SOME ASPECTS OF THE MORPHOLOGY AND HISTOCHEMISTRY OF THE CEREBRAL CHANGES IN HEPATIC COMA

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The pathomorphology of the cerebral changes occurring in the course of acute and chronic acquired lesions of the liver has a large and rich literature.

The problem has been discussed in a series of case reports and in numerous monographs, published among others by Pollak (1927), Scherer (1933), Nikolajev (1937), Stadler (1936), Waggoner and Malamud (1942), Adams and Foley (1949, 1953), Baker (1949), Inose (1952, 1961) and many others. Mc Dermott and Adams (1954) described a characteristic clinical syndrome in patients in whom a porto-caval shunt had been performed. The condition was called portal-systemic encephalopathy by Sherlock, Summershill and White (1954). Besides morphological descriptions, some histochemical studies have been carried out recently (Inose, 1961). The intention of the present investigation was to establish the pathomorphological and histochemical changes that occur in the brain when acquired liver damage has caused hepatic coma, and to compare these with the changes observed in cases of liver disease without hepatic coma. The studies were carried out on 36 cases with various types of acquired liver damage, comprising 27 cases of liver cirrhosis (in 2 a porto-caval shunt had been surgically performed), 3 cases of massive liver necrosis complicating viral hepatitis and 6 cases with neoplastic liver damage. The age of patients ranged from 8 to 81 years. Twenty-five patients died in hepatic coma. In the remaining 11 cases death was due to causes other than liver damage.

Clinical neurological signs and symptoms were present in 16 cases only one of which was in the group without hepatic coma. In two cases the typical clinical picture of so-called portal-systemic encephalopathy was present. The morphological picture in all but 4 cases was typical of hepatogenic encephalopathy. Its intensity varied a great deal from case to case, being most severe and diffuse in the cases where death occurred in hepatic coma.

The four cases without morphological changes were in the group in which hepatic coma did not occur.

The fundamental morphological changes found in our material consisted of a profound alteration in glial cells, represented by:

1. Generalized glial proliferation throughout the whole nervous system but most intense in the cerebral cortex and in the region of cortico-subcortical junction.

2. Profound pathological changes in the astroglia (Fig. 1) consisting mainly of damage to their processes (clasmatodendrosis). Numerous astrocytes lacking processes were seen. Besides the damaged astrocytes many hypertrophied glial elements were present both in gray and white matter.

3. The presence of special glial cells, mostly Alzheimer type II, and Opalski cells (Figs. 2 and 3). The latter were seen in 7 cases, 6 of whom died in hepatic coma. In

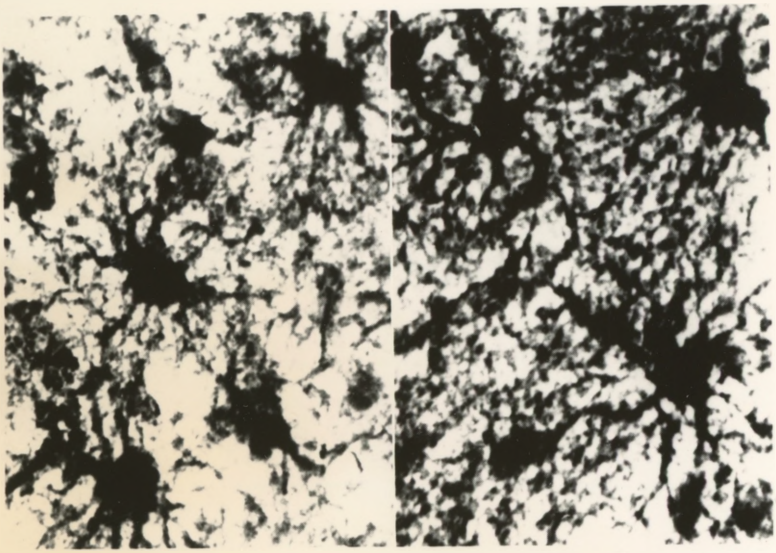

Fig. 1. Astrocytes in the region of cortico-subcortical junction, showing severe alteration of their processes. Cajal impr. Magn. x obj. 40 x oc. 15.

all cases with hepatic coma and in 5 without coma intranuclear PAS-positive inclusions were seen in the Alzheimer cells and in numerous astrocytic nuclei which otherwise appeared entirely normal. Our histochemical studies confirmed their glycogen nature (Inose, 1961), but it seemed that there was also a mucopolysaccharide component in their chemical structure. The cytoplasm of Opalski cells was filled with PAS-positive granules which also seemed to be composed of mucopolysaccharides.

4. The presence of yellowish-gray granular pigment in the vicinity of the Alzheimer cells and adjacent to some of the normal astrocytic nuclei. In some cases similar granules occurred also within glial nuclei. Their histochemical nature was identified as being polysaccharides bound with phospholipids. Their glycogen nature was not confirmed.

5. The lack of fibrillary glial reaction at the site of spongy degeneration (Figs. 4 and 5) of the nervous tissue as well as at foci of vasculogenic damage.

