Light and electron microscopic examination of amyloid-rich primitive plaques: comparison with diffuse plaques

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Summary. In Alzheimer-type dementia brains, numerous “amyloid-rich primitive plaques (PPs)” were observed with β-protein immunostaining and periodic-acid methenamine (PAM) staining. These amyloid-rich primitive plaques were accompanied by various degrees of small argyrophilic rod-like, granular or filamentous structures. Routine and modified-PAM electron microscopy revealed many bundles and flecks consisting of amyloid fibrils scattered widely throughout the plaques. Degenerate neurites, astrocytic processes and bundles of glial fibres also participated in the formation of the plaques. The similarities and differences between these amyloid-rich primitive plaques and diffuse plaques are described.

Key words: Amyloid-rich primitive plaque – Diffuse plaque – Amyloid – Periodic-acid methenamine silver method – Electron microscopy

Introduction

Many ultrastructural studies appear to have confirmed the fine structure of senile plaques (SPs) [8, 10, 11, 14–18]. According to these studies, SPs have been usually classified into three types: (1) typical plaques (TPs) consisting of amyloid cores surrounded by degenerate neurites; (2) primitive plaques (PPs) composed of many degenerate neurites and a few wisps of amyloid; and (3) compact plaques (CPs) consisting of an amyloid mass without pathological neurites. Recently, previously unknown types of SPs have been reported as “diffuse plaques” (DPs) [19, 20], “pre-plaques” [12] or “senile plaque-like structures” [5]. In this paper, we describe another type of SPs, which has been found to be composed mainly of scattered amyloid wisps using routine and modified periodic-acid methenamine (PAM) electron microscopic methods. We call this type of SPs amyloid-rich PPs and compare them with DPs in respect of the quality and quantity of amyloid.

Materials and methods

The brains used for this study were obtained at autopsy from two cases of presenile Alzheimer’s disease, one of senile dementia of the Alzheimer type, and one of adult Down’s syndrome. Formol-fixed and paraffin-embedded blocks were cut serially at 5–10 µm in thickness, and stained with methenamine-Bodian [9], modified-PAM [4–5] and anti-β-protein [6] methods. In addition, Bodian, periodic acid-Schiff (PAS), Congo red, glial fibrillary acidic protein (GFAP) and Holzer stains were also employed in some sections. For electron microscopy, small pieces were cut at autopsy from the cerebral cortex of each case and immersed in 2% glutaraldehyde solution. Sections 100 µm thick sections were made using a vibratome and stained with the modified-PAM method. After this procedure the tissues were embedded in araldite as usual. Ultrathin sections were counterstained with uranyl acetate and lead citrate.

Results

Light microscopically, numerous spherical SPs, which were densely stained with the anti-β-protein and modified-PAM methods, were observed in all four cases. They consisted of densely packed and homogeneously distributed fine granular or filamentous material in the β-protein immunostaining (Figs. 1c, 2c). The modified-PAM preparations [4, 5] also indicated a similar “ball of knitting wool-like” pattern (Figs. 1b, 2b). These staining properties suggest that this type of SP has diffusely distributed abundant amyloid. These SPs were mostly round and 20–80 µm in diameter. In the methenamine-Bodian preparations, they were variously argyrophilic, composed of very finely granular structures (Fig. 1a) accompanied by various degrees of dark rod-like, granular or filamentous materials, which are thought to be degenerate neurites (Figs. 1a, 2a). These SPs were weakly stained with GFAP immunostaining and the Holzer method. This indicates the participation of glial elements in these SPs. Small cells were often contained within them (Fig. 3a, b). These SPs are different from DPs in that they are sharply defined structures (Fig. 3a, b). On the other hand, DPs vary in shape and size, have an obscure boundary, and occasionally contain a few neurons within them. They are weakly argyrophilic in

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Figs. 1, 2. Amyloid-rich PPs. Serial sections are stained with methenamine-Bodian (Figs. 1a, 2a), PAM modified silver (Figs. 1b, 2b) and β-protein (Figs. 1c, 2c) stains. Spherical homogenous amyloid-rich PPs are accompanied by various degrees of dark rod-like, granular and/or filamentous argyrophilic bodies, which correspond to degenerate neurites (Figs. 1a, 2a). On serial sections, the same plaques seen in Figs. 1a and 2a show strong staining properties in both modified-PAM (Figs. 1b, 2b) and anti-β-protein preparations (Figs. 1c, 2c). × 200

Fig. 3. In contrast to a large obscure diffuse plaque (a, b, thick arrow), many obviously argyrophilic round primitive plaques (PPs) are seen (a arrows): On serial section stained with β-protein immunostaining these PPs demonstrate distinctly amyloid-positive staining (b arrows). Small cells are often contained within these plaques. a Methenamine-Bodian; b β-protein immunostaining. × 125

Fig. 4. Usual PPs with relatively few amyloid fibrils: a methenamine-Bodian; b modified-PAM; c β-protein immunostaining methods. × 180