

Glomerular histopathology of the contralateral kidney in experimental unilateral hydronephrosis

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Summary. The aim of this study was to examine the structural, ultrastructural and morphometric alterations which take place in the contralateral kidneys of rats with experimental unilateral hydronephrosis.

20 Wistar rats weighing 250 gr., affected by a process of unilateral hydronephrosis following the ligation of the ureter, were used; these rats were then killed 40, 50, 60, or 70 days after the ligation.

Among the perceived alterations, were immunoglobulin G deposits shown by positive immunoperoxidase reaction and increase in the size of the glomerular and corpuscle from around the fortieth day, and structural alterations that included the pedicels, electron-dense deposits in the podocytes and pseudogranular structures in the basal membrane of the capillary.

Key words: Glomerular — Hydronephrosis — Contralateral — Kidney

Introduction

The problem of hydronephritic patients has given rise to extensive studies. In cases of unilateral hydronephrosis, the contralateral kidney assumes great importance since it compensates that process.

Hydronephrosis has been described by various authors: Zollinger and Mihatsch (1978) hold that it consists of a widening of the renal pelvis due to a deterioration of the flow from the urinary tract. Robbins (1984) considers that it involves the widening of the pelvis and renal calyces associated with atrophy and the formation of renal cysts, all due to an obstruction of the urine flow.

Materials and methods

For the histopathological study of the contralateral

kidney in experimental unilateral hydronephrosis by means of the ligation of the ureter, 20 Wistar rats were used, of 250 gr. live weight.

Animals were sacrificed 40, 50, 60, and 70 days after ligation of the ureter. After sacrifice, samples of the contralateral kidney were taken, fixed in 5% glutaraldehyde and processed according to the standard technique for electron microscopy. After carving, samples were cut and contrasted with uranyl acetate and lead citrate.

The immunoperoxidase technique was used to demonstrate the presence of IgG in 4 μ section using anti-IgG rat serum obtained from rabbits.

The method was the one used by Stromberg (1970), which was modified by Baker (1971), with the aid of an MTS histoincubator.

The morphometric and statistical studies were carried out on 1 μ thick sections in paraffin, using an IVAS KONTRON AUTOMATIC image analyst. The U-Test was used for the statistical comparison of the experimental groups with control groups.

Results

The structural changes in the contralateral kidneys can be defined as increases in the mesangial matrix (Fig. 1) (detected through the use of the P.A.S. technique) and in the basal membranes (observed) with silver methenamine method (Fig.3).

These alterations were more acute in animals after 60 days of the unilateral hydronephrosis. Likewise, a positive immunoperoxidase reaction for the detection of IgG 60 and 70 days from the beginning was found (Fig.4).

The elements mainly affected in the contralateral kidney glomeruli of group I were the podocytes and filtration barrier structure.

The podocytes showed considerable development of cytoplasmic organoids, and vacuoles with electron-dense content were found to be regularly distributed in the cytoplasm.

With regard to the filtration barrier, the endothelial

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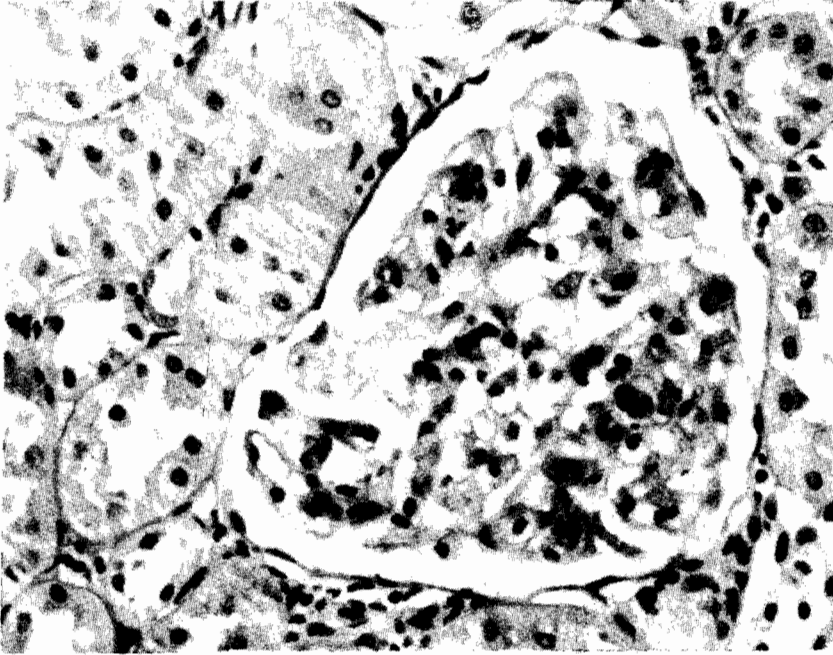