Spongy degeneration of brain tissue (frontal lobe, putamen and dentate nucleus) was typical for cases of portal-systemic encephalopathy. However less intense foci of spongy degeneration were also seen in other cases of hepatic encephalopathy with (10 cases) and without (6 cases) hepatic coma.

In addition, generalized non-specific degeneration of neurones was seen throughout the whole nervous system. This was most conspicuous in cases with prolonged hepatic coma and in those where coma had supervened in the course of viral hepatitis.

The cases with hepatic coma were characterised by marked brain edema. Vascular changes except those resulting from the patients' age were not a feature.

On the basis of the above studies we came to the following conclusions:

1. Morphological changes in the central nervous system are present in almost all cases of liver damage, whether or not death has been the result of hepatic coma.

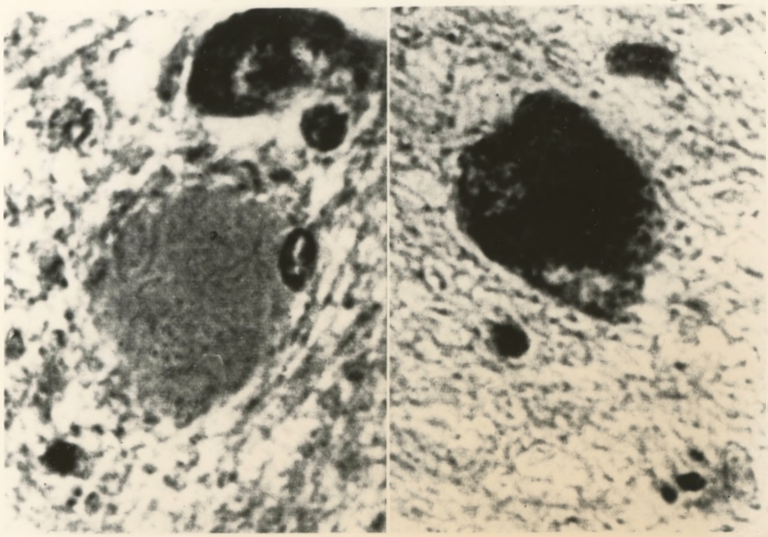

Fig. 3. Opalski cells in cases of hepatic encephalopathy.
a. Opalski cell in the cerebral cortex. Hematoxylin-eosin. Magn. x obj. 40 x oc. 15.
b. Opalski cell filled with strongly PAS-positive granules. Magn. x obj. 40 x oc. 15.

Fig. 4. Spongy degeneration in the upper portion of the putamen in a case of portal-systemic encephalopathy. Heidenhain's meth. Magn. x obj. 8 x oc. 10.

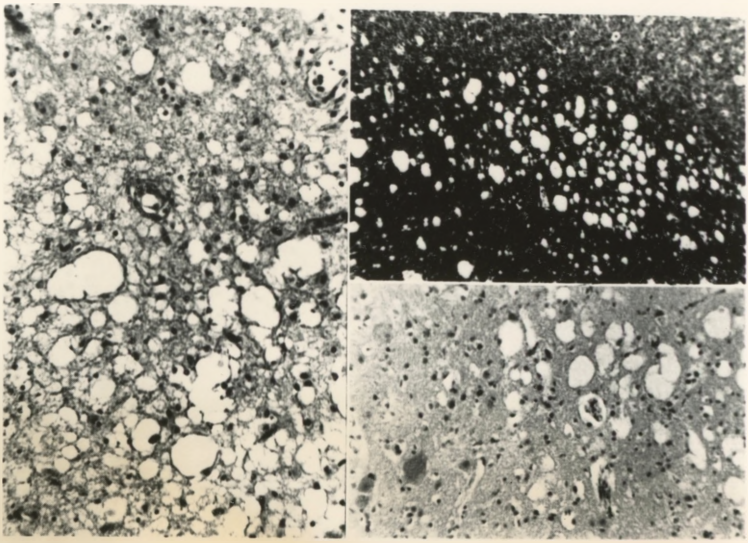

Fig. 5. Various types of spongy degeneration. Note the lack of glial proliferation.
a. Spongy degeneration in the putamen in a case of hepatic encephalopathy. Hematoxylin-eosin. Magn. x obj. 20 x oc. 10.
b. Status spongiosus in the region of cortico-subcortical junction. Heidenhain's meth. Magn. x obj. 8 x oc. 10.
c. Spongy degeneration in the Vth layer of the motor cortex in a case of portal-systemic encephalopathy. Hematoxylin-eosin. Magn. x obj. 8 x oc. 15.

suggests that vascular insufficiency, as in Wilson's disease (Konowalow, 1960; Brzezicki, 1937) contributes to its pathogenesis.

6. Our histochemical studies have shown that in addition to the intranuclear inclusions composed of glycogen in astrocytes, there are other disturbances in glial glycolipid metabolism. These are histochemically identical with those described by Mossakowski, Kasperek and Rościszewska (1964) in cases of Wilson's disease. The nature of the granules in the cytoplasm of Opalski cells is also similar to that in hepatolenticular degeneration (Mossakowski, 1965). It would appear therefore that there is a similar basic disturbance of carbohydrate metabolism within astrocytes in all of these conditions.

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