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# MORPHOLOGICAL CHANGES IN KIDNEYS AFTER PROLONGED USE OF ILLICIT DRUGS VIA INTRAVENOUS ADMINISTRATION

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**Abstract - We examined diseased addicts with prolong history of intravenous drug abuse and we found a number of macroscopic and microscopic morphological pathological changes in kidneys. Their characteristics, localization and severity depend on a number of key factors – the period of intravenous use of narcotics without complying with the main principles of aseptic treatment, the purity of the applied drug and additional substances placed in street narcotics. We studied the morphological (macro- and microscopic) changes of kidneys affecting the tubulointerstitial system, glomerules, glomerular capillary loop and damage of the glomerular capillary basement membrane.**

***Key words*: illicit drugs, drug addiction, kidneys damage, morphologic changes.**

## I. INTRODUCTION

The medical data contains descriptions of various morphological changes in different organs and tissues, related to and resulting from prolonged intravenous heroin abuse. These include different skin, cardiovascular, lung, liver, kidney and other morphological changes resulting from both the direct toxic impact of the drug and the way the dose is prepared, whether basic hygiene is maintained, and the type and amount of other substances present in the street dose. Two of the main factors behind the lethal outcome of taking "street" narcotics is that the pure content of street doses varies [1] (in Bulgaria it is between 0% and 20%, rarely more) and the presence of additional substances (from codeine, valium, rivotril, tegretol, codterpin, chinin, strychnine, etc. to flour, powdered sugar, powdered stones or sand, powdered bricks or tiles), which have various side effects and lower the threshold of the toxic, respectively lethal dose.

The aim of our study was to establish the morphological changes in kidneys of drug addicts, who died following long-term intravenous abuse. Studies by Bakir and Dunea [2] show that the complications arising from drug abuse are manifested in a specter of glomerular, interstitial and vascular diseases, including heroin-related nephropathy in African and American intravenous drug addicts, which is less frequent than the HIV-related nephropathy observed in the 1990s. There are many cases of acute and chronic tubulointerstitial nephritis [3], myoglobinuric acute renal failure [2, 3, 4], hemolytic-uremic syndrome [5], chronic renal failure [2, 3, 6], heroin-associated nephropathy, morphologically characterized as focal and segment hyalinosis and sclerosis or membrane-proliferative glomerulonephritis, clinically manifested in nephrotic syndrome, quickly progressing to terminal chronic renal failure [2, 3, 6, 7]. Some authors [8, 9, 10, 11] believe that the morphological pathological changes in multiple organs result from changes in the immune system, which are in turn due to the impact of opioid drugs on the Humoral Immune Response and cell-mediated immunity. The direct effect of analgesic drugs on the immune system is associated with lowering the resistance of the body to specific and non-specific infections, which is one of the main causes of morphological changes in the organs observed both during treatment of patients with these medications and upon examining the cadavers of long-term drug addicts.

## II. MATERIAL AND METHODS

We studied 48 kidneys of people (33 men and 15 women), who died after prolong intravenous illicit drug use (between 5 and 92 months), at the Departments of Forensic medicine and Deontology, and the department of Clinical pathology, Sofia, Bulgaria between 2006 and 2011. We searched for morphological changes in kidneys, examined up to the 6$^{th}$ hour after death, to determine the type of change and the damage caused by the toxic substances. We used light-microscopic study with Hematoxylin-eosin staining and the identified glomerulopathy - by histochemical method (PAS reaction and Congo red staining protocol) and direct immunofluorescence (DAKO). Thin slices were made (5 μm). For an ultrastructural study we used a solution of 2% paraformaldehyd and 2% glutaraldehyd, 1% solution of Os tetraoxyde, durkopan, and ultra thin slices were made (80 nm). Contrasting was implemented with Pb nitrate and examined with electron-microscope Hitachi.

