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OTS: 60-11,666

JPRS: 2697

4 June 1960

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JPRS: 2697

CSO: 3795-N

THE EFFECT OF LARGE DOSES OF RAT GAMMA GLOBULIN ON NEPHRECTOMIZED RATS

/This is a translation of an article written by N. N. Pyatnitskiy in Arkhiv Patologii (Archives of Pathology), Vol. 22, No. 1, Moscow, 1960, pages 60-62./

From the Chair of Pathological Anatomy (Head-Active Member Acad. Med. Sci. I. V. Davydovskiy) 2nd Moscow Medical Institute imeni N. I. Pirov (received by editors 3 Feb. 1958).

In the recent literature there are references to the claim that massive doses of heterologous gamma-globulin (bovine) are able to induce nephrectomized rabbits diffuse but transitory glomerulonephritis (Hown and Janeway, 1947; Moore and co-workers, 1949).

The aim of the present work is the determination of the influence of massive doses of homologous gamma-globulin on nephrectomized animals.

The experiments were conducted on 12 rats with unilateral nephrectomy. On the fifth day after surgery, rat 6.5% gamma-globulin in a dose of 0.5 ml per 100 gr. of weight was introduced intravenously to the animals every other day. Gamma-globulin was isolated from serum by means of the rivanol method of Korzheyshi; the purity of the gamma-globulin was checked by means of electrophoresis on paper; the addition of other protein fractions did not exceed 7% (Fig. 1). Each rat received from 2 to 9 injections of gamma-globulin.

On the 6-8th day after the last injection, albuminuria and hematuria originated in the rats; on 10-14th day, cylindruria. 11 rats perished on 9-30th day after the last injection; at the time of death the amount of residual blood nitrogen in them equaled 136-200 mg% (the 12th rad died of an accidental cause). Upon dissection, ascitis and hydrothorax were discovered in five rats; in all rats the kidneys appeared considerably enlarged with a grayish-yellow anemic cortex and brightly-pink medullar substance. Microscopically in the kidneys a picture was discovered which recalls proliferative intracapillary glomerulonephritis with sharp swelling of vascular loops, protein exudate into the cavity of Bowman' capsulae (Fig. 2 and 3); in 3 rats which survived until the 30th day, rich desquamation of perithelium of loops and considerable swelling of the cells of epithelium of the capsule on the side contralateral to the neck of the glomerulus were noted (Fig. 4). From the side of the epithelium of convoluted tubules, granular degeneration and hyalin-droplet degeneration of protoplasm was noted, in the lumen of straight and convoluted tubules, homogenous albumin masses and hyalin cylinders.

In the given series of experiments 12 rats also with unilateral nephrectomy served as control, at the same times and in the same doses, rat serum without gamma-globulin was introduced to them (Fig. 5). In

these animals, insignificant albuminuria (0.09-0.12%) appeared, which disappeared soon after the termination of injections.

40 days after the last injection of serum all rats were sacrificed. The residual nitrogen of the blood by this time equaled 36-42 mg%. In dissection the kidney appeared somewhat enlarged, the cortex and medulla substance were of the usual color. Under microscopic examination the glomeruli appeared somewhat enlarged, the lumen of capsules appeared free, in vascular loops with the usual density of nuclei placement, granular degeneration was observed from the side of the convoluted tubules (Fig. 6).

We also have investigated microscopically the kidneys of rats with unilateral nephrectomy (on 25-30th day after surgery), which were not subjected to any influences. No changes were discovered in these kidneys, except for insignificant increase in size of glomeruli.

On the basis of clinical and pathomorphological data concerning rats to which hemologic gamma-globulin was introduced intravenously, it is possible to assume in them proliferative intracapillary glomerulonephritis.

CONCLUSION

Proceeding from the concept of glomerulonephritis as an allergic organic reaction, it is also possible in the described experiment to find the realization of a peculiar allergic mechanism, namely: that with rat gamma-globulin, either ready antirenal antibodies have been introduced, or, under the conditions of unilateral nephrectomy, the introduced gamma-globulin assumes nephrotoxic properties.

