Ocular Manifestations Of Lafora’s Disease

By

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The association of visual disturbances and myoclonic seizures in a pre- or early adolescent child should suggest the diagnosis of Lafora’s disease. This entity has only recently been elucidated histopathologically as a specific disease. Its clinical features are those of Unverricht’s syndrome, and consist of: (1) an autosomal, recessive inheritance pattern, (2) the onset of myoclonic and grand mal seizures in pre- or early adolescence, (3) increasingly frequent and intense myoclonic movements, often limited to part of a limb or muscle, (4) a continual, diffuse, high-voltage slow-wave and wave-spike cerebral dysrhythmia, (5) progressive dementia, (6) progressive amaurosis with normal ocular fundi, (7) in-
creasing ataxia, dysarthria, dyskinesia, and rare or late spasticity, (8) progressive invalidism and muscle wasting, and atony terminally, and (9) death usually in 4 to 10 years after the onset of symptoms. The specific histopathologic abnormalities are: Lafora bodies in the central nervous system including the retina and spinal nerves, and material of similar histochemical properties in heart muscle, striated muscle, and liver cells.

We have had the opportunity to follow a young man whose history illustrates the clinical features and some of the diagnostic problems, notably the ocular ones, which characterize Lafora's disease.

Report of Patient:

This Caucasian male had an apparently healthy childhood suddenly interrupted by the development of myoclonic and grand mal epilepsy during his 15th year. Anticonvulsive medication controlled his grand mal attacks, but not the myoclonic jerks. Mental deterioration, weakness, and incoordination subsequently developed and progressed. He was institutionalized toward the end of his 19th year, because of paralysis, dementia, and apparent blindness. He remained in the institution until he died at age 23½.

Between the ages of 15 and 19 the patient experienced subjective visual symptoms consisting predominantly of blurring of vision and loss of peripheral fields. He underwent a complete ophthalmological examination, May, 1955 at age 15. Except for a slight refractive error, nothing abnormal was found. On his 2 admissions to the Hospital of the University of Pennsylvania in December, 1956 and May, 1957, his visual acuity in each eye was 6/7.5. External ocular, slit lamp, ophthalmoscopic, and peripheral and central visual field examinations were all entirely normal. The patient was seen by his ophthalmologist again in December, 1957 and May, 1959. Thorough evaluation both times yielded normal results. Although no further ophthalmic consultations were obtained, one of us (G.S.A.) periodically examined his fundi and visual fields until one year prior to death. No ophthalmoscopic abnormalities were found, yet the patient developed what seemed to be a progressive peripheral loss of vision, with preservation of central vision, which led to almost complete blindness. He did not have any further ophthalmoscopic examination before his death in December, 1962.

The patient's only sibling, and older sister, began to have grand mal seizures at age 14. Three months later myoclonic jerks developed. At age 16, coincident with the onset of incoordination, the myoclonus ceased. Visual impairment (similar to her brother's), mental deterioration, ataxia, personality alterations, and speech difficulties appeared in that order and progressed over the five years of her illness. Death occurred at age 19. No post-mortem examination was performed.

It is noteworthy that parental consanguinity was present. No other member of the family had any history of a similar disease.¹²

The results of the autopsy on the above male patient, and of extensive histochemical studies, have been the subject of previous communications.¹³ In summary, abnormal deposits were found in the cardiac and voluntary muscles, liver, and central nervous system. With respect to the visual system the retina contained deposits which were identical in morphology and staining properties to the bodies found in the brain (called Lafora bodies). These retinal Lafora bodies were found predominantly in the inner nuclear retinal layer, less prominently in the retinal ganglion cell layer, and least abundant in the inner plexiform and nerve fiber retinal layer (Figs. 1 & 2). The outer retinal layers were not affected. The optic nerves showed well-myelinated axis-cylinders. The external geniculate bodies contained some intraneuronal bodies, but they were not unusually abundant in this structure. There were numerous Lafora bodies in the calcareous cortex, similar to that seen in other parts of the cerebral cortex.
Figure 1. Retinal Lafora Bodies (black deposits) are seen in the ganglion cell layer (G), inner plexiform layer (P), and inner nuclear layer (N) of the retina. (Periodic acid-Schiff, X440.)

Figure 2. A laminated Lafora body is seen within a ganglion cell (arrow). (Hematoxylin and eosin, X575).

Discussion
The amaurosis of Lafora’s disease deserves further emphasis in the symptomatology of this disorder and consideration from the clinical and pathogenetic viewpoint. The patient and his sister had an apparent complete loss of peripheral vision with only preservation of central vision. The retina and optic nerve head, however, never presented any ophtalmoscopic abnormalities to the many examiners. No single lesion was found on histopathologic examination to explain the loss of peripheral vision. Retinal neuronal loss, possibly a few intra-axonal bodies of the optic nerves and tracts, intraneuronal bodies, and neuronal loss in the external geniculate bodies and in the calcarine cortices would seem to have all combined to produce the progressive visual defect. Since the fovola, area of the calcarine cortex is extensive, relatively less damage here would preserve central vision and might account for the kind of amaurosis our patient displayed.1

A review of the pertinent literature1 substantiates the basic facts presented herein. The association of myoclonic seizures with visual difficulties in a pre- or early adolescent child should, therefore, arouse the suspicion of Lafora’s disease. The diagnosis of this disease may be made by the rather simple procedure of liver biopsy or biopsy of striated muscle.1

Summary
Lafora’s disease appears in pre- or early adolescence. Progressive visual impairment is one of the outstanding symptoms. When this symptom is present, and a history of myoclonic seizures can be obtained, the diagnosis of Lafora’s disease should be strongly considered.

References
