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Pathomorphological Changes Developing in the Renal Arteries and Microvessels under COVID–19 Influence

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Abstract Lesion in the large arteries of the kidney, in the arcuate artery between the cortex and the medulla in a greaterdegree as well as hypertrophy of intima cells in the wall of the afferent artery of capillaries, appearance of lymphohistiocytic infiltration, proliferation of endothelium in the wall of the diverting artery are usually observed in case of COVID–19. In some cases the microvessels of the capillary network are significantly dilated and filled, but in other cases are spasmed, the basal membrane of capillaries becomes mucoid, endothelial, podocytic and mesangial cells are proliferated.

Keywords Covid–19, SARS–CoV–2 virus, ASE2, Somatic diseases, Blood vessels, Complications, Kidneys, Necrotic nephrosis

1. Topicality

Due to the influence of renin–angiotensin–aldosterone system chain, the development of reactions such as cytokine storm as well as ischemia and hypercoagulability SARS–CoV–2–induced kidney injury occurs. Because of APF2 enzyme is highly expressed in the kidney, endothelium, tubular epithelium, and podocytes of the renal blood vessels can be directly infected by SARS–CoV–2 virus. Virus–induced damage to the vascular endothelium causes their inflammation, increased discirculatory processes, the development of thrombosis causes ischemia and infarction of tissues and organs and diapedetic hemorrhages.

2. Aims and Objectives of Study

Investigation of anamnesis and autopsy protocols of those who died from COVID–19; carrying out retrospective analysis; studying the patho–morphological changes occurring in the kidney vessels.

3. Materials and Methods

Anamnesis and autopsy reports data of 86 patients who died from COVID–19 and examined at the RPAC in spring and summer 2021 have been analyzed. At autopsy, pieces of organs were cut and frozen for 72 hours in a formalin solution prepared in 10% phosphate buffer, stained by hematoxylin–eosin method.

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4. Results and Discussions

The entrance artery of the kidneys, the arcuate artery between the cortical and medulla layers, the artery delivering blood to the capillaries and the efferent artery, including secondary peritubular branches of afferent and efferent arteries have been studied during morphological examination of the renal vessels. During studying the wall of the artery flowing into the kidneys, no significant pathomorphological changes in the outer adventitia, the middle muscle layer that forms the wall of this artery has not been found. Only in the intima of the inner surface of the artery wall, slight tortuosity, flattening of endotheliocytes, hyperchromization of the basal membrane, and deformation of its connective fibers have been revealed (Fig. 1). These changes were manifested by general pathomorphological changes that developed in response to the process of viral infection, i.e., general surface disorganization of tissue structures.

While examining the wall of the arcuate arteries located between the layers of the cortical and medulla of the kidneys, it was noted that all layers of the arterial wall were equally affected by swelling and deformation. As a result, it was found that the cavity of the arteries have been narrowed, the erythrocytes in the cavity are located in a disorderly state, the wall of the artery is fused with the inner surface, and specific accumulations develop. It was noted that the intimate layer of the arterial wall was more edematous, thickened, bulged in some areas, and sank into the muscle layer in other areas.

Plasma proteins were found to be concentrated on the inner surface of the intima layer, forming a homogeneous protein with a pale eosinophilic appearance (Figure 2). Endothelial cells were stretched and deformed due to swelling and disorganization. It was revealed that the basal membrane was some degree thickened and partially deformed due to edema and plasmarrhagia. The appearance of macrophages and lymphocytes in some areas of the intima of the arterial wall was noted. When studying the muscle layer, it was found that muscle cells and myofibrils were located in the same direction, fragmented and vacuolated due to the presence of interstitial swelling in some places. Strong pathomorphological changes due to edema and disorganization in the adventitial layer, as well as in the intima, were revealed. It was noted that the vessels in the adventitia were full–blooded, blood was poured out around them by diapedesis method, the fibrous structures of the connective tissue were homogenized due to mucoid swelling, and were destroyed in places. It was revealed that the relatively smaller network of arcuate arteries between the layers of the kidney has also been greatly deformed; edema, mucoid swelling, and fibrinoid necrosis have been developed in its parietal layers. It turned out that the cavity of this artery was also significantly narrowed and the erythrocytes were located without any order.

It was revealed that some of the endothelial cells of the inner layer were swollen, some were displaced and desquamated, and lymphocytes were attached to some of them. Some areas of destruction in the muscle layer of the walls of these arteries have been observed; they have turned into a structureless tissue due to myolysis, myorhexis and destruction of muscle cells (Fig. 3). Areas of fibrinoid necrosis, hemorrhages, and severe edematous foci have been found in the interstitial connective tissue around the artery.