Fig. 1. Group 1: 40 days. Moderate proliferation of mesangial cells. P.A.S. $\times 720$



Fig. 2. Group 4: 70 days. Diffuse endotheliomesangial glomerulonephritis. P.A.S. $\times 520$



Fig. 3. Group 1: 40 days. Positive (+) immunoperoxidase reaction for the detection Ig G. $\times 560$

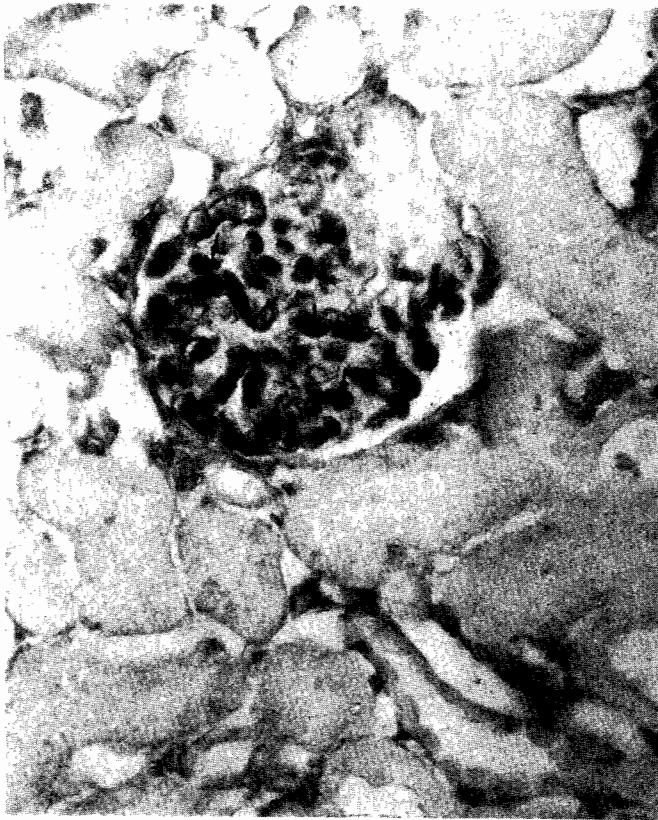


Fig. 4. Group 4: 70 days. Positive (†††) immunoperoxidase reaction for the detection Ig G. $\times 450$

