

Department of Histology and Embryology with Lab of Experimental Cytology
Skubiszewski Medical University of Lublin

AGNIESZKA PEDRYCZ, MARCIN WIECZORSKI, KRYSTYNA CZERNY

*Glomerulosclerosis 4 weeks after administration of adriamycin
in a single dose*

Glomerulosclerosis appears at any age, nevertheless, more often in children than in adults. Its signs could be limited to proteinuria, nephrotic syndrome, hematuria, and with progress of disease kidney insufficiency with uraemia could develop. It is supposed that basic lesion is abnormality of chemical building of basement membrane or configuration of its components.

The present study is performed on rats. Renal glomerules were investigated after intraperitoneal administration of adriamycin in a single dose (3).

MATERIAL AND METHODS

The experiment was performed on white female Wistar rats with initial body mass 200–250 g, aged from 2.5 to 3 months. The animals were accidentally chosen at the same time in experimental and control groups (10). In the study there were used 16 rats divided into two groups – experimental and control, 8 animals in each. At the beginning of the experiment the animals from experimental groups had administered adriamycin intraperitoneally in a dose 5 mg/kg of body weight, and animals from control group obtained 0.5 ml 0.9% NaCl intraperitoneally. The rats were decapitated 4 weeks after taking the drug dose. For histological investigation in light microscopy, left kidney was taken, which was fixed in 10% formalin, buffered to pH 7.4 (with phosphatic buffer. After dehydration of sections in increasing concentrations of ethanol (40%, 50%, 60%, 70%, 80%, 90%, “pure” ethanol), they were put in xylene and placed in paraffin. Then preparations were sectioned on slides 5 mm, which were then stained with hematoxyline and eosine, with the Masson’s method for visulisation of connective tissue, and with the McMannus’ method, for polysaccharides visulisation – PAS. Stained preparations were observed in light microscopy and documented with photographic camera Jenaval Contrast Carl Zeiss (6).

RESULTS

In control group microscopical picture of kidney, especially kidney's glomerules in all individuals did not vary from the description of manual norm.

Microscopic picture of rat kidney from experimental groups showed focal and segmental changes, which touched single glomerules (Figs. 2, 4, 6). Focal thickening and deformation of parietal lamina of glomerular capsule were observed especially in preparations stained with PAS methods (Fig. 4). In some glomerules there was present thin or completely destroyed parietal lamina. Urine space was significantly dilated. In the light of some glomerular capsules protein PAS-positive casts (deposits)

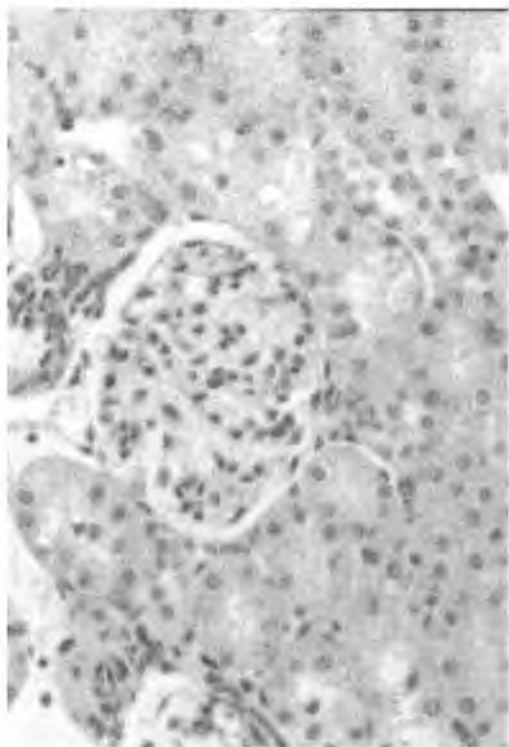


Fig. 1. Control group. The picture of part of rat female kidney in light microscopy. Stained with H&E. Magn. 320x

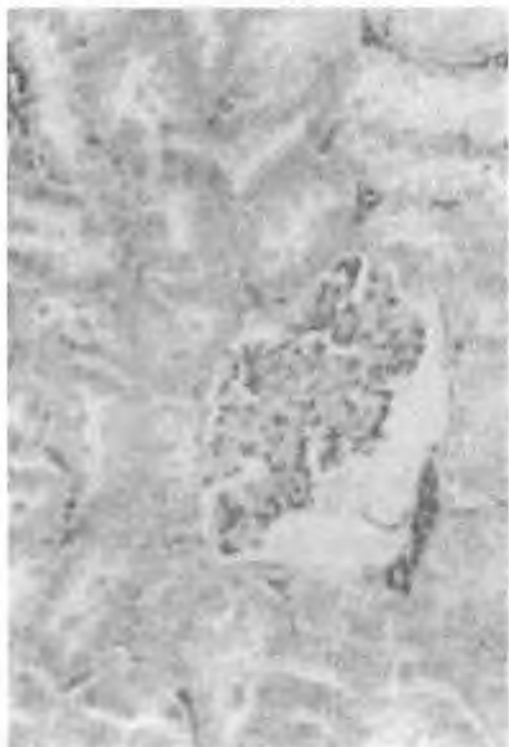


Fig. 2. Experimental group. The picture of part of rat female kidney in light microscopy. In glomerules – present urine space dilatation. Irregular shape of visceral lamina of glomerular capsule. Dilated and damaged loop vessels. Stained with H&E. Magn. 320x

