandibular joints...
by cephalometric measurements and underdeveloped paranasal sinuses.

The present study focused on evaluation of the orbits in LS by MR imaging and adds new data on their shape and size. We found that the bony orbits in the study group were smaller and shallower but wider than those in the control subjects without LS (Table). The lateral wall length was smaller, and the angle of the orbit was larger. There was a lesser medial distance between the orbits than that in controls, with no significant difference in the most anterior orbital diameter (Fig 2).

The significantly smaller maximal diameter of the globe in the patients with LS is probably a direct effect of deficient IGF-1 as well as part of the impaired growth of the upper face. The ocular axis (the angle between the optic nerves) diminishes slightly from childhood to adulthood. We did not measure this angle, but the orbital angle was found to be larger in the patients with LS.

The refraction of the eye depends on 3 variables and their interaction: corneal power, lens power, and axial length. The human eye is programmed to achieve emmetropia in youth, despite the changes in these variables. The eye grows rapidly during the first year of life, concomitant with flattening of the cornea and a decrease in the power of the lens. After 6 years of age, refraction is modified mainly by increases in axial length. In an earlier clinical study of 12 untreated patients with LS, refraction examination yielded only a tendency toward hyperopia related to the small globe axis, thick lens, and steep corneal curvature. These differences from normal values in the literature reflect the influence of IGF-1 on the various components of the eye. There is anecdotal evidence that the small anteroposterior dimension of the orbit and the anterior position of the globe may manifest clinically. Ophthalmologic examination revealed increased proptosis and midface hypoplasia, most probably associated with small orbits (Z. Laron, personal communication, 2005).

The major weakness of the study is its retrospective design. We could neither perform volumetric measurements of the bony orbit and its content, which are more reliable, nor base our measurements on high-resolution studies of the orbits.

In conclusion, shallow and wide orbits and small globes relative to orbital size are seen in LS and may be secondary to IGF-1 deficiency. Further studies are needed to elucidate the influence of IGF-1 on ocular growth.

References
1. Laron Z. Extensive personal experience: Laron syndrome (primary growth hormone resistance or insensitivity)—the personal experience 1958–2003. J Clin Endocrinol Metab 2004;89:1031–44
2. Guevara-Aguirre J, Rosenblum AL, Fielder PJ, et al. Growth hormone receptor deficiency in Ecuador: clinical and biochemical phenotype in two populations. J Clin Endocrinol Metab 1993;76:417–23
3. Kornreich L, Horev G, Schwartz M, et al. Craniofacial and brain abnormalities in Laron syndrome (primary growth hormone insensitivity). Eur J Endocrinol 2002;146:499–503
4. Bourla DH, Laron Z, Snir M, et al. Insulin-like growth factor I affects ocular development: a study of untreated and treated patients with Laron syndrome. Ophthalmology 2006;113:1197–200
5. Laron Z. Laron syndrome: primary growth hormone resistance. In: Jameson JL, ed. Contemporary Endocrinology. Totowa, New Jersey: Humana Press; 1999;17–37
6. Scharf A, Laron Z. Skull changes in pituitary dwarfism and the syndrome of familial dwarfism with high plasma immunoreactive growth hormone: a roentgenologic study. Hum Metab Res 1972;4:93–97
7. Parentini F, Perissutti P. Congenital growth hormone deficiency and eye refraction: a longitudinal study. Ophthalmologica 2005;219:226–31
8. Parentini F, Tonini G, Perissutti P. Refractive evaluation in children with growth defect. Curr Eye Res 2004;28:11–15
9. Fredrick DR. Pre and postnatal growth of the eye, adnexa, visual system and emmetropization. In: Taylor DI, Hoyt CS, eds. Pediatric Ophthalmology and Strabismus. 3rd ed. London, UK: Elsevier Saunders; 2005:26–31
10. Waiting AA, Posnick JC, Armstrong DC, et al. Craniofacial skeletal measurements based on computed tomography. Part II. Normal values and growth trends. Cleft Palate Craniofac J 1992;29:118–28
11. Fleidius HC, Christensen AC. Reappraisal of the human ocular growth curve in fetal life, infancy, and early childhood. Br J Ophthalmol 1996;80:918–21
12. Peyster RG, Ginsberg F, Silber JH, et al. Exophthalmos caused by excessive fat: CT volumetric analysis and differential diagnostic. AJR Am J Roentgenol 1986;146:459–64
13. Laron Z, Klinger B. Body fat in Laron syndrome patients: effects of insulin-like growth factor I treatment. Horm Res 1993;40:16–22