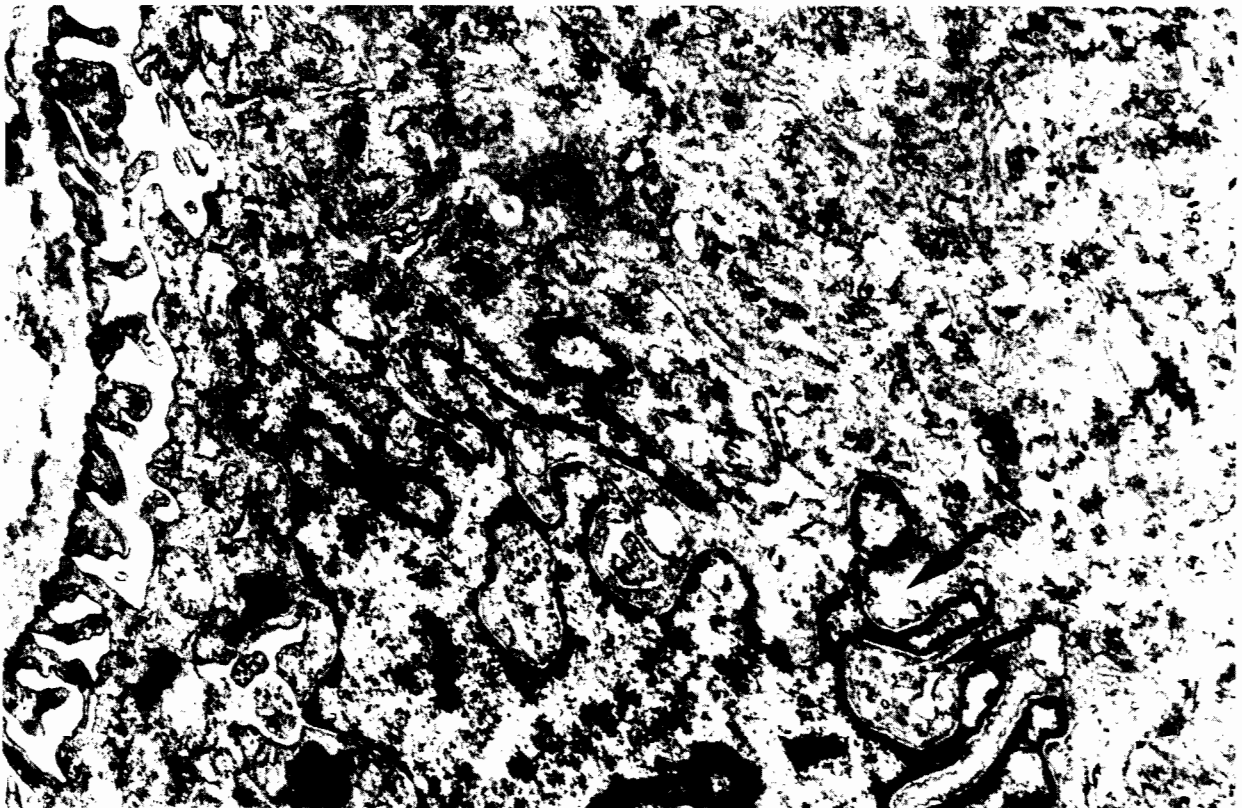


Fig. 5. Detail of the podocytes where increased development organoids and numerous cytoplasmic inclusions in the nucleus can be observed. $\times 15,700$

