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Renal Biopsy in Children's Schoenlein Henoch Syndrome

By

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Immuno-fluorescencent and electron microscopic examination of renal biopsy specimens obtained in two cases of Schoenlein—Henoch syndrome revealed a picture suggestive of acute glomerulonephritis and of membranous glomerulonephritis, respectively. The findings are compared with the clinical signs and the laboratory results.

In one third of the patients with Schoenlein—Henoch syndrome nephritis or, less frequently, a condition reminding of nephrosis develops [8]. Histological examination performed in cases accompanied by renal failure, which is rarely fatal, reveals the presence of extracapillary proliferative glomerulonephritis which used to be regarded as a characteristic feature of the disease. Vernier et al. [13] were the first to suggest that histological changes of another type, viz. a segmental adhesion to Bowman's capsule of the pathologic glomerular loop may also accompany the disease; in its gravity, four degrees were distinguished, viz. (a) absence of light-microscopic changes; (b) segmental-focal process; (c) segmental-diffuse process; (d) diffuse extracapillary (proliferative) process. The last-named form is usually observed in necropsy material, but may sometimes be detected also at the onset of the disease; in this case it carries a grave prognosis [9]. The clinical picture is dominated in types (a) and (b) by nephritis with haematuria, in type (c) rather by nephrosis [3].

Kobayashi [5] by means of immuno fluorescence demonstrated glomerular deposits of gamma globulin in three of seven children suffering from Schoenlein–Henoch syndrome. This argues in favour of an immunopathologic character of the renal lesion and raises the question of whether immuno-suppressive treatment, successfully applied in other immune-pathologic forms of nephritis and nephrosis, might be indicated when the syndrome is accompanied by a grave histological picture and serious clinical manifestations [1, 11].

Data concerning electron-microscopic changes in this syndrome are scarce [12]. In our material the two

displayed cases here represent the nephritic and nephrotic forms of the disease and in these pathological states a diagnostically significant parallelism could be observed between the clinical picture, the laboratory results and the renal changes.

Methods

Material was obtained by renal biopsy carried out by a modified version of Lurz's technique.

The surgically removed specimen was immediately fixed in 70% ethanol of 4°C. Sections for light-microscopic examination were embedded in paraffin, then stained with haematoxylin-eosin, PAS, silver methenamine and according to Hart. Specimens for immuno-fluorescence examination were prepared by the method of Sainte-Maria [10]. They were incubated with fluorescein isothiocyanate-bound (FITC) anti-human IgG, anti-human IgM, anti-human fibrin and anti-human $beta_1C$. The so-called blocking test served for control: before incubating the kidney pieces with FITC-bound anti-human sera they had been incubated with unbound anti-human sera. No fluorescence was seen in such cases. An OPTON type microscope and, for fluorescence examinations, a 200 W HBO type bulb were used.

For electron-microscopic examination the preparations were fixed in 2% osmium tetroxide solution, embedded in araldite and stained with uranyl acetate-lead oxide [4]. The sections made by means of an LKB Ultrotome were examined under a type SEM-3—1 electron microscope.

Report of Cases

Case No. 1. L. K., male, 6 years old, was admitted to a county hospital in September, 1968, with the diagnosis of Schoenlein—Henoch syndrome. Purpura, petechiae and melaena were increasing, grave oedema and gross haematuria developed and 8.0 g of protein/per day were excreted. The child was referred to our Department. At admission total serum protein was 3.9 g%, albumin 30.2%, $alpha_1$ globulin 9.2%, $alpha_2$ globulin 27.5%, beta globulin 20.2%, gamma globulin 11.9%; serum complement 50 $C'H_{50}$ (normal). Ascites formed, and the patient developed a right-side hydrothorax and then pneumonia. The condition remained grave for several weeks, but after a treatment with antibiotics, digitalis, spironolactone and furosemide the pneumonia and the oedema disappeared, proteinuria decreased to about 3.0 g/24 hrs and the condition was satisfactory three months after admission.

Histological examination of the biopsy specimen showed that the majority of glomeruli were enlarged and rich in cells. Proliferation of the endothelial cells was observed in some segments of the glomerular loops and, at some places, over the entire glomerulus; accumulation of PAS-positive matter also occurred (Fig. 1). There appeared a crescent-shaped figure in one of the glomeruli. Staining with silver methenamine revealed focal accumulation of argentophile fibres in the glomeruli (Fig. 2).

