CONTRIBUTIONS AT THE MORPHOPATHOLOGICAL STUDY OF DOG NEPHROPATHIES

SUMMARY

The meaning of the present work consists upon the identification and morphological framing of kidney pathological processes at dog, reviewing the criteria of recognizing and labelling the morphological types of nephropathies, their evaluation as marker for diagnosis and prognosis inside a general disease and eventual correlation with some environment factors.

The doctoral thesis has 231 pages and it is structured in 2 distinctive parts: first part, which contains bibliographical data concerning the thesis theme and the second part, concerning a personal research made during the elaboration of the present thesis.

The first part "The stage of knowledge regarding the morphology of the dog nephropathies" is structured in two chapters in which is systematized the information collected from 202 bibliographical sources.

In Chapter 1 is presented data concerning morphological particularities of dog kidneys (embryological origin of the kidney, anatomical and histological structure).

Chapter 2 contains the dog kidney morphopathology, the classification of nephropathies, the pathogenesis of the inflammatory process and the presentation of the morphological and histological particularities of the main dog nephropathies (bioplastical adaptive changes, circulatory changes, dystrophies, inflammations and tumours). In this chapter, was underlined the description of the immune glomerulopathies etiomorphopathogenesis, this subject not being a very interesting one for the veterinarians from our country. Similarly with the histological aspects of the human glomerulopathies, were treated the immune glomerulopathies of animals, especially pets (dogs and cats).

The original part of the thesis, developed on 120 pages, contains material and methods of work, the obtained results and their interpretation and general conclusions.

The investigations were made during 2002-2007 on material taken from corpses of deceased or euthanasiated dogs, among which communitarian dogs with different organopathies. The cases came from the clinics of the Veterinary Medicine Faculty and also private clinics from Iasi.

The study material consisted upon 215 dogs of different ages, males and females, from which 167 presented kidney morphopathological changes of different intensity.

The samples that resulted from the necropsies were photographed and listed and after that, in order to be histologically examined, were selected and taken 3 to 6 fragments of kidney from each case and also other organs that are closely related (heart, liver, lung, intestine, spleen, etc.).

In this matter the samples were fixed in formaldehide, water solution 10% and /or fixing liquid Bouin, processed, included in paraffin and sectioned at 5 μm. From almost 650 fragments of organs were realised 2400 preparates, then coloured using usual or special methods: Hematoxiline -Eosine (bichromic coloration HE), Hematoxiline-Eosine-Metil Blue (trichromic coloration Masson, HEA), Haematoxiline-Eosine-Saphrane (HES), Periodic Acide- Schiff fuxine (PAS) and Periodic Acide - Schiff fuxine - light green (PAS - Light green).

Imunohistology lays at the disposition of the researcher efficient methods of showing some cellular or molecular markers able to bring diagnosis arguments.

Inside the research made was used the imunohistochemical method of evidencing the proliferating cell nuclear antigen (PCNA) protein associated DNA - polymerases from fibroblasts in course of mitosis, using monoclonal antibodies applied upon paraffin included sections after a deparaffination, in order to show the tissular antigenical epitopes.

PCNA is a DNA-polymerases associated protein that plays an important part in the cellular proliferation, put in evidence at the nucleus (not nucleolus) during the cellular cycle. PCNA is described by having a granular, diffuse aspect of the nuclei in which DNA synthesis already begin for cellular proliferation.

The PCNA level varies during the cellular cycle stages. So, in nucleus, it is increased by the end of G1, immediately before the DNA synthesis, becoming maximum during S phase and decreasing in G2 phase and M phase. So, it's level is correlated directly with the rate of cellular proliferation and DNA synthesis.

Coloured histological preparates, clarified and set with Canada balm were examined at optical microscope and photographed at different resolution powers.

Histopathological examination of the permanent preparates from the cases taken in study allowed the identification and classification of the pathological processes with kidney

localisation, respecting the classification, hierarchysation and morphological criteria of identification of lesions from speciality comparative pathology lesions.

This way, are described and illustrated by photos the following kidney pathological processes (groups of lesions): adaptative bioplastical changes, circulatory changes, dystrophies, inflammations and tumours.

Inside bioplastical adaptative changes were observed and described kidney hyperplasia, kidney cysts (polycystic kidney) and kidney compressive athrophy.