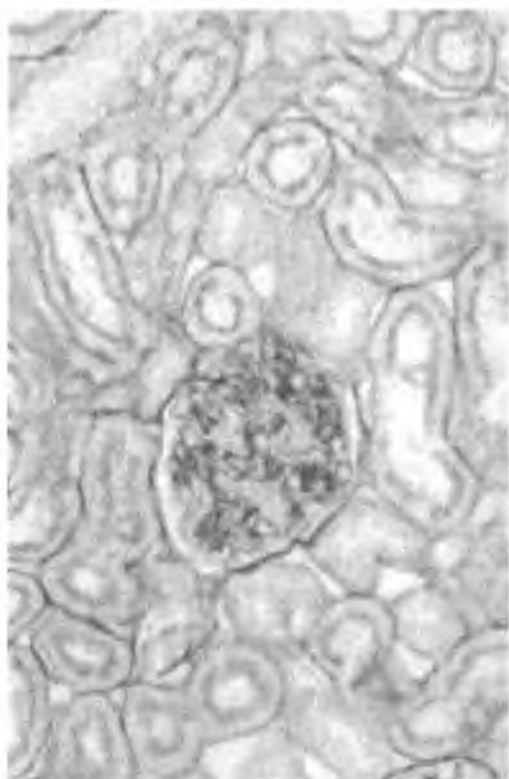


Fig. 3. Control group. The picture of part of kidney of rat female in light microscopy. Stained by PAS method. Magn. 320x



Fig. 4. Experimental group. The picture of part of rat female kidney in light microscopy. In glomerules – present urine space dilatation. Irregular shape of visceral lamina of glomerular capsule. Thickening of basal membrane. Irregular, damaged loops of capillary vessels. Proliferation of PAS(+) mezangial matrix. Stained by PAS method. Magn. 320x

were present, which sometimes had fulfilled all urine space. In glomerular vessels thickening of basement membrane, especially visible in preparations stained with the PAS method was observed. The amount of PAS-positive mesangial matrix was increased. Vessel loops were dilated and deformed, in some glomerules partially or completely destroyed. As regards the amount of fibres and cells of connective tissue present between vessel loops (mesangium) – glomerular sclerosis was observed, especially in preparations stained with the Masson's method (Fig. 6).

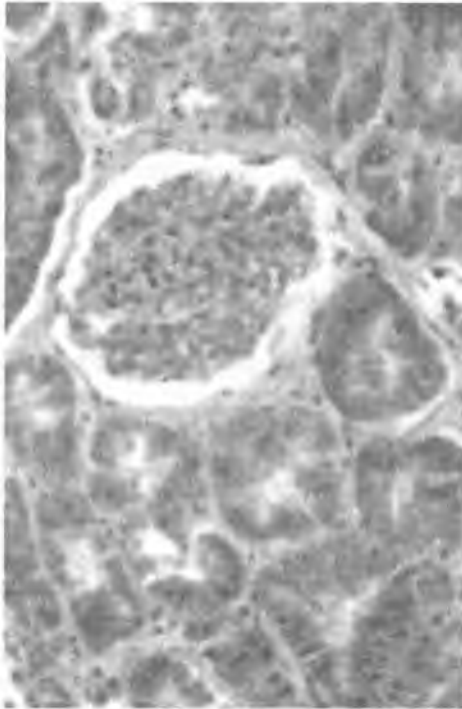


Fig. 5. Control group. The picture of part of rat female kidney in light microscopy. Stained by Masson's method. Magn. 320x

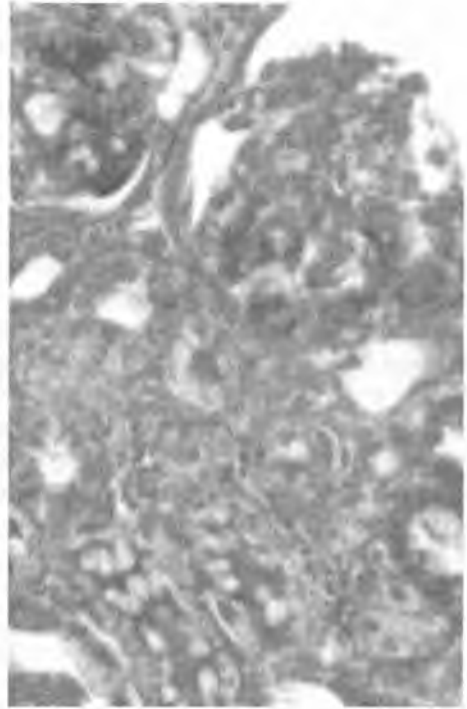


Fig. 6. Experimental group. The picture of part of rat female kidney in light microscopy. Glomerules with irregular shape of visceral lamina of glomerular capsule. Urine space dilatation present. Irregular capillary vessels loops. Increased ammount of connective tissue in glomerules. Focal thickening of basal membrane. Stained by Masson's method. Magn. 320x

DISCUSSION

Changes in glomerules observed in the present study in light microscopy were the following: an increased amount of fibres and cells of connective tissue – mesangium – glomerulosclerosis.