Immuno-fluorescence examination revealed focal deposits of IgG on the basement membrane of the glomerular loops (Fig. 3). IgM or fibrin were not observed.

Electronmicroscopic investigation in the glomeruli disclosed thickening of the basement membrane. Its processes extended at many points deeply into the cytoplasm of the epithelial cells. Numerous subepithelial deposits were seen. The lamina densa was stratified. The foot processes of the podocytes had fused. The great number of cytoplasmic organelles and the segmentation of nuclei pointed to intense epithelial and endothelial cell activity (Fig. 4).

Diagnosis: segmental diffuse glomerulonephritis of third degree according to Vernier.

Immuno-suppressive treatment was prescribed with 3 mg/kg of cyclophosphamide

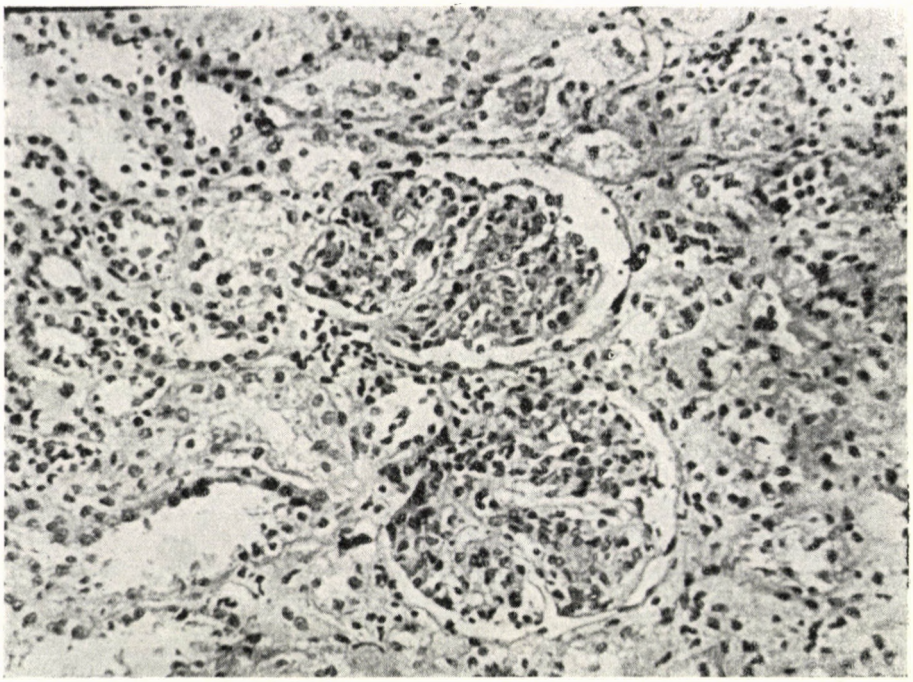

FIG. 1. Enlarged glomeruli. Endothelial proliferation in certain glomerular segments. The tubular epithelium is finely granular, the lumen contains a granular substance. Lymphocytic infiltration in interstitial spaces. Haematoxylin-eosin

