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Case Report

Unusual Glomerular Change in Cytomegalic Inclusion Disease

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Summary. This paper reviews a case of a newborn child which died soon after birth in consequence of a cytomegalic inclusion disease involving the brain, liver, lungs and kidneys. The interest of the case lies in the unusual finding of lesions of the vascular loops of the renal glomeruli.

These lesions were represented by focal areas of homogeneous appearance which were strongly basophilic and PAS-positive. Although the nature of these areas has not been completely established, the renal lesions can be tentatively defined as focal, probably necrotizing glomerulonephritis. The association of this type of glomerular lesions with cytomegalic inclusion disease has not been previously reported.

Key words: Virus Diseases — Cytomegalic Inclusion Disease — Kidney — Kidney Diseases — Glomerulonephritis.

Introduction

In patients with generalized cytomegalic inclusion disease, renal involvement usually includes the presence of characteristic inclusion-bearing cells in renal tubules with concomitant interstitial lymphocytic infiltrates. Rarely, cytomegalic inclusion cells may also be found in glomeruli (Wagner, 1930; Raso, 1942; Fetterman *et al.*, 1968; Le Tan Vinh *et al.*, 1969; Pyanov, 1969). Other kinds of renal alterations, in the course of cytomegalic inclusion disease, were reported. They include focal or total necrosis of glomerular loops, extracapillary glomerulonephritis, formation of small glomerular cysts (Pyanov, 1969), thickening of basement membranes with consequent nephrotic syndrome (De Luca *et al.*, 1964). But such alterations are extremely rare. For this reason we are reporting the autopsy findings of a focal apparently necrotizing glomerulonephritis in a newborn infant which died from the effects of cytomegalic inclusion disease soon after birth.

The histochemical features of this case of glomerulonephritis are so outstanding that a study of the literature was carried out to ascertain whether similar cases have been reported previously.

Case Report

Clinical Data. Male infant born during the 39th week of pregnancy to a 28-year-old woman with a history of diabetes. Weight and length were respectively 2.0 Kg. and 41 cm. The infant showed cutaneous hemorrhages and bullous desquamative dermatitis of the hands and feet. Dyspnoea occurred rapidly, accompanied by a progressive increase in cardiac frequency. Furthermore, hematemesis took place repeatedly and the baby died 30 hours after birth. We have no detailed information about treatment.

Autopsy. At autopsy the most prominent lesions were a periventricular necrotizing encephalitis with coexisting hydrocephalic dilatation of the ventricular cavities and a bilateral bronchopneumonia which was most pronounced in the left lung. The spleen was moderately enlarged and congested. The liver showed a slight condition of fatty degeneration. The gastric mucosa was the site of hemorrhagic purpura, from which a coagulated mass of blood had originated. The kidneys showed intense congestion.

Microscope Findings. Tissue samples from various organs were fixed in a 10% formalin solution and embedded in paraffin. The following stains were employed: hematoxylin-eosin, Van Gieson, Mallory trichromatic reaction, phosphotungstic acid-hematoxylin (PTAH), Gomori, PAS, Feulgen, colloidal iron, Von Kossa, Congo red, cresyl violet and alcian blue at pH 4, 2.8 and 1.5.

Inclusion bearing cells were found in the brain, lungs, liver, bile ducts and kidneys. In the kidneys, many glomeruli showed small amounts of an intensely basophilic, amorphous or finely granular material with roundish or polycyclic contours. The normal structure of the glomerular loops in correspondence of this material was lost. The extension of these foci in a single glomerulus was variable, sometimes being limited to one or more cotyledons and sometimes extending to the entire glomerulus (Figs. 1, 2). The affected glomeruli were fairly numerous and with uniform distribution. These lesions were often accompanied, in the same glomerulus, by inclusion-bearing cells, but the latter were never detectable inside the basophilic necrotic areas, but always nearby undamaged or not completely damaged cotyledons (Figs. 1, 3, 4). Pathological findings in the kidneys also included thickening and apparent necrosis of the wall of some small arteries with histochemical features similar to those seen in the glomerular areas (Figs. 5, 6). Furthermore, as shown in figures 4, 5 and 6 even outside the striking basophilic foci, the glomerular loops could show areas of degeneration or necrosis, demonstrated by the progressive disappearance of capillaries and nuclear structures and substitution with an amorphous material.