## III. RESULTS

Our data unequivocally indicate that prolonged intravenous illicit drug abuse often affects the kidneys. Different changes concerning the tubulointerstitial system and glomerules can take place. The percent of sclerotic glomerules in drug addicts, including the ones we studied is much higher compared to people who are not addicted to drugs. Morphological changes to the tubulointerstitial system (fibrosis, inflammatory interstitial infiltration and atrophic ducts) are often observed in such individuals. Changes to the kidneys of the glomerulopathy type are less frequent. We observed notable morphological changes to the glomerules like segmental glomerulosclerosis and hyalinosis (Fig. 1A), tearing of glomerule basament membrane with

necrosis (Fig. 1B), and membrane-proliferative glomerulopathy with thickening of the glomerular capillary basement membrane (Fig. 1C).

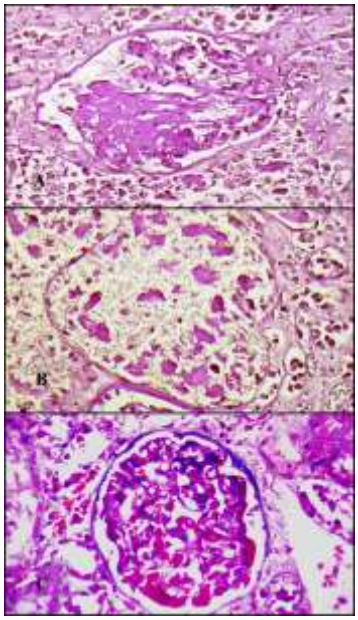

**Fig. 1. A: Segmental glomerulosclerosis and hyalinosis in the glomerule. PAS reaction. Magnification (x250). B: Tearing of glomerule basal membrane with necrosis. PAS reaction. Magnification (x250). C: Notable (ribbon-shaped) thickening of the glomerular capillary basement membrane. Stain: Hematoxylin and eosin. Magnification (x250).**

Pseudolinear deposits of IgG in glomerules with direct immunofluorescence studies were observed (Fig. 2A). In other cases we identified massive mesangial deposits of amyloid in a glomerular capillary loop (Fig. 2B, 2C).

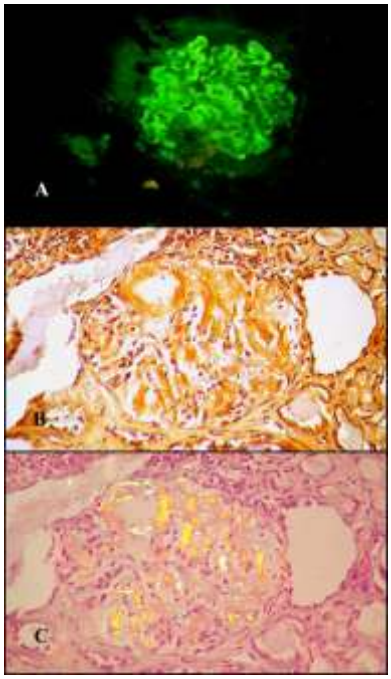

**Fig. 2. A: Pseudolinear deposits of IgG in glomerules. (DAKO) direct immunofluorescence. Magnification (x250). B: Massive mesangial deposits of amyliod in a glomerular capillary loop. Stain: Congo red. Magnification (x250). C: Massive mesangial deposits of amyliod in a glomerular capillary loop. Stain: Congo red. Polarized light. Magnification (x250).**

The ultrastructural examination showed smooth podocytes (Fig. 3A), subendothelial osmiophilic deposits in a glomerular capillary loop and damage of the glomerular capillary basement membrane (Fig. 3B, 3C).

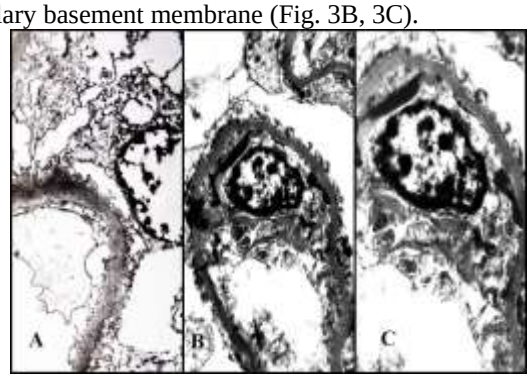

**Fig. 3. A: Smooth out of podocytes-Podocyte disease. Magnification (x4900). B: Subendothelial osmiophilic deposits in a glomerular capillary loop. Magnification (x4300). C: Subendothelial osmiophilic deposits in a glomerular capillary loop. Magnification (x7000).**

In some cases we found massive mesangial and subendothelial osmiophilic deposits in the glomerular capillary loop (Fig. 4A, 4B, 4C).