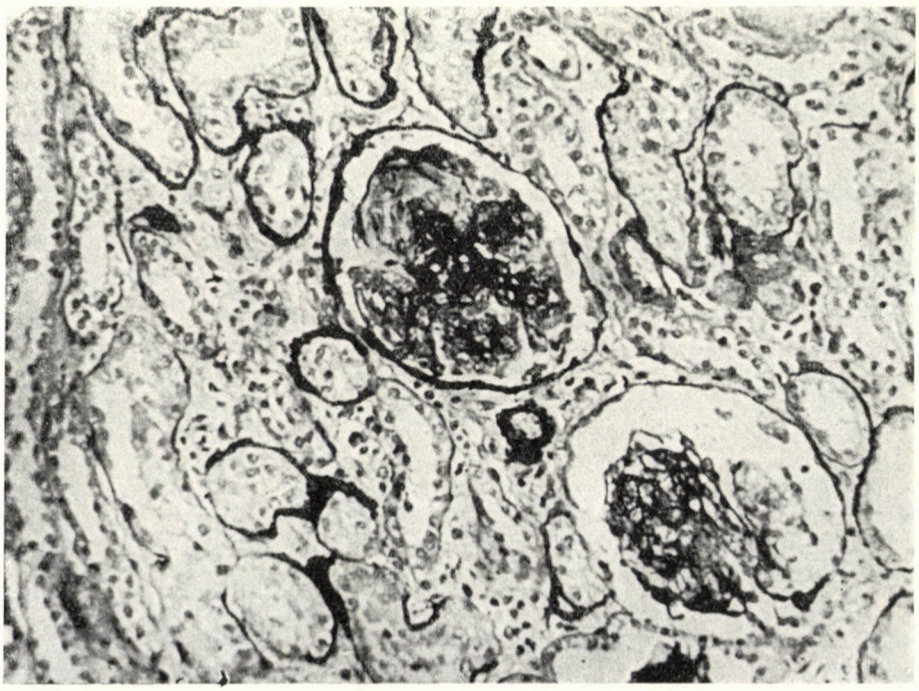

FIG. 2. Focal accumulation of argyrophile fibres in the glomeruli. Occasional thickening of tubular basement membrane. Silver methenamine

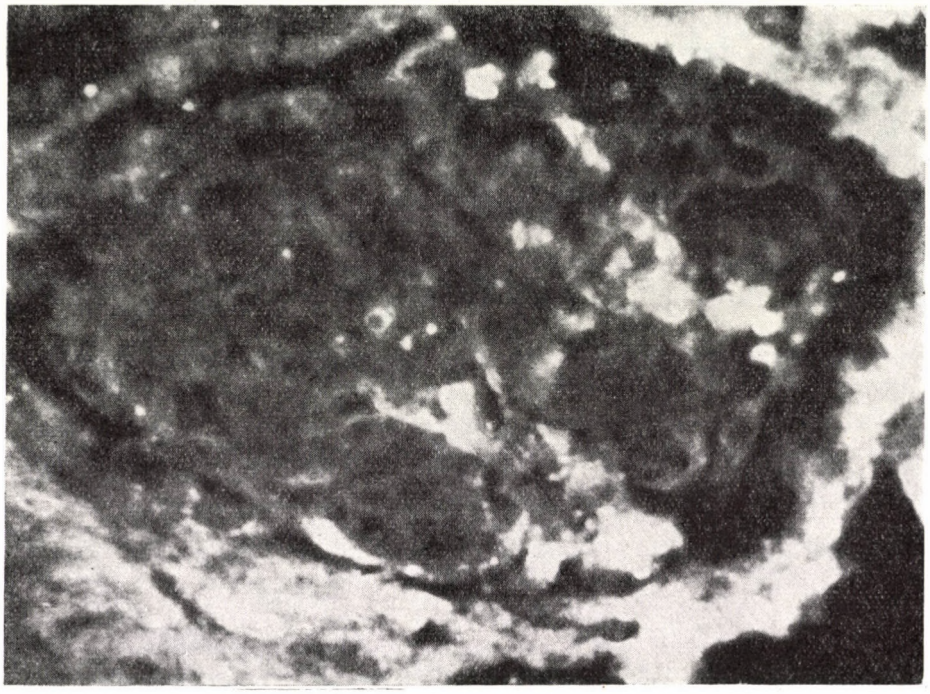

FIG. 3. Focal accumulation of gamma globulin in the glomeruli (after incubation with anti-human IgG bound to fluorescein isothiocyanate)

