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Intraneuritic Corpora Amylacea

Demonstration in Orbital Cortex of Elderly Subjects by Means of Early Postmortem Brain Sampling and Electron Microscopy

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Summary. Within the framework of an Early Postmortem Brain Sampling Program we had the opportunity to make some light and electron microscopic observations on the orbital cortex of two elderly subjects known to have been free of neurologic and psychiatric disease. Filamentous deposits with the ultrastructural appearance of corpora amylacea were seen inside astrocytic and, more rarely, inside neuronal processes. The findings and their interpretation are discussed in the light of current views on cerebral corpora amylacea and Lafora bodies. It is concluded that today's views on this matter do not account satisfactorily for the present observation or for observations we have quoted from the literature.

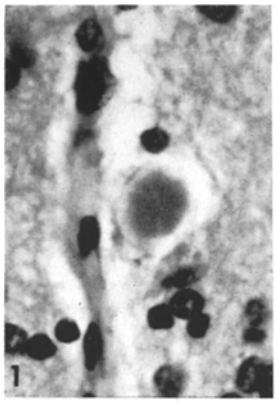
Since Ramsey's publication (1965) it is generally admitted that cerebral corpora amylacea occur invariably in astrocytic processes and cell bodies. Likewise, it is a matter of common knowledge that the basophilic brain deposits known as Lafora bodies have a similar ultrastructure but a strictly intraneuronal location (Schochet, 1972). In the course of our Early Postmortem Brain Sampling Program we made some observations which leave little doubt as to the occurrence of corpora amylacea type of inclusions not only in astrocytic but also in neuronal processes. In this paper we report our findings and we discuss them in the light of current views on corpora amylacea and Lafora bodies of the central nervous system.

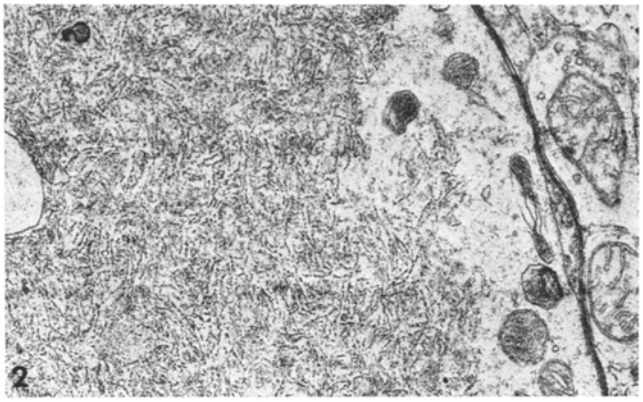
Material and Methods

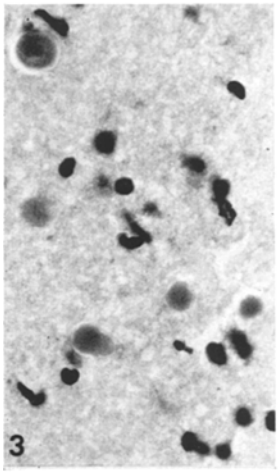
Approximately fifteen minutes after the patients had been pronounced dead and permission from next of kin had been obtained, a needle was inserted between eyeball and upper lid, through the intraorbital soft tissues, past the orbital roof and into the frontal lobe. Retrieved cylinders of orbital cortex and white matter were immediately fixed in 4% glutaraldehyde, stored at 4° C and processed later for light and electron microscopy. Details of the method have been published severally together with a preliminary account of the ultrastructural observations on a small series of unselected cases out of a large number of consecutive deaths in the medical ward of an acute general hospital (Herrlinger *et al.*, 1974). Brief clinical information on the two cases dealt with in this report is given in the legends appended to the illustrations. A conventional autopsy was not performed.

