Basement Membrane Changes in Membranoproliferative Glomerulonephritis

II. Characterization of a Third Type by Silver Impregnation of Ultra Thin Sections*

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Summary. In a previous study on membranoproliferative glomerulonephritis (MPGN) we reported the preliminary result that a basement membrane (b.m.) lesion incompatible with the criteria of subendothelial deposits (type I) or intramembranous dense “deposits” (type II) can be recognized by silver impregnation (s.i.) of ultra-thin sections. This technique has been further evaluated and applied firstly to control cases with normal b.m., perimembranous GN, diffuse proliferative (“MPGN-like”) lupus nephritis and, secondly to additional cases of idiopathic MPGN comprising 10 biopsies with doubtful findings as judged by electron microscopy with conventional impregnation. S.i. of ultra-thin sections proved to be a reliable method, of particular value in the visualization of fine structural details of b.m. changes in the field of MPGN. The light microscopic (l.m.) equivalent of the new lesion is defined. Accordingly, the series of 31 patients with idiopathic MPGN has been subdivided into three groups: Type I (19), type II (3), type III (9 patients). Type III is understood to be an intermediate type lesion, distinguished from type I by true membranous changes (discontinuity of the lamina densa) and from type II by the lack of the intramembranous electron-dense (argyrophilic) material. It resembles in part, however, perimembranous GN due to segmental spike formation and little proliferation.

The clinical course of the patients with the type III lesion did not significantly differ from that of the other groups. The details are given in short case reports. Serum C3 was persistently depressed in 6, initially depressed in 2 patients and normal in one. As in type II, a predominant or isolated presence of C3 can be seen by immunofluorescence microscopy. Therefore, type III is likely to be mistaken for type II on the basis of immunological and l.m. data, and for type I on the basis of e.m. with conventional impregnation. The resultant inconsistencies so far inherent in the dual subclassification concept of MPGN can probably be solved—at least in part—by the accep-
tance of the type III lesion as defined by its appearance in silver impregnated ultra-thin sections.

Both lesions, type II and type III, are understood to be conditions in which the notional difference between “deposits” and a substantial alteration of the b.m. is poorly defined.

Key words: Membranoproliferative glomerulonephritis — Ultrastructure of basement membrane changes — Silver impregnation in electron microscopy.

Introduction

Until now the morphological pattern of membranoproliferative glomerulonephritis (MPGN) has been subdivided into two different types: type I with subendothelial deposits and type II with so called intramembranous dense deposits or electron-dense alteration of the basement membrane (b.m.) (Habib et al., 1973). In type I the b.m. is believed to remain essentially intact whereas in type II the b.m. material is itself characteristically involved in the disease process. As a rule, type II is associated with persistent depression of serum complement (C3) suggestive of a pathogenetic mechanism with complement activation via the alternate pathway.

In a previous study we have reported on our findings in a series of 31 renal biopsies from patients with idiopathic MPGN (Anders and Thoenes, 1975). Our main interest was focussed on the light and electron microscopic characterization of the material causing glomerular capillary wall thickening. The light microscopic (l.m.) findings were classified according to the presence or absence of a lobular pattern, the electron microscopic (e.m.) findings according to the presence or absence of the intramembranous dense material. Our results differed from those of other groups in that 1. the type I lesion with an intact b.m. could not be demonstrated in a similar percentage to that given in the literature, 2. almost half of the hypocomplementemic cases examined by e.m. failed to show the classical electron-dense alteration of the b.m. Most of these cases were characterized by an irregular, more or less extensive, ill defined b.m. thickening which in uranyl and lead (U/Pb) impregnated sections did not allow a clear distinction between the b.m. proper and the abnormal material. Therefore, we hesitated to ascribe this medium dense alteration to the incorporation of deposits into the b.m. and wondered whether it represented a distention of the b.m. with loss of its original properties (such as electron-density and argyrophilia of the lamina densa). On l.m. examination these doubtful cases gave the impression of “dense deposits” with little or no apparent double contour formation. But neither the presence of electron-dense material nor well defined subendothelial deposits could be demonstrated by e.m. with conventional impregnation.

The only technique we found to yield conclusive results in investigating this particular problem was silver impregnation (s.i.) of ultra thin sections. Using this technique it was possible to delineate a so far undescribed lesion (Anders and Thoenes, 1975; Fig. 8) which cannot be described by the criteria of the types I or II, and therefore may have to be considered as a separate lesion, type III.