A Case of Juvenile Lipidosis: Electron Microscopic, Histochemical and Biochemical Studies*

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Summary. Electron microscopic, histochemical and biochemical studies of a case of juvenile lipidosis have been presented. The neuronal inclusions were mostly unit membrane-bound with fingerprint-like patterns. Membranovesicular bodies were also found in the neuronal perikarya, but "typical" granular lipofuscin bodies were not seen. Cortical astrocytes contained a similar type of inclusion but the inclusions in the astrocytes in the white matter were quite different. The localization of acid phosphatase activity in all types of inclusions suggests their possible lysosomal nature. Biochemical analysis failed to pin-point any specific abnormalities.


Key-Words: Juvenile Lipidosis — Electron Microscopy — Histochemistry — Biochemistry — Granular Lipid Inclusions.

Juvenile amaurotic familial idiocy (Juvenile Lipidosis; Spielmeyer-Vogt disease; Batten’s disease) has up to now been classified clinically as a type of cerebral lipidosis. Recent biochemical and electron microscopic studies, however, suggest that it may be a distinct disease entity rather than one of the cerebral lipidoses (Klenk, 1953; Jervis, 1959; Folk-Pi, 1959; Zeman and Hoffman, 1962; Gonatas et al., 1963; Svennerholm, 1963). Unlike Tay-Sachs disease (Klenk, 1939) or G_{M1}-gangliosidosis (Jatzkewitz and Sandhoff, 1963; Suzuki and Chen, 1967; Gonatas and Gonatas, 1965; O’Brien et al., 1965), in all of which there is an abnormal accumulation of gangliosides, such an accumulation is not present in juvenile lipidosis (Klenk, 1953; Folk-Pi, 1959; Gonatas et al., 1963; Svennerholm 1963). Furthermore, the abnormal neuronal inclusions in the latter do not resemble those of the other lipidoses.

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Studies of juvenile lipidosis by Zeman and Donahue (1963) and Donahue et al. (1967) revealed multiloculated and granular osmiophilic lipid inclusions in the cytoplasm of neurons, glia, and endothelial cells; they suggested that the inclusions might originate from the mitochondria. In a detailed study of a cerebral biopsy specimen from a patient at a relatively early stage of the disease, Gonatas et al. (1963) found normal astrocytes and oligodendroglia; neurons and microglia contained numerous lysosome-like bodies, membranovesicular bodies and lipofuscin bodies with many intermediate forms in the cytoplasm. In their opinion, these intermediate forms suggested progressive transformation of the three types of inclusions.

The histologic, electron microscopic, histochemical, and biochemical observations reported here were carried out on a cerebral biopsy sample from a patient with juvenile lipidosis. The unusual cortical astrocytes and the prominent cytoplasmic inclusions in the neurons and glia differed in many respects from those described in other studies of juvenile lipidosis.

Case Report

History. The patient, a 13 year old, non-Jewish, white girl, was admitted to the Bronx Municipal Hospital Center for a diagnostic cerebral biopsy. Development of the patient had been normal until the age of 5 years; then a visual defect became apparent. The I.Q. at that time was 95. By the age of 10, grand mal seizures had developed, and a diagnosis of neurolipidosis was made at another hospital. Mild seizures continued despite Dilantin and phenobarbital. A year later, her sense of balance had become disturbed, and the following year mental retardation had progressed to forgetfulness of words, dysarthria and an I.Q. of 69.

During the 6 months before admission to the Bronx Municipal Hospital for the biopsy, her mother noticed sporadic jerking, which may have been a form of myoclonus.

Examination. The results of the general physical examination and laboratory studies were uninformative. The neurological examination established the following: normal head size; severe mental retardation; failure to perceive light or a moving object; coarse horizontal nystagmus; optic atrophy with bilateral pigmentary degeneration of retina; slurred speech; slightly broad-based, unsteady gait; absent Romberg sign; bilaterally significantly hyperactive deep tendon reflexes; intact corneal and gag reflexes. The sensory examination was non-contributory.

Family History. The only pertinent family history concerned the patient's one sibling, a 7 year old boy. He was blind with pigmentary degeneration of retina and was considered clinically to have juvenile lipidosis, although his I.Q. was 125. Other siblings (11 years old girl, 6 and 4 years boy) are doing well.

Material and Methods

About 2 g of tissue were taken from the right superior frontal gyrus and were prepared for histologic, electron microscopic, histochemical and biochemical studies.

Histological Study. Small pieces of tissue were fixed in 10 percent formalin, embedded in paraffin, and stained with hematoxylin-eosin, periodic acid-Schiff (PAS), Heidenhain's, Bodian's, oil red 0, Sudan black, indophenol HCl (Albert et al., 1960), and for acid fastness. A small piece was prepared for frozen sections, stained with Sudan IV and PAS, and Bielschowsky's and Cajal's methods.

Electron Microscopic Study. The cerebral tissue was fixed for 90 min at 4°C immediately after biopsy in Palade's Vernal-al buffered O₂O₄ (Palade 1952) with added sucrose (Cautfield, 1957) or in Dalton's chrom osmium fixative (Dalton, 1955). Another piece of tissue was fixed for 150 min in 3 percent glutaraldehyde in 0.1 M cacodylate buffer, pH 7.4, then for 90 min in one or the other of the osmium fixatives. After fixation, the tissue was dehydrated with graded ethanol and embedded in Araldite and studied with a Siemens Elmiskop 1.