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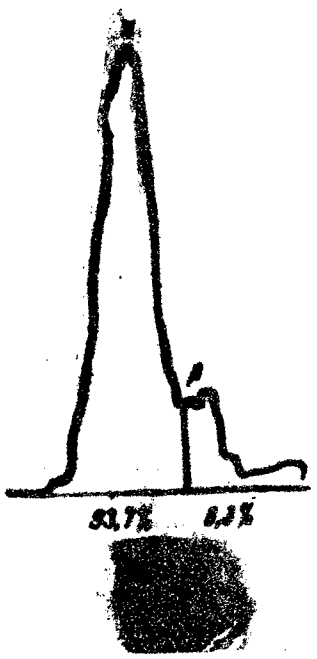

Fig. 1. The curve characterizes the content of admixtures in the introduced gamma-globulin of veronal-medinal buffer; pH= 8.6. At the bottom electrophoregram: wide dark band corresponds to the fraction of gamma-globulin.

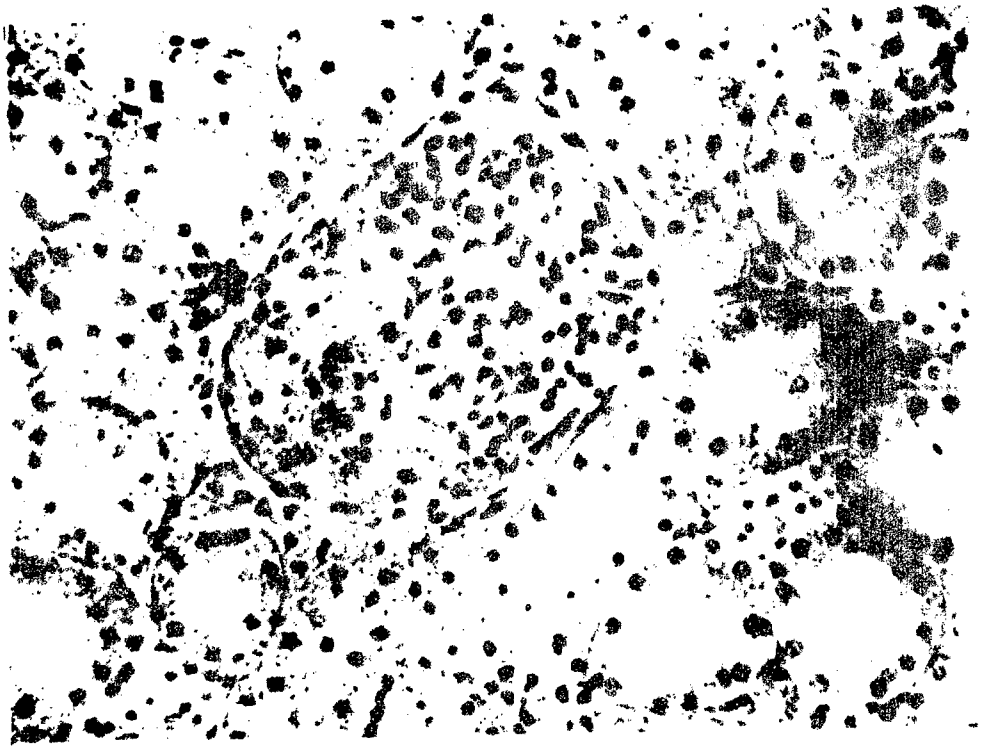

Fig. 2. Intracapillary productive glomerulonephritis; death on 16th day after the last introduction of gamma-globulin (staining with hematoxylin-eosin. X 200).

Fig. 3. Fibrinoid swelling and homogenization of the glomerulal loops. Death on 7th day after the last introduction of gamma-globulin (staining with hematoxylin-eosin. X 200).