We know from the literature that the tissue of the kidneys has a perfect histological structure, that is, all layers of the wall tissue are well developed and structured. When studying the walls of the arteries that carry blood to the kidneys in patients who died from COVID–19 infection, it was noticed that the cavity of the arteries was narrowed and the walls were thickened. It was noted that the inner layer of the wall intima consists of a relatively dense tissue, and endothelial cells on the inner surface have a single–layer elongated structure. It was found that beneath the intima its shape is elongated, the nuclei are dark–colored, the fibrous structures are also dense, dark and eosinophilic. Only between the intima and muscle layers, the development of pathomorphological changes was revealed, consisting in marked edema and lymphohistiocytic infiltration (Fig. 4). This inflammatory infiltrate was located in the intimate layer of the arterial wall and consisted of young connective tissue cells, macrophages and lymphocytes. As a result of infiltration, it was found that the connective tissue structures in the intimate layer of the arterial wall were destroyed. It was revealed that the muscle layer consists of circularly located relatively hypertrophied smooth muscle cells.

Swelling and disorganization of connective tissue structures in the outer adventitial layer have been revealed, lymphohistiocytic cell infiltrates appear in some places.

It has been established that the wall of the artery carrying blood from the capillaries of the kidney differs in structure from the wall of the feeding artery. In the wall of the efferent artery, it was found that the inner layer of the intima is thin, consists only of endothelial cells and the basal membrane, while the muscular layer is thick and well developed. Examining the kidneys of patients who died from COVID–19 infection, it was found that dystrophic and inflammatory changes developed in the intima of the arterial wall that carries blood from the capillaries, and both endothelial and intimal cells have been proliferated (Fig. 5). It was revealed that the muscle layer was greatly thickened, ciliary muscle cells were hypertrophied and randomly located. Severe edema and disorganization of fibrous structures have been observed in the adventitia. As a result of a morphological study of the kidneys of patients who died from COVID–19 disease under the influence of all associated diseases, characteristic pathomorphological changes have been revealed.

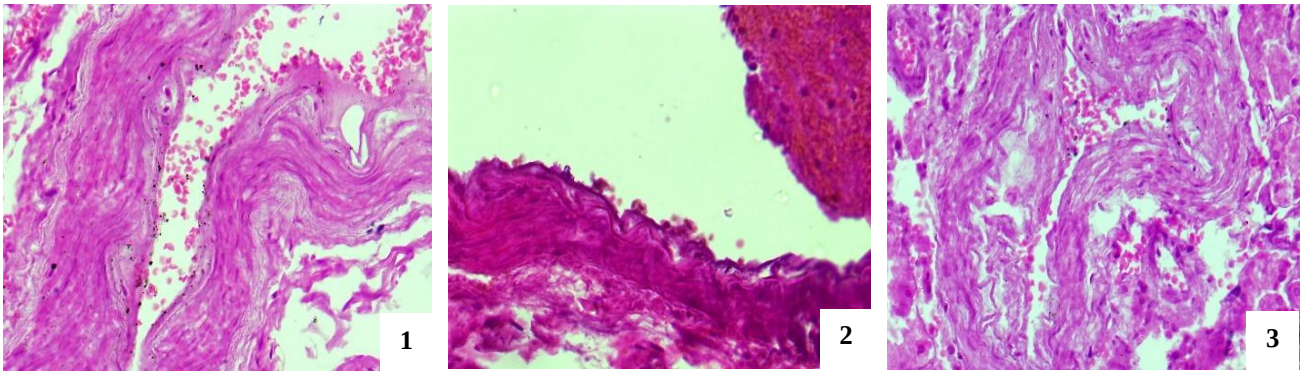

Figure 1-3. 1. Superficial disorganization of the walls and structures of the intima flowing into the kidney artery; 2. An arcuate artery between the layers of the kidney, its wall is deformed due to swelling, adhesion of plasma proteins and erythrocytes to its inner surface; 3. Arcuate artery between the layers of the kidney, its deformation, the presence of fibrinoid necrosis in its wall, foci of destruction. Staining: G–E. Scale: 10x40