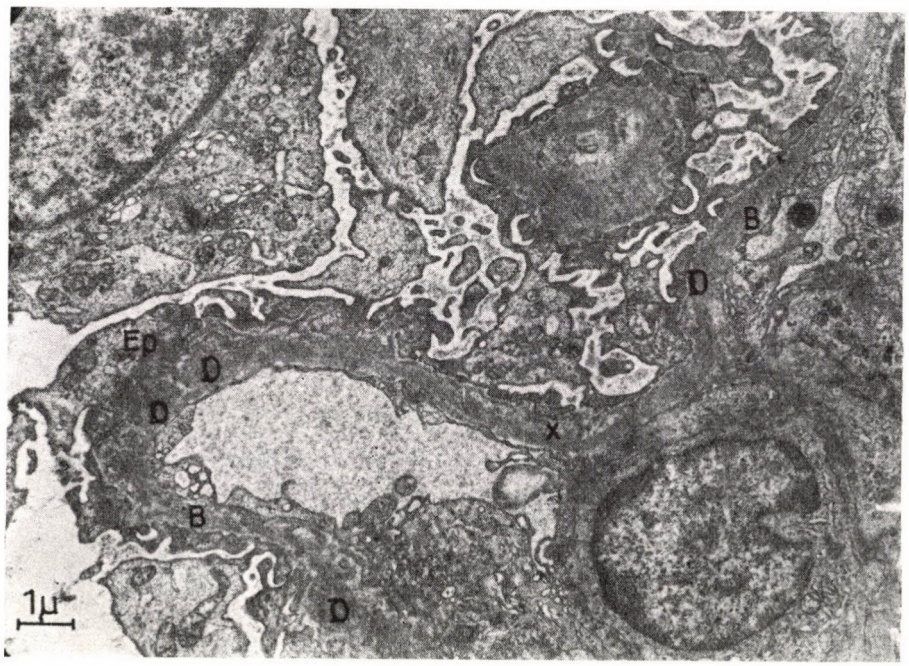

FIG. 4. Thickening of basement membrane (B) and stratification of lamina densa (x). Massive subepithelial deposits (D). Fusion of foot processes of epithelial cells (Ep). ×6000

and 10 mg of prednisolone daily. Although continued for 10 weeks, this therapy was not convincing. Proteinuria decreased transitorily to about 1.0 g/24 hrs, and was accompanied by microscopic haematuria. The serum protein level then was 5.6 g per 100 ml, creatinine clearance amounted to 117 ml/min/1.73 cm² body surface. Now, after six months the urine still contains variable amounts of protein.

Case No. 2. I. V., female, 5 year of age, was admitted in March 1969 with the diagnosis of Schoenlein—Henoch syndrome. On the seventh day after admission, proteinuria of about 2.0 g/24 hrs began, with the appearing of 20 to 30 red and 8 to 10 white cells per HPF. The serum protein level then was 6 3 g per 100 ml; with albumin 46 7%, alpha$_1$ globulin 3.7%, alpha$_2$ globulin 17.1%, beta globulin 14.1%, gamma globulin 18.4%. Serum complement was normal (68 U).

After a month of unchanged urinary values, renal biopsy was performed. The specimen displayed a number of richly cellular and enlarged glomeruli. Abundant cellularity was limited to particular segments of the glomerular loops; these segments displayed a proliferation of endothelial and mesangial cells (Fig. 5). Silver methenamine staining revealed focal accumulation of argyrophile fibres in the glomeruli (Fig. 6) Immunofluorescencent examination showed IgG deposits on the basement membrane which extended over the entire glomerulus in some places and only to part of it in others (Fig 7) Again certain glomeruli contained no IgG whereas at some points IgG appeared also on the basement membrane of

