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ON THE ASSOCIATION OF VARIOUS TYPES OF CEREBRAL LIPIDOSES

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Demyelination of the white matter is a common feature in neuronal storage diseases. The pathogenic interpretation of these findings is not univocal. There exists a group of lipid storage diseases in which the nature, intensity and distribution of white matter alteration suggest either the existence of of a leucodystrophic component or coexistence of two different pathological processes. The observation presented below suggests the coexistence of a neuronal storage disease with a leucodystrophic process.

Case history: 13-month-old boy in whom at the age of 5 months the parents noticed progressive enlargement of the head as well as arrest and later deterioration of physical and mental ability. Optic fundi were normal. Enormous hepatosplenomegaly was found. X-ray examination revealed kyphosis of lumbar spine, chondrodystrophic changes of lumbar vertebrae and extensive craniolacunia (Fig. 1). The child died of bronchopneumonia after 3 weeks of hospitalisation.

Pathological examination revealed vacuolisation of hepatic cells, foamy transformation of histiocytes in liver and spleen and swelling and vacuolisation of epithelial cells of renal tubuli and of Malpighian glomeruli (Fig. 2).

In megalencephalic brain two fundamental types of microscopic changes were present: 1) generalized storage process involving to a different degree all neurons of the central nervous system (Figs 3 and 4).

The glycolipid accumulated in the nerve cells was histochemically identified as ganglioside; 2) profuse demyelination of cerebral (Figs 5, 6, 7) and cerebellar white matter involving also the axis of cerebral gyri. No sudanophilic myelin breakdown products, inflammatory and macrophagic reaction were present either in the areas completely devoid of myelin or in the fields where an active demyelination process was occurring. The scanty cellular reaction to demyeli-

nation was purely astrocytic (Fig. 8). The cytoplasm of astrocytes was filled with glycolipid which stained metachromatically red with acid cresyl violet.

Ultrastructural study of needle biopsy material from the frontal cortex exhibited a great variability of intracytoplasmic inclusions both in neurons

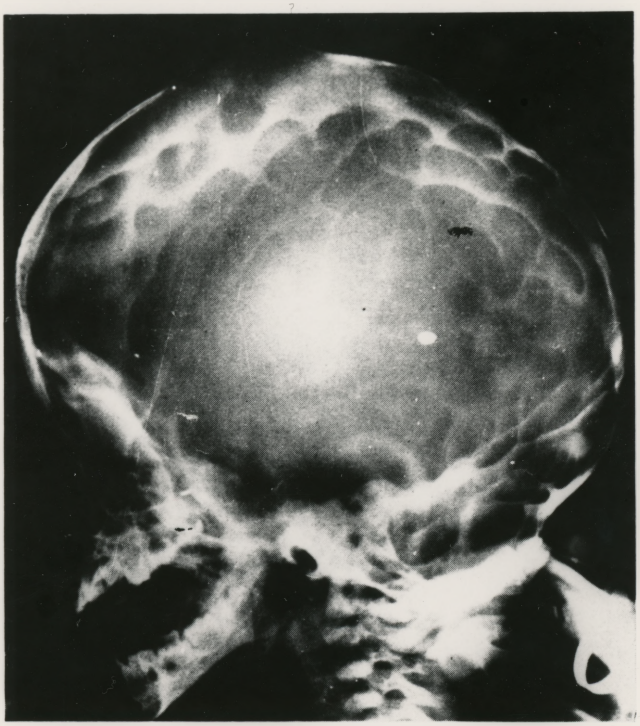

Fig. 1. Lateral projection of skull. Numerous bone defects in skull cap.