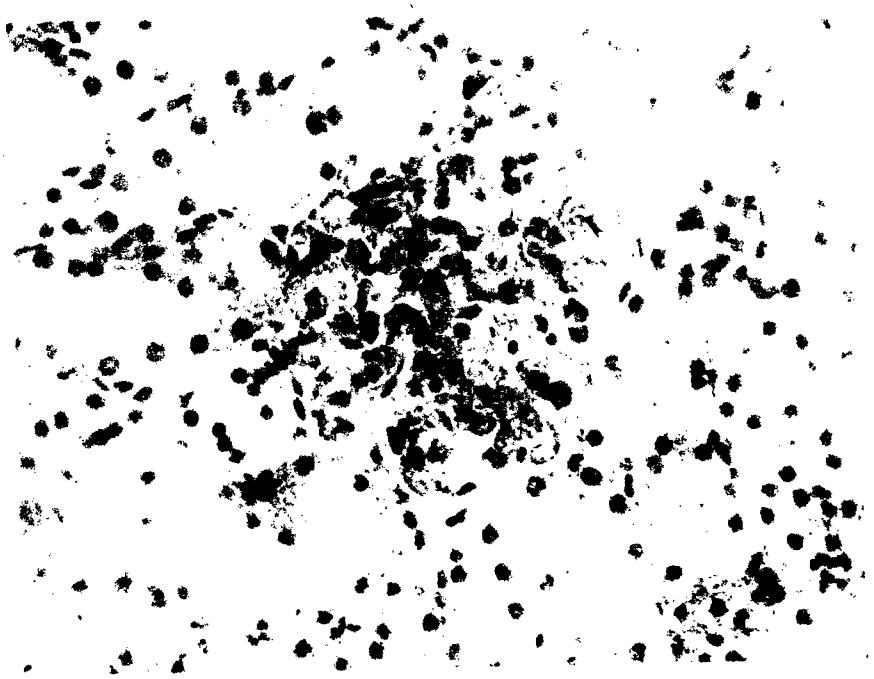

Fig. 4. The beginning of the formation of a crescent (left segment of glomerulus). Death on 28th day after last introduction (staining with hematoxylin-eosin. X 200).

Fig. 5. Solid line-serum deprived of gamma-globulin; the upper electrophoregram corresponds to it; dotted line-normal rat serum; the lower electrophoregram corresponds to it. The conditions of electrophoresis are the same.

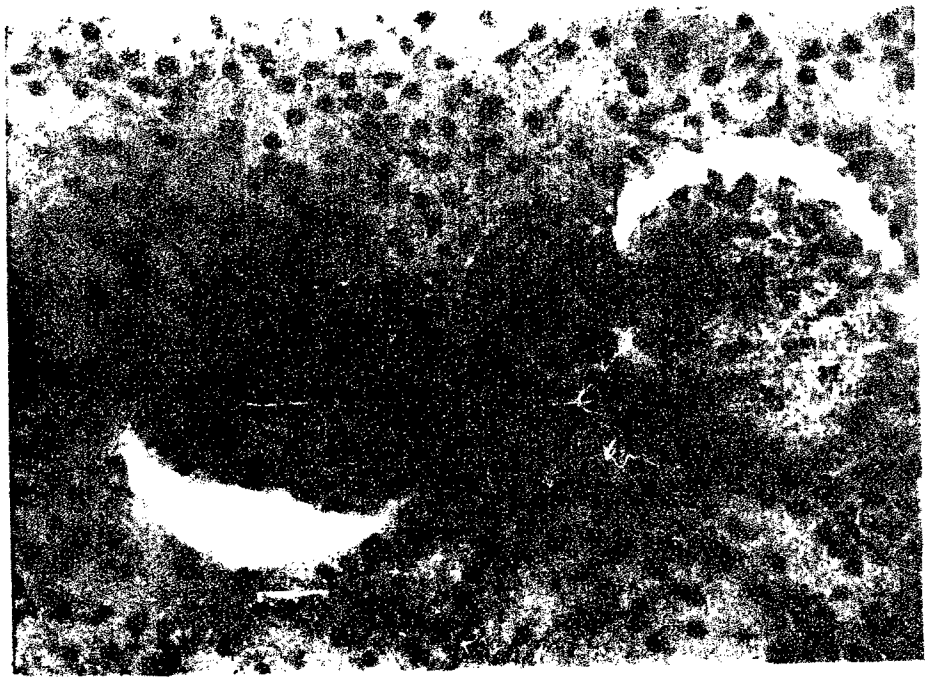

Fig. 6. The kidney of a rat from the control group - certain increase of glomeruli size, granular dystrophy of epithelium of convoluted tubules; 40 days after the last introduction (staining hematoxylin-eosin. X 200).

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