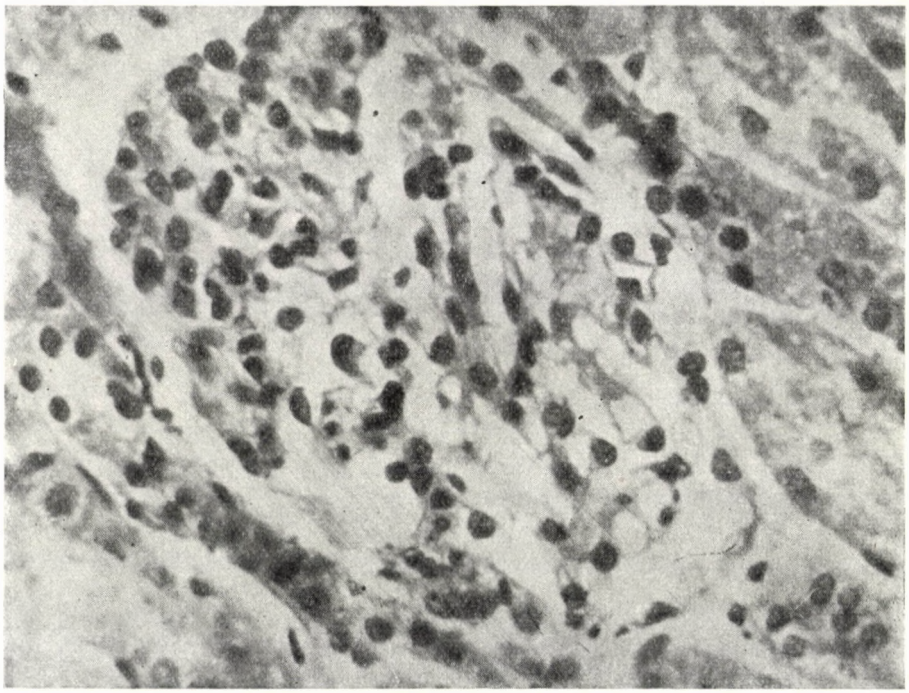

FIG. 5. Endothelial proliferation in a glomerular segment. Accumulation of PAS-positive matter in glomerulus. PAS

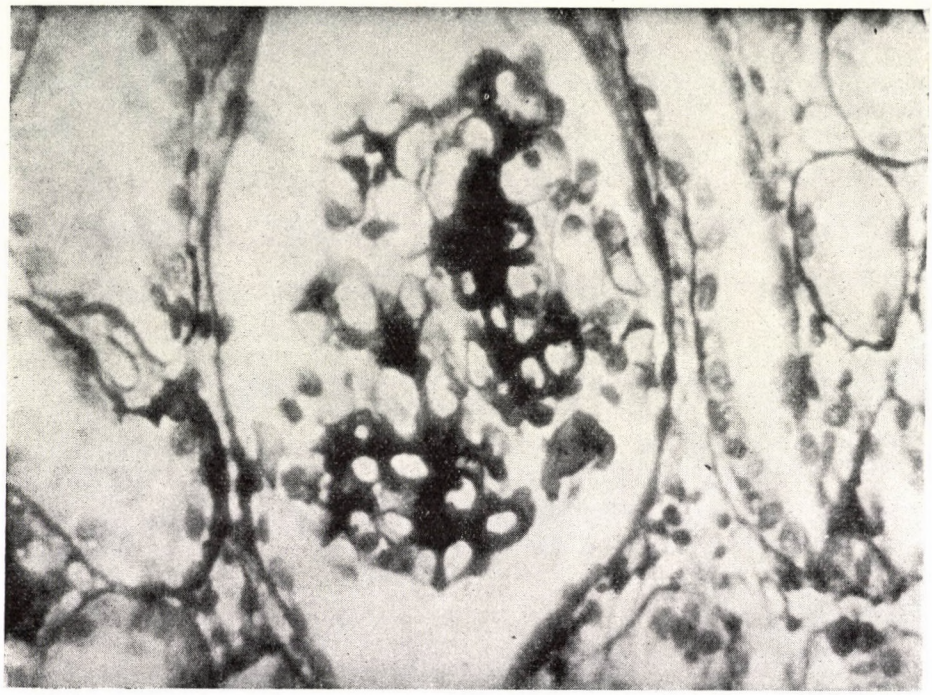

FIG. 6. Focal accumulation of argyrophile fibres in a glomerulus. Silver-methenamine