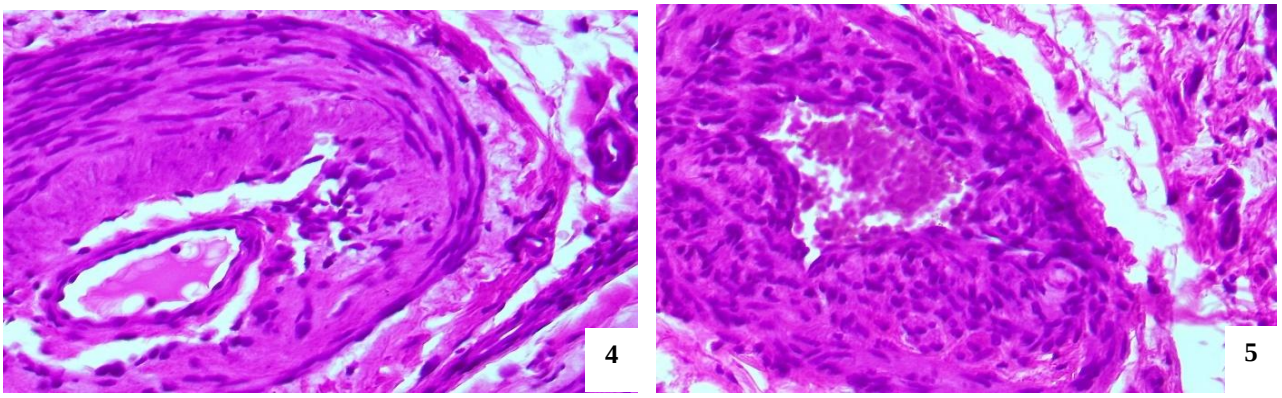

Figure 4-5. 4. The development of inflammation with lymphohistiocytic infiltration and edema in the intimate layer of the artery flowing into the kidney glomerulus; 5. Thickening of the efferent artery, glomerulus intima cells, uneven placement of the muscle layer. Staining: G–E. Scale: 10x40

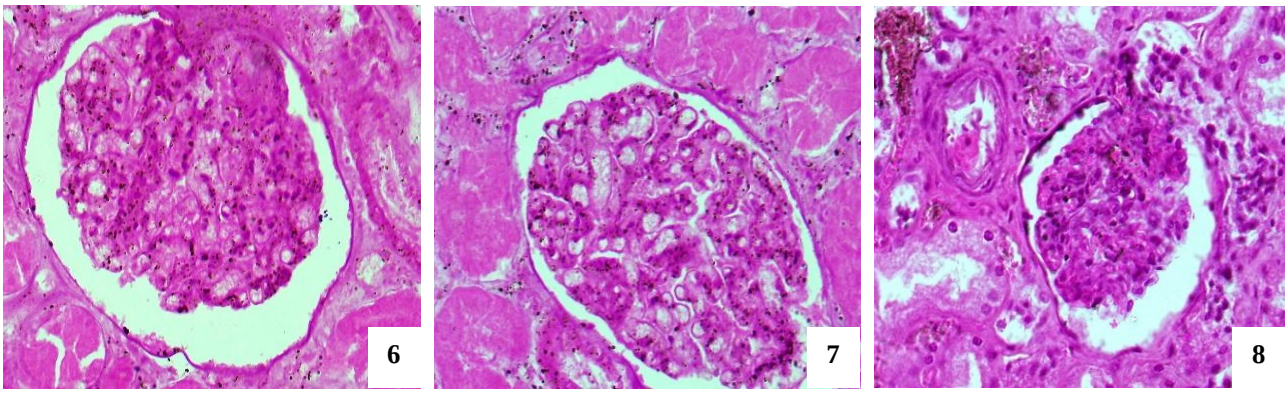

Figure 6-8. 6. Kidney glomerulus, capillaries are dilated, filled with blood, mesangium is proliferated; 7. Kidney glomerulus, part of the capillaries are dilated, another part is filled with a protein substance; 8. Kidney glomerulus and its arteries, efferent artery is narrowed, thrombosis, afferent artery is dilated and filled with lymphocytes and macrophages. Staining: G–E. Scale: 10x40

