An Electron Microscopic Study on an Avascular Glomerulus in the Rat

Hidekazu Shigematsu

Summary. An avascular glomerulus, measuring about 30 μ in diameter, composed only of atrophic epithelial and undifferentiated mesenchymal cells was found in the kidney of a normal male rat. There were no afferent and efferent arterioles associated with this glomerulus, but a blood capillary with some juxtaglomerular cells occurred at its pole. This glomerulus was considered to be derived from a malformation in nephrogenesis and to be in the process of becoming hyalinized. Discussion was made with reference to the pathogenesis of so-called congenital glomerulosclerosis.

Some light microscopic studies have been made on so-called congenital glomerulosclerosis, but its pathogenesis is still obscure. In this short report, the fine structure of a rat glomerulus lacking vascular elements is presented. The ultrastructural analysis will give some information about the collapsed glomeruli which condition is due to the abnormal development of glomerular capillary loops.

Materials and Methods

In studying normal and pathological glomeruli, the author encountered an avascular glomerulus in a young untreated male rat (3 months). The tissues were fixed in 3% glutaraldehyde and then 1% osmium tetroxide. After dehydration with graded ethanol, the tissue blocks were embedded in Epon 812. The thin and thick (1 μ) sections were made alternatively on a Porter-Blum microtome. The thin sections were stained doubly with uranyl acetate and lead citrate, and the thick ones were stained with toluidine blue. Electron and photomicrographs were matched with corresponding structures of the same single glomerulus.

Results

An avascular glomerulus with atrophic renal tubules was found to occur singly in the normal renal cortex of a rat. The other glomeruli and renal tubules in the vicinity of this abnormal glomerulus were seen to be normal (Fig. 1).

The abnormal glomerulus was about 30 μ in diameter, and was made up of several lobular divisions (lobuli) with the axial matrix surrounded by some visceral epithelial cells. Electron microscopy showed that neither vascular lumens, endothelial cells nor blood cells were present in any part of this glomerulus (Fig. 2, 6). The visceral epithelial cells (podocytes) were mostly atrophic and their cytoplasm contained a small Golgi apparatus, several strands of the granular endoplasmic reticulum as well as scattered mitochondria (Fig. 2, 4, 6). The basal parts of the podocytes were mostly flattened and showed a wavy attachment line to the basement membrane. Some of
them projected deeply in the axial direction of the lobuli showing an islet-like appearance in some cross sections (Fig. 5a, b, 6).
Fig. 3. A part of a normal glomerulus in the same kidney. Well developed foot processes appear on the smooth basement membrane of the patent glomerular capillary loop. ×6,600

Fig. 4. A part of the abnormal glomerulus of the same magnification as in Figure 3. Atrophic podocytes with undeveloped foot processes are seen on the irregularly thickened and loosened basement membrane. Mesenchymal cells (Ms) are in contact with the basement membrane. ×6,600

Fig. 5. a. The epithelial cytoplasm projects deeply into the matrix. The lamina densa shows modifications such as enmeshing (Em) and splitting (Sp). ×5,700 b. Another sectional level of the same lobule. The epithelial cells are attached to the basement membrane from both sides. The continuity between the outer and the inner cytoplasm is interrupted in this section, forming the lumen (Lu) in the center. Note the undeveloped foot processes (arrows). ×6,900
The basement membrane was composed of a dense layer grossly about 3,000 Å in width (lamina densa) and an outer electron lucent layer about 700 Å in width (lamina rara externa) just beneath the epithelial cell (Fig. 4). The former layer was quite irregular in outline showing a moth-eaten appearance and irregularity in electron density.

Fig. 6. A section after the levels shown in Figures 1 and 2. Three nuclei of undifferentiated mesenchymal cells (Ms) are seen. Deposits of finely granular material (Dp) debris-like materials (Db) and vacuolar structures (V) are detected inside the thickened basement membrane which shows a meandering course with nodulations (Nd) or fusions (Fw). Foot processes of the epithelial cells are flattened. Epithelial cytoplasm (Epp) protrudes deeply into the matrix, and is seen isletlike in the cross section. ×8,300
Fig. 7. Vascular pole of the glomerulus at a level after Figure 6. Three glomerular epithelial cells (Ep) are seen. The urinary space (Us) is separated from the blood vessel (V) by the basement membrane and the matrix. However the capillary does not extend deeply into the matrix but touches only slightly on this pole. An atrophic distal tubule (ADT) is present adjacent to the glomerulus. En Endothelial cell nuclei. ×2,800 Inset. Incomplete juxtaglomerular apparatus. A section after the levels shown in Figure 7. Some of the glomerular epithelial cells (Ep) are still present. The succeeding capillary lumen (V) appears at the left of the figure. Two kinds of juxtaglomerular cells are to be seen. One of them, agranular cell (A) has a distended, granular endoplasmic reticulum with evident perinuclear cisternae and the other, granular cell (G) has osmiophilic granules. Each of them has the basement membrane (Bm) around its cell membrane. ×4,900
density (Fig. 2, 4, 5ab, 6), when compared with the lamina densa of the normal glomerular capillary loop in the same kidney (Fig. 3).