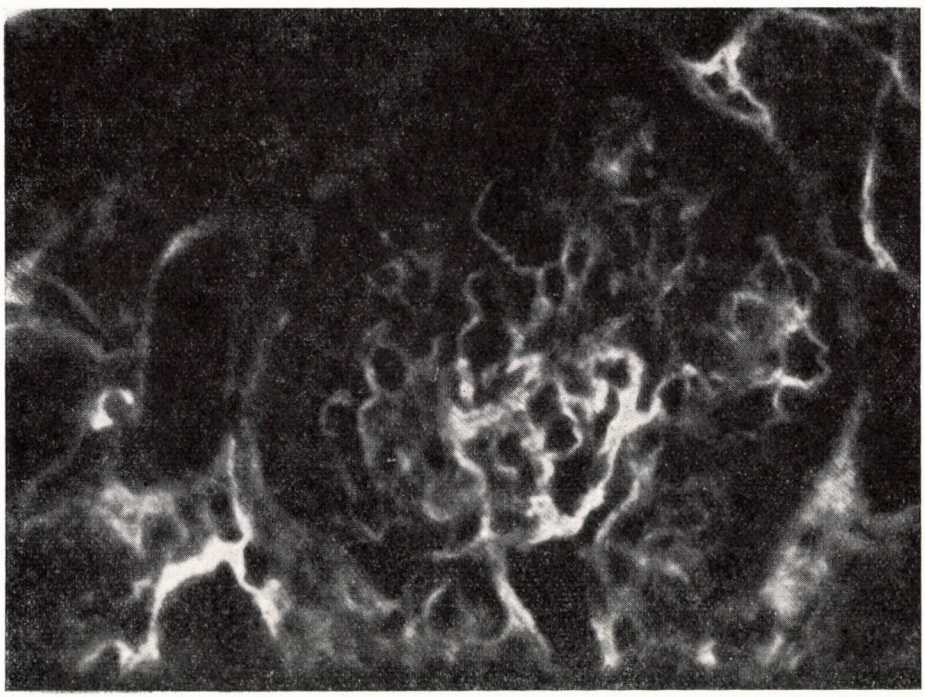

FIG. 7. Gamma globulin on the basement membrane of a glomerulus and of the tubules. (Incubation with anti-human IgG bound to fluorescein isothiocyanate)

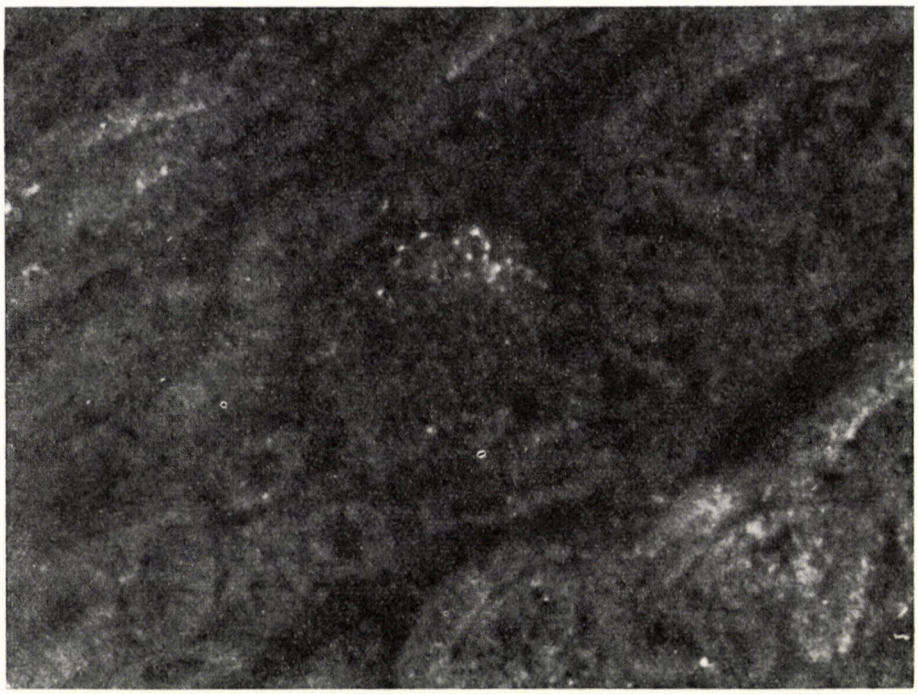

FIG. 8. Granular gamma-M globulin in glomerulus (after incubation with anti-human gamma-M globulin bound to fluorescein isothiocyanate)