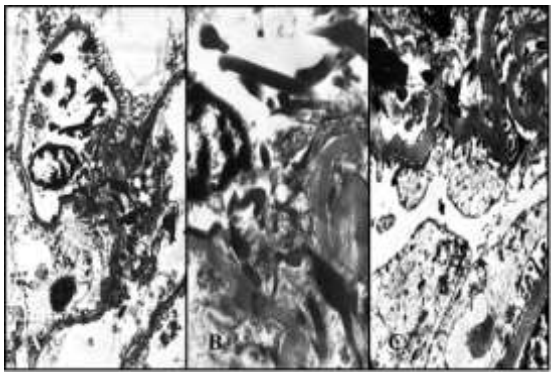

**Fig. 4. A: Mesangial and subendothelial osmiophilic deposits in a glomerular capillary loop. Magnification (x2750). B, C: Massive mesangial and subendothelial osmiophilic deposits in a glomerular capillary loop. Magnification (x7500).**

Parallel with increasing of heroin abuse, young peoples incidence of HIV infection and associated renal diseases has increased. Also interstitial mononuclear cell infiltration and vacuolization in the cells were found.

## IV. DISCUSSION

The pathogenesis of heroin-associated nephropathy is unknown, but the following factors are believed to play a role: the antigen role of heroin and/or substances found in it [3]; acute and chronic infections and the related immune complex [2, 3, 6] or acute post-infectious glomerulonephritis; chronic hepatitis B and C with extrahepatic manifestations (membranous, mesangiocapillary and IgA glomerulonephritis, mixed cryoglobulinemia, vasculitis, aplastic anemia, thyroiditis, Type 1 diabetes, sialadenitis and Sjogren's syndrome, Behcet's disease, lichen rubber planus, autoimmune and lymphoproliferative diseases);direct damage from hepatitis and HIV to the glomerular structures with development of immune complex glomerulonephritis or HIV-associated nephropathy [2, 6]). It seems that macrophages play an important role in the development of glomerulosclerosis. Morphine enhances the migration of monocytes, which

could be a factor contributing to the development of glomerulosclerosis in patients abusing heroin [12]. Our data suggest that addicts who inject the drug under the skin ("skin popping") are prone to develop amyloidosis. Chronic infections are believed to play a pathogenic role. Patients who inject cocaine and heroin under the skin develop nephrotic syndrome with increase of serum creatinine and creatinine clearance [10]. R. Dettmeyer et al. [13] conducted a post-mortem examination on 179 intravenous drug addicts, from whom they took kidney specimens. Monolymphocytic membrane-proliferative glomerulonephritis was found in 61.7% of the cases. The case of the heroin addict with membrane-proliferative glomerulonephritis that we observed was morphologically similar. The pathogenesis of this type of glomerulonephritis is of immune complex-type. Such cases of glomerulonephritis have been described by many authors [3, 6] as well as in the transplanted kidneys [14]. Hepatitis antibodies were found in the serum in 32 of our 48 cases, while three of these 48 patients were HIV-positive. Chronic hepatitis B and C are known to be connected to glomerulonephritis. Unlike drug addicts in Africa and America, drug addicts in Europe do not develop focal segment glomerulosclerosis. They develop monolymphocytic membrane-proliferative glomerulonephritis, in part due to heroin use or to the other substances mixed in with the drug and obviously independent of the hepatitis infection [6]. We must point out that these patients were not tested for hepatitis and HIV, which makes it possible to attribute the morphological changes to the kidneys and liver to these viruses.

## V. CONCLUSION

As the evidence shows, the most common used drug – heroin – causes morphological changes and damage of varying intensity and clinical significance in kidneys when injected over a long period of time. Possessing knowledge of the morphological substrate of these changes enables experts of forensic medicine and pathology to give a quick and correct diagnosis of cases in their practice, thereby assisting clinicians, law enforcement officials and investigators.

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