The results obtained from the previously reported staining techniques can be summarized as follows. The focal areas were strongly PAS-positive and stainable with colloidal iron at pH 1.8 (Mowry, 1958). Moreover they were stainable with the Mallory and Van Gieson reactions. They were not stained when the Feulgen, Von Kossa, Weigert, Gomori and Congo red techniques were employed The alcian blue reaction was clearly positive at pH 4, slightly positive at pH 2.8 an almost negative at pH 1.5. Toluidine blue metachromatic reaction was negative.

Fig. 1. Glomerular focal necrosis with accumulation of intensely basophilic material. The arrows indicate two inclusion-bearing cells in the glomerular area uninvolved by necrosis. H and E, × 200

Fig. 2. Necrosis involving almost completely a glomerulus. H and E, × 200

Fig. 3. Two inclusion-bearing giant cells in close proximity of a necrotic area. H and E, × 320

Fig. 4. Two inclusion-bearing giant cells (arrows) in a glomerular loop showing initial degenerative changes. H and E, × 800

Fig. 5. Basophilic necrosis of a small artery running near a glomerulus showing two necrotic foci and other less severe degenerative changes. H and E, × 320

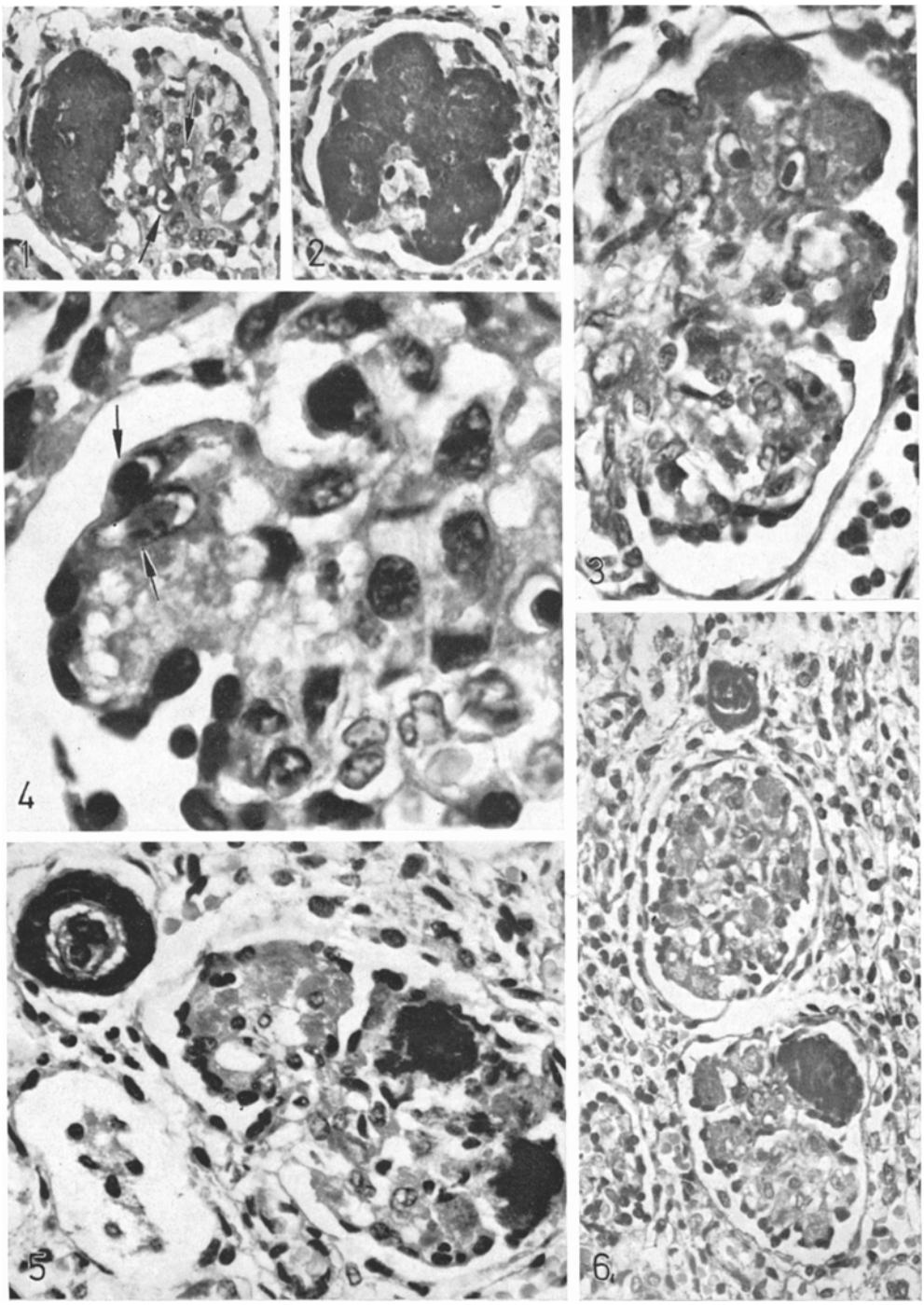

Fig. 6. Basophilic necrosis of an afferent arteriole with two glomeruli showing degenerative changes and a focus of basophilic necrosis in one of them. H and E, × 200

From all these chromatic properties the following information can be deduced about the composition of the material. The PAS-positivity indicates the presence of glycoproteins. The colloidal iron reaction would suggest the presence of acid mucopolysaccharides, but this is denied by the alcian blue negativity at pH 1,5 and by the absence of metachromasia. In the same way the material also seems to contain collagen; however this finding is debatable since there are no argyrophilic fibrils and birefringence is absent.

In conclusion, the only certain feature in the composition of the material is the presence of abundant glycoproteins.

Comments

The localization of inclusion-bearing cells in kidneys, liver, lungs and brain, together with the findings of a necrotizing encephalitis, strongly suggest a diagnosis of cytomegalic inclusion disease. Regarding the most prominent aspect of the case, namely the focal glomerular lesions, a study of the literature in search of similar or comparable cases was made.