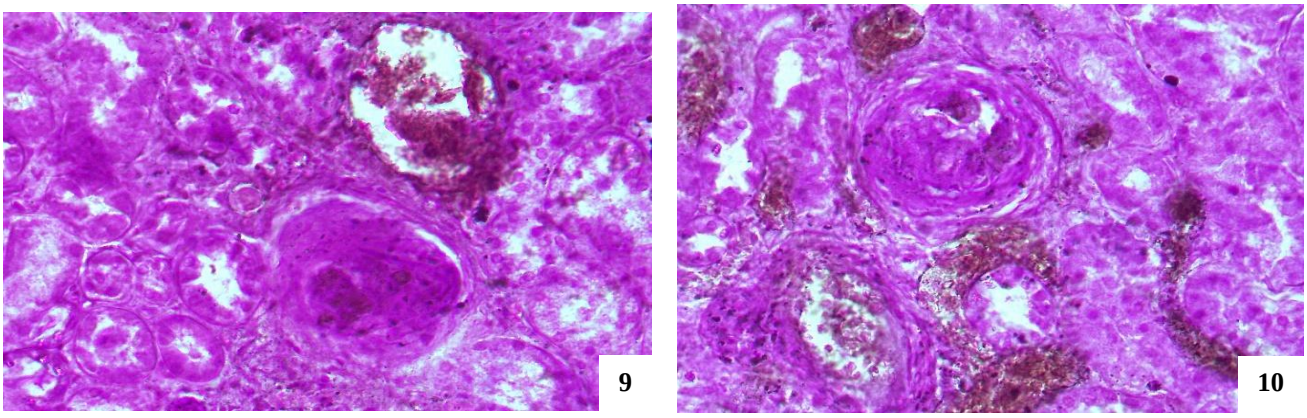

Figure 9-10. 9. The peritubular branch of the efferent artery, its cavity is completely obturated by a thrombus; 10. Formation of multiple thrombi in the cavity of the peritubular branch of the efferent artery. Staining: G–E.Scale: 10x40

Paralytic dilation of glomeruli in the capillary network, thinning of the wall, close placement of plasma proteins and erythrocytes in the cavity have been observed. It was noted that the endothelial cell of the capillary wall was stretched and thinned, and the cytoplasm of the surrounding podocytes was undergone the vacuolar degeneration with small drops. The mesangial cells were relatively proliferated and hyperchromic (Fig. 6). As it was revealed, capillaries network of glomerulus was dilated and blood–filled as a result of significant narrowing of efferent artery and stasis of the blood. In other cases, it was seen that the network of capillaries of the kidney glomeruli became collapsed and decreased a little in size. In one part of the capillary network, the capillaries were seen in a state of expansion similar to that described above, while in the cavity of the other part, it was found that the cavity of the capillary is filled with a protein substance strongly stained by eosinophils and became denser (Fig. 7). Endothelial, podocyte and mesangial cells were at the level of proliferative activity, they were slightly enlarged.

In a number of cases, it was observed that the network of capillaries and capillaries collapsed and became smaller, and

the tissue structures inside it did not swell, but condensed. When examining the afferent and efferent arteries, it was observed that the afferent artery was somewhat narrowed, and a thrombus appeared in its cavity, consisting of fibrin fibers, erythrocytes and lymphocytes (Fig. 8). It can be seen that the wall of this artery is thickened due to the proliferation and increase in cells in it. It was noted that the inner surface of the artery is uneven, one of the endothelial cells in it is displaced, and the other is hypertrophied. Therefore, this process has been confirmed by the fact that the thrombus developed as a result of damage to the inner surface of the artery. It was revealed that closely located to glomeruli efferent artery was significantly dilated, lymphocytes and macrophages were accumulated in the cavity. As a result, an expansion of the efferent artery, an impairment of the integrity of some areas have been occurred.

It was revealed that the secondary peritubular arteries of the kidney of patients who died from COVID–19 in some cases thickening of the wall of the efferent artery and narrowing of the cavity, in other cases the wall is thinned and dilated, in one more case the cavity of the artery is obturated by a thrombus, in another case several thrombi adhered to the wall in the artery cavity. Pathological changes of such a type in the efferent artery usually result in ischemia in the convoluted tubules, their epithelium becomes necrotic.

This micrograph (Fig. 9) shows that the cavity of the efferent artery is completely obstructed by a thrombus, artery wall is thinned and destroyed. As it was determined, the epithelium of the convoluted tubules around the artery was necrotic and destroyed, the nuclei have disappeared, and the cytoplasm turned into a tiny–grained structureless mass. It was observed that Henley's duct tubule is healthy, its diameter is small, the single–layer prismatic epithelium and all histological structures has preserved unimpaired. It was noticed that the vein next to the artery suddenly became dilated and filled with blood.

5. Conclusions

In case of COVID–19 disease, minor arcuate artery between the cortical and medulla layers was damaged in greater degree than the major arteries of the kidney, all layers of the walls of these arteries were diffusely swollen and disorganized, desquamation of the endothelium in the intima showed adhesion of plasma proteins and erythrocytes.

Various changes develop in the afferent and efferent kidney arteries demonstrating thickening of the intima cells in the wall of the afferent artery due to hypertrophy of the intima cells and the development of lymphohistiocytic infiltrate, endothelial proliferation in the wall of the efferent artery, thickening of the muscle layer and disruption of the location in the it muscle cells have been observed.

It has been established that in some cases the microvessels of the capillary network of renal glomeruli are significantly dilated and blood-filled, in others they are spasmodic, the basal membrane of the capillaries is thickened and mucoid, the cells of the endothelium, podocytes and mesangium are proliferatively activated, the capillary network in one case was dilated and increased, and in another collapsed and wrinkled.

It was noted that the peritubular artery in the interstitium of the cortical layer of the kidney proved to be more damaged, an obstructive thrombus developed in its cavity, several fragments of a thrombus of different sizes appeared in one vessel, the veins around it were well–filled.

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