LIGHT AND ELECTRON MICROSCOPIC OBSERVATIONS OF DIFFUSE PLAQUE
AND ITS RELATED CONDITIONS

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INTRODUCTION

Many ultrastructural studies appear to have confirmed the fine structures of senile plaques (SPs). SPs have been usually classified into three types: 1) typical plaques with amyloid cores surrounded by degenerate neurites, 2) primitive plaques composed of many degenerate neurites and a few amyloid wisps, and 3) compact plaques consisting of a mass of amyloid without pathological neurites. Recent advances in staining methods such as β-protein immuno-histochemistry and the modified periodic-acid methenamine silver (PAM) method have offered important information concerning amyloid substance. In the present study, diffuse plaques (DPs), a type of SP, were investigated light and electron microscopically using various staining methods including modified-PAM electron microscopy. Ultrastructural findings characteristically seen in DPs were similar to those obtained in the superficial layer of the cerebral cortex and occasionally in peripheral coronas of typical SPs. Based on these observations we discuss the morphological origin of SP amyloid.

MATERIALS AND METHODS

The brains used for this study were obtained at autopsy from two (44 and 79 years old) male patients with Alzheimer-type dementia (ATD). Formalin-fixed, paraffin-embedded 5-μm serial sections of the cerebral cortex were stained with the methenamine-Bodian, modified-PAM, and β-protein immunostaining methods. For electron microscopy, small pieces were cut from the fresh cerebral cortex of the two ATD cases and immersed in 2% glutaraldehyde solution. Some of the tissue was refixed in 1% OsO₄ solution and embedded in Araldite for routine electron microscopic examination. Using the remaining parts of the tissue, we cut 100-μm-thick sections using a vibratome and appropriated them for the modified-PAM electron microscopic examination, which shows the specific deposition of silver particles on amyloid substance.

RESULTS

Diffuse plaques

DPs were, though fainter than SPs, clearly stained by the methenamine-Bodian method, but were never recognized with the original Bodian method, which has been widely used to detect SPs. DPs were less argyrophilic than
other types of SPs, and were seen as diffuse and uniform deposits of fine silver granules. They were irregular in form and variable in size. Large ones often contained a few neurons (Fig.1-A). No apparent glial reaction was seen within or around DPs. The plaques were clearly stained with β-protein immunostaining (Fig.1-C), as well as with the modified-PAM method (Fig.1-B), which was proved to stain SP amyloid specifically. The predilection sites of DPs were similar to those of other types of SPs in the cerebrum. By the modified-PAM electron microscopic examination, DPs were revealed as sparse aggregates of fusiform or bundle-like amyloid-like wisps accompanied by the deposition of silver granules (Fig.2). At higher magnification, no obvious amyloid fibrils were confirmed, but weakly electron-dense amorphous substances were recognized, on which silver granules had been deposited (Fig.2, inset). Upon routine electron microscopy, DPs were also shown as aggregates of scattered fusiform or bundle-like wisps (Fig.3) consisting of weakly electron-dense amorphous and partially fibrous substances (Fig.3, inset). A few small degenerate neurites and astrocytic processes were occasionally observed. The ground substance of DPs seemed to be somewhat rough in comparison with the surrounding tissue. Although the amorphous and partially fibrous amyloid-like wisps seemed to be free in the tissue and it was