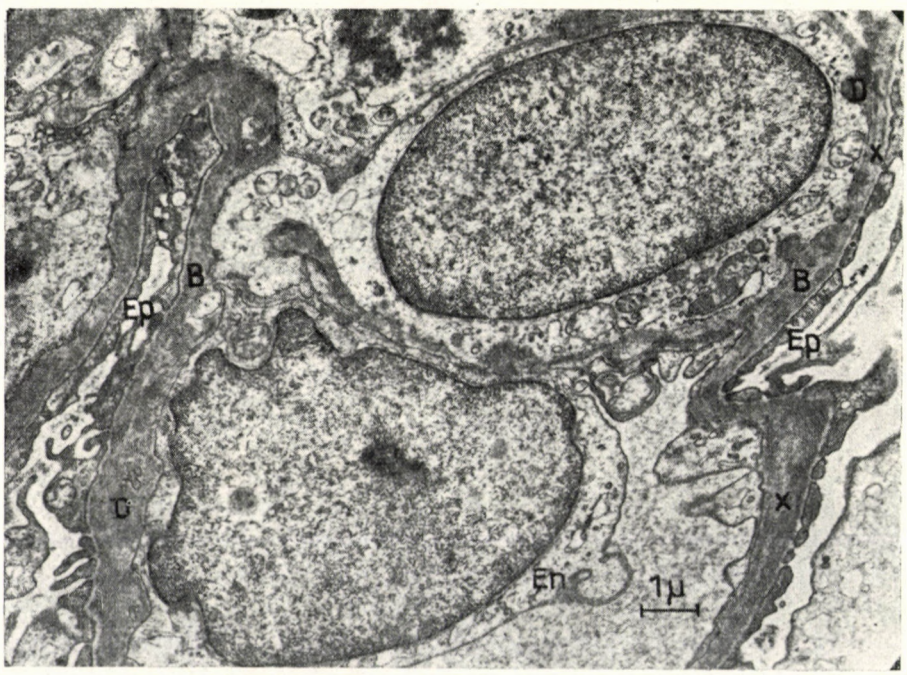

FIG. 9. Thickened basement membrane (B); stratification of lamina densa into 2—3 layers (x). Extensive fusion of foot processes of epithelial cells. Deposits (D) at certain points beneath the swollen endothelial cells (En). ×7500

the tubules. IgM granules (Fig. 8) and small foci of fibrin were observed on the basement membrane of some glomeruli.

Electronmicroscopic investigation showed variously thickened basement membranes and a stratification of the lamina densa into 2 or 3 layers. Endothelial cells were distended, the capillaries partly obliterated. Subendothelial deposits of electron-dense material were observed. The foot processes of podocytes were extensively fused (Fig. 9).

Diagnosis: segmental focal glomerulonephritis of second degree according to VERNIER.

Proteinuria and haematuria subsided spontaneously after two months of hospitalization. The Addis count was normal; endogenous creatinine clearance amounted to 88 ml/min/1.73 cm^2 body surface.

DISCUSSION

The nephropathies developing in connection with Schoenlein–Henoch's syndrome have to be regarded as immune-pathologic diseases, although immune-fluorescence tests are positive mostly in fresh cases only when steroid treatment has not yet been started. Gamma globulin deposits were found on the basement membrane of glomeruli in our material as well.

The type of gamma globulin deposited in renal diseases is an intriguing question. KOBAYASHI [5] found in the kidneys mostly IgM in acute glomerulonephritis and IgG in lipoid nephrosis. It was only IgG which appeared in the glomeruli in our case No. 1 with nephrosis, whereas deposits of IgM were also seen in case No. 2 where the nephritic signs were dominant. Nephrosis in case No. 1 presented a graver clinical and histological picture, and also its short-term prognosis was more unfavourable. Immuno-suppressive therapy had no effect in this patient, although such treatment had yielded good results in other cases of steroid-resistant nephrosis (membranous glomerulonephritis) in children [7].

Fibrin deposits were found in case No. 2, a fact which seems to support the assumption [2] that a reduction of fibrinolytic activity might play a decisive role in Schoenlein—Henoch's syndrome.

Serum complement activity was normal in these cases; this is a remarkable finding because activity is usually reduced in acute glomerulonephritis and sometimes in the nephrosis syndrome [6]. This phenomenon may be useful in the differential diagnosis too.

The behaviour of serum-protein fractions was characteristic on nephrosis and nephritis. Hypalbuminaemia and the increase of alpha and beta globulins were accompanied by hypogammaglobulinaemia in case No. 1, while in case No. 2. a slight hypergammaglobulinaemia occurred.

The ultrastructural pattern seemed to be in harmony with the clinical and light-microscopic findings. The changes in case No. 1, i. e. thickening of the basement membrane in the direction of the epithelial cells and the subepithelial deposits are rather typical on lipoid nephrosis, whereas endothelial changes and subendothelial deposits, as observed in case No. 2, are characteristic mainly of nephritis [12]. Although the gravity

of the disease was clearly shown by the light microscopic findings in both cases, it was only by means of the electron microscope that we were able to get an exact picture about the endothelial and epithelial changes occurring in the glomeruli, and to localize the deposits.

From the foregoing it is clear that in the case of persisting renal complications the clinical and laboratory findings have to be supplemented by renal biopsy in order to obtain reliable information about the character and the prognosis of Schoenlein–Henoch's kidney alterations.

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