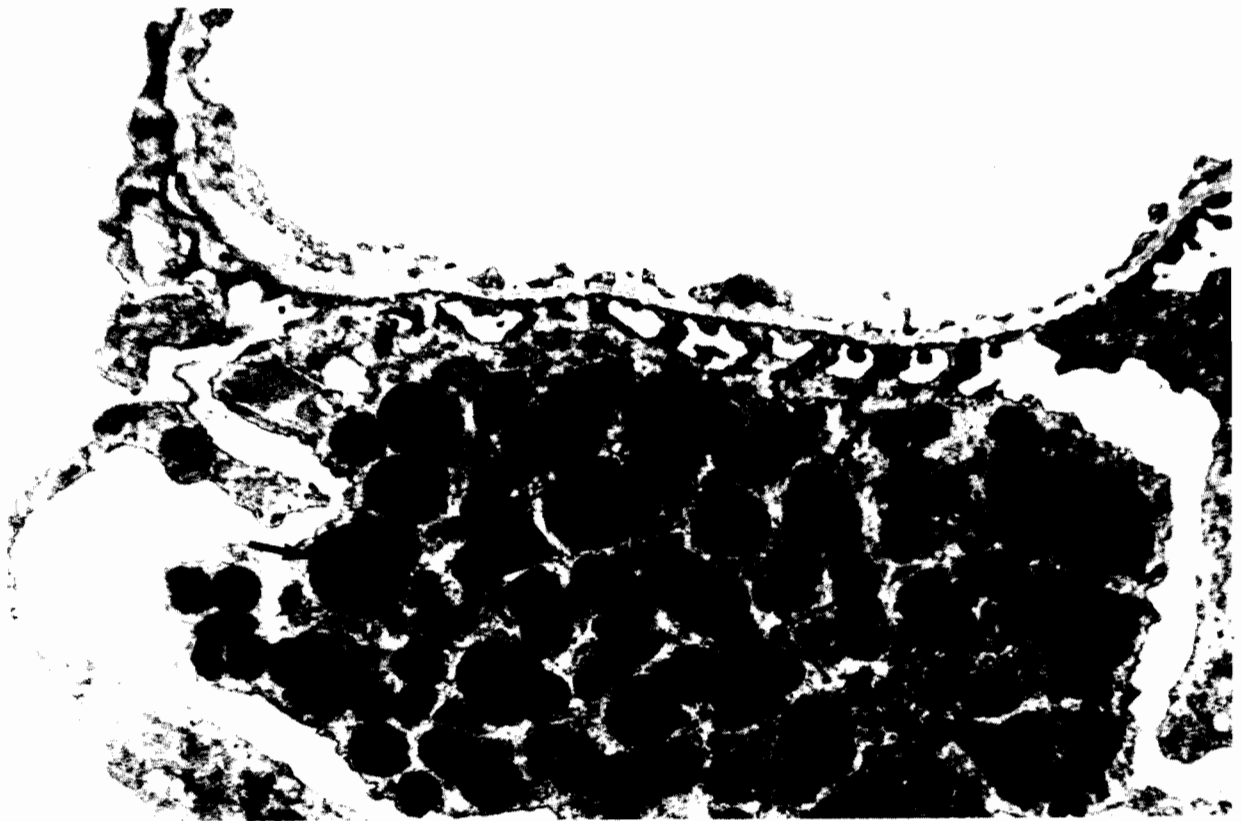


Fig. 6. The cytoplasm of a podocyte with numerous electron-dense polymorphic granules. $\times 12,700$



Fig. 7. Detail of the pedicels showing degeneration in the fingerprints. $\times 11,600$

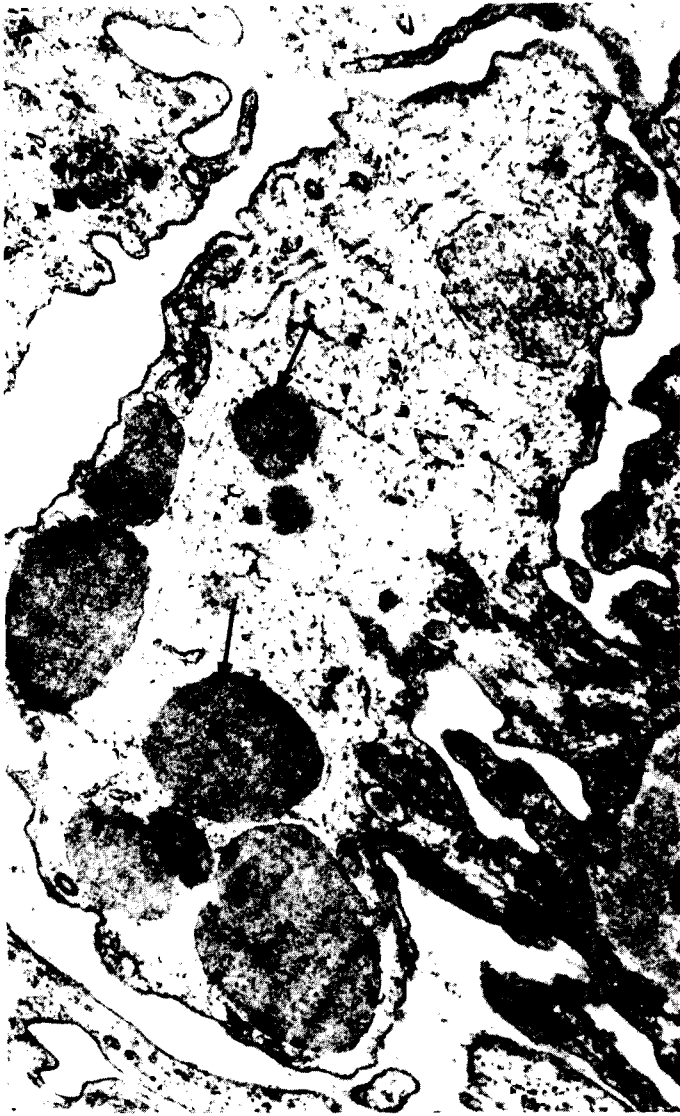
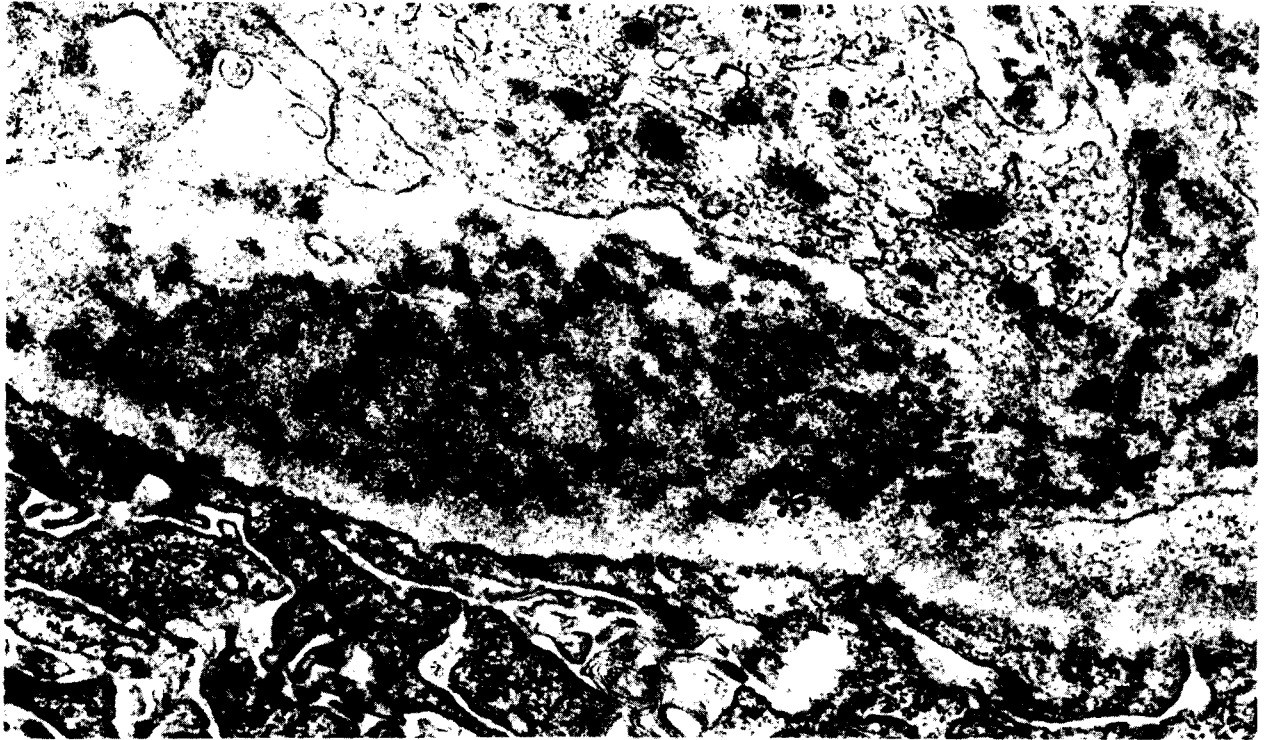