Focal necrosis of glomerular loops has been noted previously together with other histological glomerulonephritic alterations by Pyanov (1969), as stated in the introduction. Pyanov's paper represents the only report of glomerulonephritic lesions in the course of cytomegalovirus disease that we have been able to find in the literature. However, since no abnormal histochemical data were reported, it must be assumed that Pyanov's cases represented focal necrotizing glomerulonephritis having ordinary histochemical aspects.

In a wide range of viral infections with renal involvement many glomerulonephritic lesions are reported (Jensen, 1967; Reimann, 1968). These include focal necrosis of glomerular loops, hypernucleosis, fibrin deposits and hyperplasia of endothelial cells, but these various lesions do not correspond to the particular findings observed in this case. A partial similarity exists between the lesions in our case and the so called "hematoxylin bodies", occurring as small lilac-staining bodies in hematoxylin-eosin preparations, and affecting renal glomeruli in the course of systemic lupus erythematosus and in some forms of focal glomerulonephritis. This similarity is more pronounced where our glomerular foci are less basophilic and less compact. Hematoxylin bodies are described as showing, at least in vivo, reduced Feulgen staining and to be PAS-positive and not metachromatic (Heptinstall, 1966).

The absence of previous observations in the literature and the strange histochemical features of the glomerular lesions in this case do not make a definite interpretation possible. After employing many stains, we obtained some data which suggested a partial composition of the glomerular material. This is different from any other previously reported necrotic material in glomerulonephritic lesions. But any attempt to clarify the functional meaning of this material must remain, at the present time, a purely speculative exercise.

In the expectation of further clinical and pathologic information, our case could be temporarily considered in a broad sense as a peculiar focal necrotizing glomerulonephritis concomitant with a generalized cytomegalic inclusion disease.

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