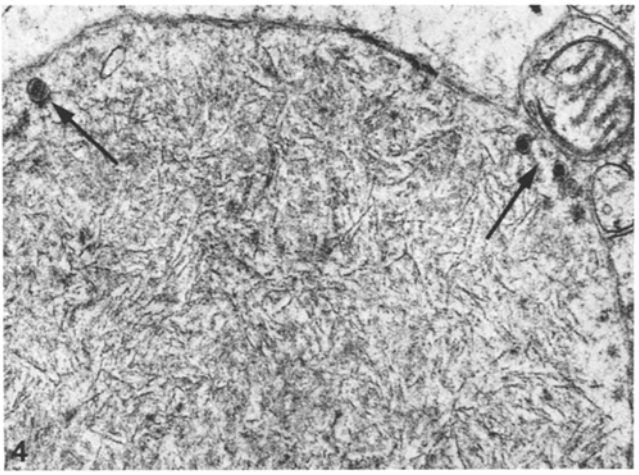
Observations

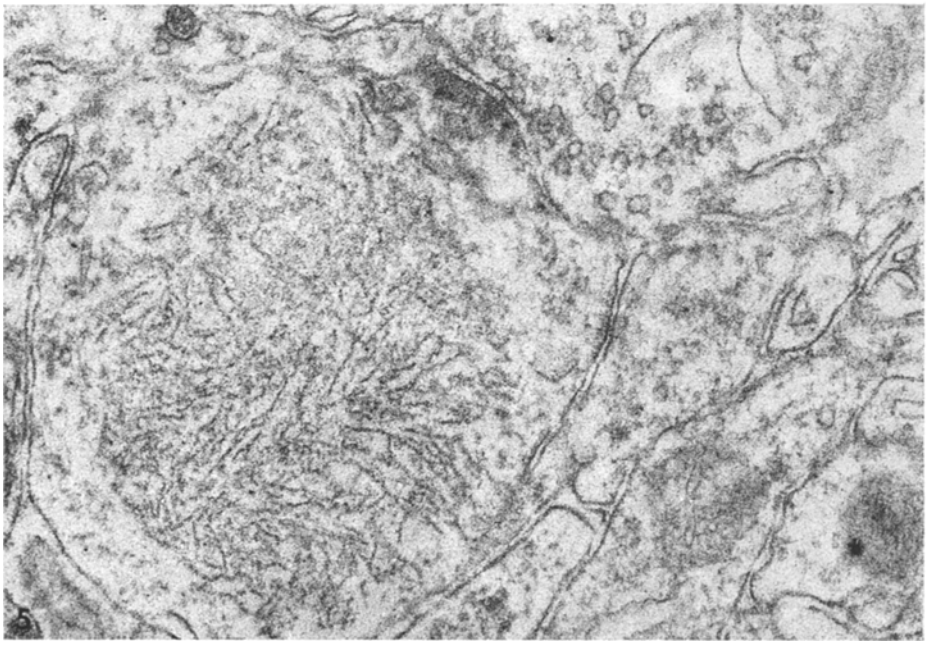
Light Microscopy. Paraffin sections stained with haematoxylin and eosin, cresyl violet and periodic acid-Schiff reagent were available for study. In both











cases several corpora amylacea were seen along the blood vessels (Fig. 1) and scattered about in the cortical gray matter (Fig. 3). They appeared as variably basophilic, periodic acid-Schiff positive, round bodies measuring up to 40 μ in diameter and displaying a hyaline texture with or without a suggestion of a central core of different staining qualities. An assessment of the location of these structures in relation to the various components of the neuropil was not possible. Histologic evidence of neurologic disease was not found in either of the two cases.

Electron Microscopy. Ultrathin sections prepared from glutaraldehyde-osmium fixed and Epon-embedded blocks were stained with uranyl acetate and lead citrate and examined with a Zeiss EM 9A electron microscope.

In both cases several filamentous bodies were observed inside cell processes but never inside perikarya (Figs. 2, 4, 5). They consisted of an unbounded mass of randomly oriented, slightly bent, branching filaments measuring about 65Å in tickness and bathing in a thinly spread background matrix of low density. A focally whorled pattern and punctate densities were seen inside some tangled masses; a differently structured central core was not found. The majority of these bodies were in every respect consistent with written accounts and published electron micrographs of cerebral corpora amylacea. However, few isolated exemplars, apart from being otherwise typical and quite comparable with the others, lay embedded in cell processes which were suggestedly or undoubtedly neuronal in nature. For instance, Fig. 2 depicts a portion of a corpus amylaceum whose cell membrane is sheathed with a few attenuated lamellae not unlike myelin lamellae. Inside the cell process scattered mitochondria are more evocative of a myelinated axon than of an astrocytic process. Dense-cored vesicles are seen along the edge of the corpus amylaceum depicted in Fig. 4. A few isolated "osmiophilic particles" of this kind are not unknown to occur in astrocytes (Gonatas *et al.*, 1967) but are by far more likely to be seen in the average neuronal than in the average astrocytic cell process. And finally, Fig. 5 shows a small corpus amylaceum with a typical synaptic specialization along the cell membrane surrounding the inclusion. Intraneuritic corpora amylacea occurred