Fig. 8. Moderately electron-dense polymorphic granules with pseudogranular structure can be appreciated in the podocyte. $\times 12,700$

Fig. 9. Electron-dense pseudogranular deposits in the basal membrane of a glomerular capillary. $\times 21,500$



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Table 1. The distribution of the animals was as follows:

GROUPS	CONTROL	EXPERIMENT	SACRIFICE POSTLIGATURE
I	1	5	40 Days
II	1	5	50 Days
III	1	5	60 Days
IV	1	5	70 Days

Table 2. Morphometric study

Group	Glomeruli		Corpuscle	
	Area	Vol	Area	Vol
Control	4,5-0,15	361-32	5,5-0,19	561-44
1	6,3-0,26	1.002-180	10.5-0,36	1640-335
2	6,9-0,37	1.052-280	12.4-0,51	2712-518
3	8,8-0,29	1.359-248	15.4-0,43	3520-495
4	8,4-0,31	1.212-314	14.3-0,51	2993-341

cells showed shortened polymorphic microvilli and focal fusion of pedicels; similarly, the basal lamina was focally expanded.

Bowman's space was occupied by a moderately electron-dense granular substance; in contrast, the parietal epithelium of Bowman's capsule showed no modification worthy of mention.

The above mentioned alterations were also found in group 2, although there were certain differences; thus, the podocytes showed extensive cytoplasmic areas free from organelles next to other areas with a large number of them (Fig. 5).

The fusion of the pedicels in the second group was more evident, and the basal lamina of the glomerular loops contained a pseudo-fibrillar substance.