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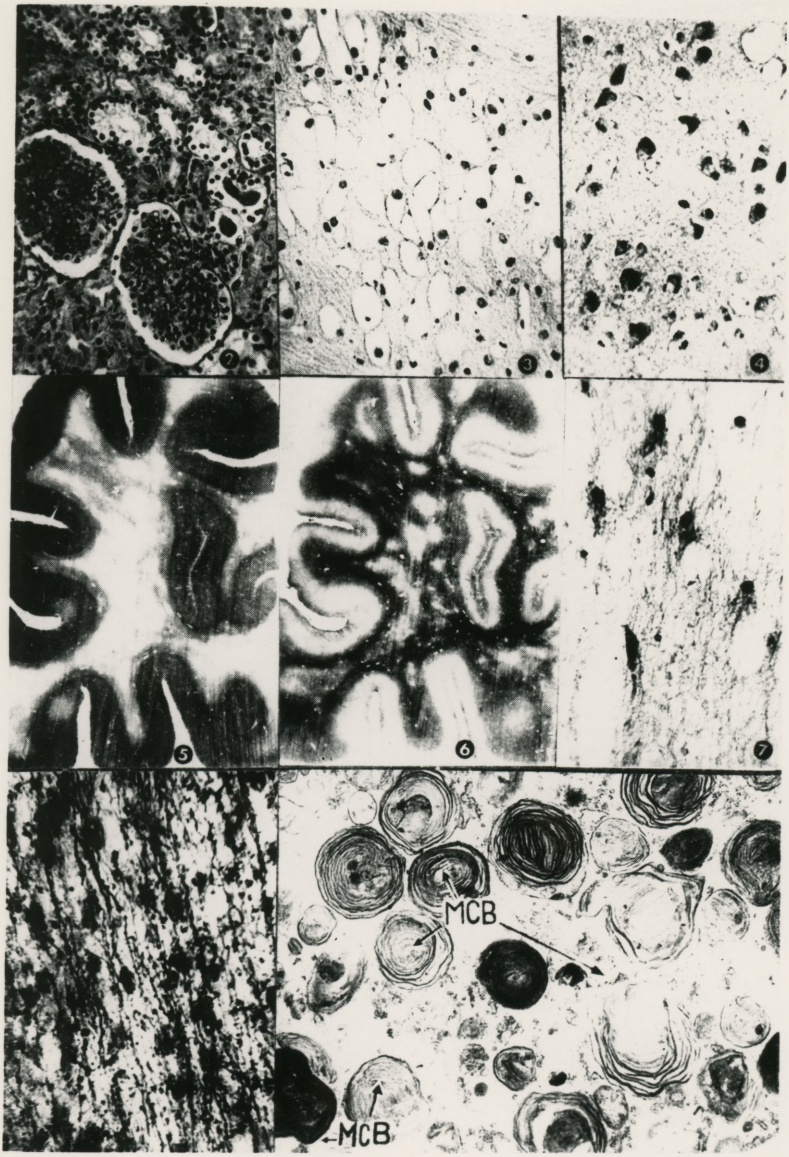
Fig. 1. In text. *Fig. 2.* Kidney. Epithelial cells of renal tubules swollen and vacuolated. The same changes in the cytoplasm of glomerular epithelium. Subcapsular spaces widened. In tubules PAS-positive hyaline deposits. Paraffin. Periodic acid Schiff. × cca 140 — *Fig. 3.* Pons. Severe damage of nuclei pontis. Paraffin. H-E. × cca 260 — *Fig. 4.* Abundant lipid accumulation in neuronal cytoplasm of frontal cortex. Frozen section. Sudan black B. × 140 — *Fig. 5.* Frontal lobe. White matter completely devoid of myelin. Paraffin. Heidenhain. Magn. glass — *Fig. 6.* Same section. Widespread gliosis in demyelinated area, most pronounced in subcortical region. Paraffin. Kanzler-Arendt. Magn. glass — *Fig. 7.* White matter of centrum semiovale with residual myelin sheaths and lipid-containing astrocytes. Frozen section. Sudan black B. × cca 260 — *Fig. 8.* Frontal white matter. Scanty regressively changed astrocytes in demyelinated area. Paraffin. H-E. × cca 260 — *Fig. 9.* Electron micrograph of cortex. Cytoplasm of the neuron contains numerous characteristic membrano-cytoplasmic bodies. × cca 10,000.



and glial cells among which membranocytoplasmic bodies and membranovesicular bodies prevailed (Figs 9, 10).

