LEBER'S CONGENITAL AMAUROSIS

Clinical Heterogeneity and Electroretinography in 27 Patients

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1. SUMMARY

Purpose: Clinical evaluation of 42 patients with primarily suspected diagnosis of Leber’s congenital amaurosis (LCA).

Methods: We used the electroretinogram (ERG), visual acuity, fundus appearance, age of onset, and systemic findings to confirm or revise the diagnosis of LCA.

Results: Twenty-four patients had a non-recordable ERG, and 3 showed small, residual, mainly cone-driven b-waves. Profound visual loss ranged from no light perception to 20/200. Visual acuity of light perception was frequent at <1 year of age. Three patients never had light perception. Most patients had a stable visual acuity despite progressive retinal pigmentary changes. A normal fundus was seen predominantly in patients younger than 1 year of age, but could also be found in patients of all age groups. The first, and frequently the only pigmentary changes were vascular attenuation and rarefaction, later in life heterogeneous retinal findings appeared. None of the 9 reexamined patients showed a normal fundus. Nystagmus and strabismus were principal presenting symptoms. Eleven patients presented with the oculodigital sign, three of them were enophthalmic, and 12 patients showed roving eye movements. Patients with additional (nonocular) findings such as mental retardation (n = 12), renal (n = 3) and skeletal (n = 4) abnormalities revealed no different ERG- or
ophthalmoscopic findings than the remaining patients. Twelve patients revealed abnormal psychomotor development.

From the initial cohort of 42 patients with suspected LCA, the diagnosis had to be revised in 15 cases as follows: juvenile RP (n = 8), infantile Refsum syndrome (n = 1), and 6 patients could not yet be classified with certainty.

Conclusion: Bilateral visual impairment in infants should be assessed clinically and electroretinographically within the first year. Later in life, the diagnosis of LCA can be a challenge due to its phenotypical heterogeneity. Systemic disorders are independent of ocular findings. In patients older than two years with non-recordable ERG, visual acuity better than 20/200, progressive visual loss, normal pupillary responses, absent oculodigital sign and absence of systemic abnormalities, juvenile retinitis pigmentosa should be considered.

2. INTRODUCTION

Leber’s congenital amaurosis (LCA) is the earliest and most severe form of inherited retinopathy as described by Theodor Leber. The autosomal recessive disease is characterized by profound visual loss or total blindness, searching nystagmus, hyperopia, and eye poking (oculodigital sign), usually recognized within the first months of life. The highly reduced or non-recordable electroretinogram (ERG) and exclusion of metabolic disorders corroborate the diagnosis.

We present 27 patients with the diagnosis of LCA, that evolved from revising the diagnoses of 42 cases with primarily suspected congenital amaurosis. Clinical and electroretinographic results were often obtained under general anesthesia and reevaluated at times by repeat examination or assessment of the patients’ history.

3. PATIENTS AND METHODS

We reviewed 42 patients retrospectively in whom LCA was suspected between 1968 and 1996 at the Department of Ophthalmology, University Hospital of Zürich. The initial diagnosis was based on an absent or highly reduced ERG in infancy. Out of these 42 patients, 27 met the following inclusion criteria for LCA: (1) markedly reduced or non-recordable ERG, (2) profound visual loss documented during the first year, (3) no evidence for a metabolic disorder.

A thorough history was taken and a complete ocular examination was performed in most patients, assessing visual acuity, testing of the pupillary responses to light if possible, eye movements, slit-lamp biomicroscopy, retinoscopy in cycloplegia, direct, and indirect ophthalmoscopy and fundus photography. We revised the diagnosis in 15 cases out of the total of 42 patients with suspected LCA.

3.1. Electroretinography

Complementing the clinical observations electrophysiology is used to objectively assess or exclude retinal degeneration in infants. The electrophysiological technique, recording with Henkes contact lens electrodes, was full-field, single flash ERG with selective stimulation of the rod-system following 20 min. of dark adaptation and subsequently using a rod-desensitizing white background to assess the function of the cone-system.