Significant changes in glomerular structures were also observed in group III. Thus, the podocytes in the primary pedicels showed a large number of vacuoles with electron-dense content, in addition to the alterations previously mentioned. Moreover fusion of the secondary and tertiary pedicels was evident. Similarly, a considerable development of their cytoplasmic organelles was observed (figs 6 and 7).

A large number of microvilli, which are directed towards the vascular light, were observed in the endothelial cells. The basal membrane showed a focal hump-like swelling, and next to it the fusion of the pedicels was observed (Fig. 8).

However, the most important modifications were found in the fourth group, where it was possible to highlight the presence of electron-dense pseudogranular deposits in the basal membrane of the filtration barrier, whilst electron-dense vacuoles were still evident in the cytoplasm of the podocytes, above all in the primary pedicels. The parietal epithelium of Bowman's capsule showed a clear swelling and lamination of the basal lamina (Fig. 9).

The same things observed in other groups were also observed, but in greater proportions. The morphometric

study of the glomerulars of the contralateral kidneys showed a gradual increase in the areas (table 2) and in the volumes of the glomeruli and corpuscles. After analysing the Bowman space it was observed that the increase was maximum in the third group, and that it had decreased in the fourth group.

Discussion

The sudden suspension in the urine flow that follows ligation of the ureter, gives rise to a hydronephrosis which, according to Zollinger and Mihatsch (1978), with whom we agree, implies a process of compensatory hypertrophy in the contralateral kidney.

The hydronephrosis thus provoked can be classified as a complete and total unilateral hydronephrosis, according to Anderson and Scotti (1980). One of the most important alterations is the thickening of the basal lamina, reported by Bermann and Maizels (1982), who consider it fundamental to the appearance of compensatory hypertrophic processes.

The compensatory reaction is a proven phenomenon which takes place in the contralateral kidney when a morbid unilateral process exists. Our studies show that this compensation can reach pathological limits, as we have demonstrated.

The compensatory hypertrophy principally affects the glomerular structures; we have observed that ultrastructurally they mainly affect the podocytes and those structures which form the filtration barrier.

These alterations coincide with those reported by Walker (1973), Jennings and Earle (1961) and Dustin and Dourov (1981) in similar processes.

At the same level as the luminal surface of the endothelial cells of the vascular loops, there are focally arranged microvilli; this can be explained in terms of a surface increase caused by endothelial hyperactivity, due, according to Castillo (1984), to a process of hyperfiltration which is in this case compensatory.

The most important phenomenon, however, is the thickening of the basal membrane which forms the filtration barrier. In some cases it is a focal process, in others it is diffuse. Focal swellings are sometimes distributed in the form of «humps», a fact which may be explained, as Walker (1973) reports, in terms of the deposit of fibrinoid, detected in our own studies by means of P.A.S. and metanamine silver techniques.

Cochrane and Koffler (1973) consider that this swelling may be caused either by metabolic disorders or by the presence of glomerular Ig G, C3, fibrin or fibrinogen which cannot be detected by means of electron density, as Zollinger and Mihatch (1978) have reported. With the immunoperoxidase technique, this thickening of the basal membrane, mainly when due to electron-dense deposits within, has proved positive to the presence of Ig G. For this reason, we agree with Wilson and Dixon (1979) that these may be deposits of glomerular Ig G.

The presence of electron-dense pseudogranular deposits which form groups and «humps» in the basal

membrane is due, according to Zollinger and Mihatch (1978), to immunocomplexes.

Wilson and Dixon (1979) also report that these are intermembrane deposits related to morbid processes in which there is a release of antigenic proteins. This would explain the presence of deposits in the case under study, where there is a destruction of structures in the hydronephrotic kidney.

The clusters of polymorphic vacuoles with homogeneous electron-dense content or really large bodies may be due either to a hyperformation of the basal membrane, as suggested by Fillit (1978), or to residues of immunocomplexes, as Zollinger and Mihatch (1978) have proposed. We favour the latter explanation.

Similarly, the podocytes show a considerable increase in organelles, which we believe is a compensatory process of hyperactivity, as reported by Cabanne and Bonenfant (1982). However, the most important phenomenon, among the alterations of podocyte structures, is the fusion of the pedicels which form the filtration barrier. This finding could explain the absence of proteinuria, which Fillit et al. (1978) consider to be a characteristic sign of this type of fusion.

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