The circulatory changes identified at dog were frequent enough: kidney congestion, glomerular and interstitial haemorrhage, disseminated intravascular coagulation (shock kidney), thrombosis, emboli, kidney infarct and kidney oedema.

The kidney dystrophies were: steatosis, granular and hydric nephrosis, hyalinosis, amiloidosis, haemosiderosis, jaundiced, uricosis, calcification, oxalosis and litiasis.

At our cases were described after the localisation of the inflammatory process: glomerulitis (glomerulonephritis), tubulonephritis and interstitial nephritis, especially immune ones and interstitial nephritis (limphohistiocitary and fibrous).

Glomerulonephritis with immune underground were diagnosed especially at adult dogs.

Were diagnosed:

- **membranous glomerulonephritis**, translated histologically throught thickening (5-6 times) of the basal glomerular membrane especially at the peripheric glomerular capillaries (solitary) being distortional and with plied aspect (wire loop), accompanied by a slight proliferation of mesangial cells and increase of the mesangial matrix.

The evolution is favourable the lesions being reversible in the most part, at others being observed a slow progressive evolution to glomerular sclerosis, due to capillaries obliteration.

The majority of the membranous glomerulonephrities evolve generalized or globally, being idiopathic (competition of the circulant immune complexes could not be identified), expression of some pathological processes (infections, neoplasic processes, intoxications or autoimmune diseases).

Membranous glomerulonephrities can be the expression of old age (synthesis of membranous material), intoxication with heavy metals (gold, mercury), chronical septical diseases (piometer at dogs), parasitic infestations, association with chronical interstitial

nephrities (at dog), systemic metabolical changes (diabetes, tiroiditis) or idiopatical (unidentified immune complex).

- **proliferative mesangio-glomerulonephrities**, are histologically dominated by cellular proliferations that lead to a pluricelularity aspect or polinucleosis of the Malpighi corpuscle.

This type of immune glomerulonephritis was most frequently met in our casuistic, being dominated by cellular and matrix changes of the glomerular mesangium, translated morphologically through an increase of the number of cells from it`s structure, as a consequence of the mesangial and endothelial cell proliferation associated with inflammatory cells (polinuclear, mononucleated cells), increase of mesangial matrix and accumulation of mesangial deposits.

Hyperplasic phenomena from the structure of glomerule (glomerular polinucleosis) produced a remarkable reducement of glomerular capillaries through external compression, going to complete stenosis, realising this way the decrease glomerular blood perfusion and finally the sclerosis.

- **membrane-proliferative glomerulonephrities** called also capilar-mesangial glomerulonephrities represents a morphoclinical entity that is characterized by the proliferation of the mesangial cells and at the same time by the thickening and duplication of the glomerular basal membrane. So it has both aspects of the membranous and mesangio-proliferative glomerulonephrities.

In chronical evolution were noticed conjunctive periglomerular and peritubular proliferations and atrophy of the nephrone. These morphological aspects are considered intermediary lesions that finalise with generalised chronical glomerulonephrities and then lead to chronical kidney insufficiency.

- **sclerosant glomerulonephrities**; from morphological point of view were observed many aspects in the evolution of this lesion: activation of the mesangial cells and increase of synthesis of the mesangial matrix, accumulation of eosinophilical homogeneous material on the structures of Malpighi corpuscle, thickening of the glomerular basal membrane, thickening of the basal membrane of Bowman capsule and even doubling it, degeneration of the visceral epithelium, apparition of the inter-epithelial glomerular sinechies (visceral epithelium-wall epithelium), cell proliferation and conjunctive fibres in the glomerular and periglomerular mesangium.

At same cases sclerosis begun centrifugally, from the mesangium and the glomerular capillaries towards the Bowman capsule, at others was observed a centripet sclerosis, proliferation of conjunctive fibres starting from the glomerular capsule containing then the whole glomerule.

Glomerular sclerosis ends with glomerule transformation or only of the vascular hank in a mass of concentrical stratified conjunctive cells and fibres or can be resumed only at the constitutions of a fibrous scar in which can be distinguished vague remains from the vascular mass structure.

Kidney tumours, rare at the examined cases, were represented by the mixed kidney carcinoma, tubular colangiocarcinoma, kidney lymphoma and melanoma.

The thesis is concluded with general conclusions, in which the principal lesions of the kidneys are briefly exposed through anatomopathological and histopathological investigations, their importance and value to the direct and differential diagnostic.