O'Donnell et al. (5) investigated as well kidneys five weeks from single dose of drug. He observed dilatation of glomerular capillaries and focal, segmental glomerulosclerosis. In the same period (4 weeks) Podjary (8) did not notice any changes. He has administered adriamycin to rats, in a dose 3.5 mg/kg of body weight, so a bit lower dose than in the present study. The same dose (5 mg/kg of body

weight) as in this study used Wang (14). He did not notice any changes in kidney in light microscopy, either.

Other observations performed Zimma (16), who 3 weeks after drug administration in a dose 5 mg/kg of body weight described minimal mesangium proliferation and infiltration around vessels. Similar changes to those described in the present study noticed Sternberg et al. (12) 4 weeks after drug administration in a dose 20 mg/kg of body weight. Hall (2) investigated kidneys 13 weeks after giving rats a single dose. He noticed urine space dilatation, and even focal atrophie of glomerules and focal and generalized glomerulosclerosis.

Most of the authors describing kidney after adriamycin paid attention to hyalinisation and sclerosis of glomerules (glomerulosclerosis) (1, 7, 11, 13, 15). Sclerosis depends on hyaline deposition (3), and then deposition of substances with features of acidophilic PAS-positive mesangium matrix with a few collagen fibres (4).

With progression of disease glomerules hyalinised completely. Proliferation of mesangium cells and matrix (3) has an influence on prognosis.

Authors observed different degree of glomerulosclerosis development in kidneys. From minimal proliferation of mesangium and infiltration around vessels within 3 weeks after drug administration in a dose 5 mg/kg of body weight (16), to generalized glomerulosclerosis within 3 and 6 weeks in the same single dose of the drug (11). Remuzzi described changes similar to changes in human in the course of nephropathy with minimal changes (3 weeks after drug administration a in dose 5 mg/kg of body weight) (9). It is difficult to find the relation between the degree of sclerotic changes and magnitude of a given dose. It was possible that different regions of kidneys were investigated. Glomerulosclerosis was started in paramedullary glomerules and then gradually glomerules placed close to the surface were involved. The section of kidney taken from subcapsular area could not disclose any changes. Then minimal changes occurred. In the time when the disease develops, the chance to find changed glomerules is increasing (3).

There exists the relation between the intensity of sclerotic changes, and time which passed from drug administration.

Yoshida (15) administered adriamycin to rats in a few dose (till total dose 16 mg/kg of body weight) and examined kidneys after 14 and 28 weeks. Sclerotisation index (SI scale 0–4) was 1.49 after 14 weeks and was above 2.0 after 28 weeks. The dose of drug was bigger than in present study.

Bertani et al. (1) had given adriamycin in a dose 5 mg/kg of body weight and carried out long observation. After 6 months of extensive proteinuria 40% of rats had no signs of glomerulosclerosis; and in 60% of rats there was observed mild glomerulosclerosis with big casts in tubules and inflammatory infiltration. After 9 months all rats in picture of kidney had obvious glomerulosclerosis. Bertani (1) stated that progression of the disease and sclerotic changes depend probably on tubular casts' formation and are the consequences of inflammatory changes.

The mechanism of arising glomerulosclerosis after adriamycin study Paczek et al. (7). He examined the endoglomerular proteinase activity after 7, 12, 22 weeks from drug administration. He noticed that it decreased slowly in time and stated that it could be important in glomerular growth development – an important factor of glomerulosclerosis.

Similarly as in the present study, 4, 5 weeks after giving a single dose of the drug, kidneys were observed by O'Donnell (5). He noticed the mesangium proliferation (matrix and cells). Soares (11) administered 3 mg/kg of body weight and observed, like in the present study, focal, segmental glomerulosclerosis.

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SUMMARY

The purpose of this study was the histological assessment of kidney glomerules in light microscopy after a single dose of adriamycin. Results of lab investigation showed that as soon as 4 weeks after adriamycin administration given peritoneally appears focal, segmental glomerulosclerosis.

Glomeruloskleroza w 4 tygodnie po podaniu jednorazowej dawki adriamycyny

Celem pracy była ocena histologiczna w mikroskopie świetlnym kłębków nerkowych szczura po jednorazowym podaniu adriamycyny. Wyniki badań wskazują na to, że już po 4 tygodniach od dawki leku podanej dootrzewnowo pojawia się ogniskowa, segmentalna glomeruloskleroza.