Fig. 1. Histologic section from orbital cortex of a male aged 72 with bronchial asthma and death in status asthmaticus and heart failure (Case 1): typical corpus amylaceum along a small blood vessel. H & E, ×745

Fig. 2. Electron micrograph from Case 1: section of corpus amylaceum occupying an unidentified cell process, possibly a myelinated axon, ensheathed by myelin-like lamellae. ×21000

Fig. 3. Histologic section from orbital cortex of a male aged 65 with ventricular tachicardia of unknown origin and death in ventricular fibrillation (Case 2): several corpora amylacea lie scattered about in the grey matter. H & E, ×597

Fig. 4. Electron micrograph from Case 2: section of a corpus amylaceum occupying an unidentified cell process, possibly a neurite, containing also some dense-cored vesicles (arrows). ×30000

Fig. 5. Electron micrograph from Case 1: small corpus amylaceum in a postsynaptic ending. ×54000

singly in the neuropil showing no topographic predilection for vascular structures. Ultrastructural evidence of an underlying neurologic disease was not obtained.

Discussion

No matter what one chooses to call the filamentous inclusions the electron microscopic features of which we have described and illustrated, it is obvious that they possess essentially the ultrastructural appearance of corpora amylacea and Lafora bodies; and it is further evident that a few of these bodies take on an intraneuronal rather than an intra-astrocytic position. That being the case, our findings raise the following questions.

It may be that our filamentous structures are bona fide Lafora bodies which occur in neuronal processes of elderly subjects without neurologic or psychiatric involvement of any kind. It is not our intention to uphold this thesis which runs against some traditional tenets on this subject (Schochet, 1972). However, a survey of the literature reveals that intraneuronal inclusions interpreted as "Lafora-like" or as Lafora bodies have been reported in the brain of patients without myoclonus epilepsy (Suzuki *et al.*, 1971; Petito *et al.*, 1973) and in the brain of dogs with only questionable, if any, neurologic disease (Holland *et al.*, 1970). An alternate possibility is that our filamentous structures represent average corpora amylacea which, on rare occasions, happen to occupy an intraneuronal position instead of having the more common intra-astrocytic situation. This, again, does not conform to today's prevailing views on corpora amylacea. However, the advanced age of our patients and the basal location of our cortical specimens argue in favor of rather than against such an interpretation and so does the reported finding of intra-axonal and presynaptic corpora amylacea type of filamentous masses in three cortical biopsy cases of Pick disease (Brion and Mikol, 1971).

The third and last possibility is that corpora amylacea and Lafora bodies may be only two names for one and the same type of intracellular deposit with variable prevalence inside astrocytes and neurons alike in advancing age, in myoclonus epilepsy and in other diseases as well. Preferential involvement of one cell type with partial and possibly total sparing of the other may merely reflect the different severity of the process in the different cytological types rather than bear upon the chemical compositon of the material(s) being stored. And furthermore, similar if not identical ultrastructural and chemical substrates (Sakai *et al.*, 1969; Austin *et al.*, 1970; Sakai *et al.*, 1970; Nikaido *et al.*, 1971) may have the same morphogenesis and yet be polyetiological: distinct structural and/or regulatory defects of cell's metabolism may play the causative role in the different situations here under consideration.

We have no evidence to offer along these lines. Only future observations may shed some light on these problems. For the time being the least that one can say is the following. First, intracellular inclusions best identifiable as cerebral corpora amylacea of old age can occur also, though rarely, inside nerve cell processes. Secondly, our findings and some of the findings we have quoted from the literature do not fit in with present-day thinking on the subject of corpora amylacea and Lafora bodies.

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