Biochemical study of brain tissue fixed in formalin revealed a high increase of ganglioside content both in gray and white matter. TLC of the ganglioside fraction from gray matter showed an increase of G_{M1}-ganglioside corresponding to 67.1 per cent NANA. These results permit in the presented case the diagnosis of generalized gangliosidosis (O'Brien, et al. 1965). Landing disease (Landing, et al. 1964) or G_{M1}-gangliosidosis (Suzuki, et al. 1968). From the clinical point of view the case reprents this type of disease in which neurological symptomatology is accompanied by severe visceral involvement and damage of the skeletal system (Derry, et al. 1968). In the morphological picture noteworthy are pathological changes in the white matter which took the form of severe demyelination accompanied by diffuse fibrogliosis and only weak astrocytic

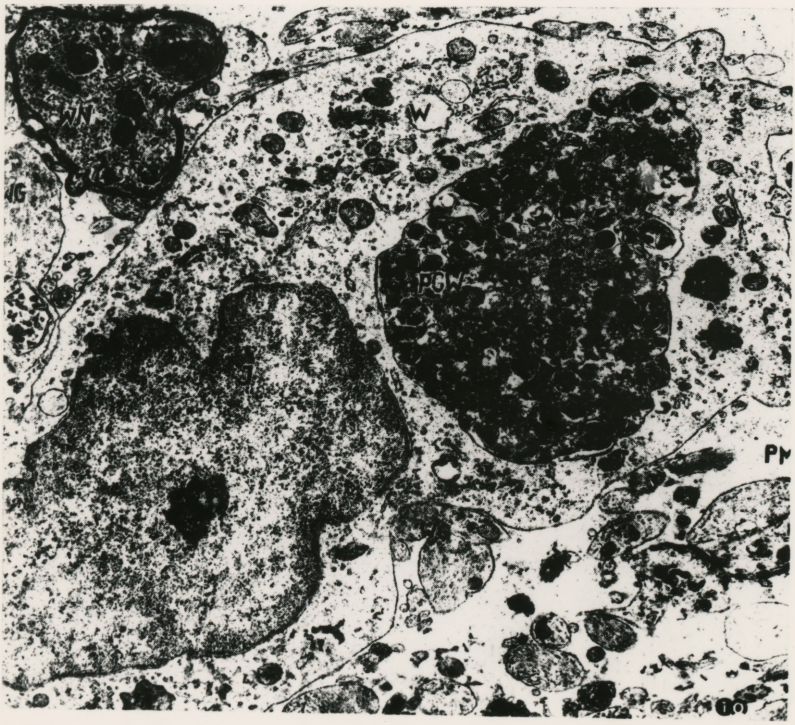


Fig. 10. Electron micrograph. Glia cell, probably astrocyte with pleomorphic membrane limited inclusion body (POW). Considerable widening of extracellular space (PM) with numerous glia fibers (WG). cca 10.000

cellular reaction. Macrophages were not seen in any areas of the white matter, despite the enormous accumulation of free lying granular products of myelin breakdown (Fig. 7). In all areas of white matter accumulation of PAS- and Sudan black B-positive substances was seen in the scanty astroglia cells.

Varying in degree myelin disintegration is a common element of the pathological picture of generalized gangliosidosis. Suzuki et al. (1968, 1969) consider this myelin involvement as a secondary type of demyelination. However, he also stresses the abnormal ganglioside pattern in white matter tissue. Some authors (Attal, et al. 1967, Bargeton, 1963, Fardeau and Lapresle, 1963) consider that the pathological process taking the form of neuronal storage involves also to the same extent the myelin sheath and is an integral component of the fundamental process.

The pathological changes in the white matter in the present case vary widely from those in other cases of G_{M1}-gangliosidosis. The coexistence of cerebral gangliosidoses with metachromatic leucodystrophy (Mossakowski, et al. 1961, Lüthy, et al. 1966, Pilz and Jatzkewitz, 1968) suggest that the single metabolic defect may affect the normal pathway of several sphingolipids located in different structural components of the brain. Such a possibility could be taken into account in our observation in which the character of myelin damage and glial insufficiency suggests such a nature of pathological process.

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