In the matrix of the lobular divisions, a few mesenchymal cells, some vacuolar structures and vesicular debris of unknown origin were observed just beneath the meandering basement membrane. Focal depositions of finely granular material, probably hyalin, were also found in the matrix. The mesenchymal cells showed numerous cytoplasmic processes protruding into the matrix (Fig. 2, 6). There were, however, no mesenchymal cell elements in the axial matrix in some lobuli (Fig. 5a, b).

A periglomerular blood capillary was observed in contact with the tip of the avascular glomerulus. However, the vascular space did not extend deeply into the glomerulus, but touched only slightly the pole of this glomerulus (Fig. 7). This capillary was accompanied by juxtaglomerular cells. Some of these cells contained numerous dense granules with a fine texture surrounded by a membrane. The other cells were devoid of granules and were characterized by a predominance in the cytoplasm of the distended cisternae of the granular endoplasmic reticulum. Perinuclear cisternae in these cells were also dilated (Fig. 7, inset). The distal tubule apparently originating from the avascular glomerulus was atrophic to a considerable extent and the tubular lumen was nearly closed (Fig. 7).

Discussion

The most striking feature of the abnormal glomerulus described in the present study was the absence of the glomerular capillary loops. Similar avascular glomeruloid structures have been reported only in the case of Wilm's tumor, in which the origin is suggested in the metanephrogenic blastema (Balsaver et al., 1968). The atrophic epithelial cells on the winding thick basement membrane, a small number of the mesenchymal cells in the matrix of lobular divisions, and only one capillary with some juxtaglomerular cells intimately related to the pole highly suggest that this glomerulus may be derived from a malformation of a glomerulus in its development. It is possible under the present concepts of nephrogenesis (Du Bois, 1969) that the embryonal primitive vessels could not extend into the cleft formed in the metanephric vesicle, or that the capillary buds were unable to develop in situ from the metanephric mesenchymal cells. Kurtz (1958) reported in a study of developing glomeruli that the epithelial foot processes in the glomerulus are present only where the epithelial cells were apposed to the developing capillary tuft. The undeveloped, mostly flattened foot processes observed in the present study suggest the presence of vascular disorders during development. It is probable that the debris-like materials found between the basement membrane and the axial matrix might be derived from the once-developed and vanished endothelium of the blood capillary. The irregularity in the electron density and other findings in the lamina densa seem to be the result of the abnormal metabolism of the podocytes. It is known on the basis of some experimental studies (Kurtz and Feldman, 1962; Andres et al., 1962; Pierce and Nakane, 1967; Striker and Smuckler, 1970) that podocytes participate in the basement membrane formation. The hypoactivity of the epithelial cells which appear mostly atrophic in the present study, and the absence of blood supply might possibly cause the low turnover rate and low level of wear and tear resulting in this abnormal basement membrane.
Regressive sclerotic changes of glomeruli in the kidneys of new born infants or fetuses have been systematically studied since HERXHEIMER in 1909 (SCHWARZ, 1928; FRIEDMAN et al., 1942; LENNARTZ and RUDOLPH, 1959; TAKEUCHI et al., 1959; FRIEDLI, 1966). Concerning its etiology, up to date literature is divided into two different concepts. One is the vascular congenital view and the other is the inflammatory origin concept. FRIEDMAN et al. (1942) used for the first time the term "congenital glomerulosclerosis" referring to the former concept. In the present study the avascular matrix was found to be in the course of hyalinization. The glomeruloid structures which thus missed capillary development could undergo regressive changes observed as a hyalinized or fibrous mass. Some regressive hyalinized glomerular lesions have been observed with a close correlation to post natal infection of the respiratory tract. In contrast, whether or not the inflammation could occur in the developing glomeruli is quite disputable. In the present study the inflammatory signs were absent in the vicinity of the abnormal glomerulus or in the vascular wall, so the glomeruloid structure could not be regarded as a postinflammatory product. In fact, it is known that inflammation is observed as strikingly confined to the developed juxtamedullary glomeruli when nephritis is induced in pups (STEBLAY, 1963). Thus it seems possible that the present study has presented additional data to the concept of embryonal vascular origin in so-called glomerulosclerosis.

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ラットの腎臓にみられた無血管性系球体の電子顕微鏡的観察

重 松 秀一

無処置の雄ラット（3ヶ月）の腎皮質に血管成分を欠如した系球体を観察した。この系球体は、約30μの最大径を有し、その中には萎縮性の上皮細胞と未分化の間葉細胞が認められ、輸入、輸出動脈は認められなかったが、数個の旁系球体細胞を有する毛細血管がこの系球体に接触していた。この系球体は系球体発生過程の異常によって生じたと考えられ、病変に至る途中とみられる。いわゆる先天性系球体硬化症の病理発生に関連して考察を試みた。

References


重 松 秀一
〒280 千葉市美鼻町
千葉大学医学部
第二病理学教室

Dr. Hidekazu Shigematsu
Department of Pathology
Chiba University School of Medicine
Chiba, 280 Japan