Histological aspects in immune-mediated glomerulonephritis in dogs

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Abstract
The kidney is often the target of agressions of extra-renal origins. Its structure and function make it vulnerable and oftenly affected by the pathological changes that take place inside the living organism. Glomerulonephritis are pathological processes characterized morphologically and functionally firstly by the alteration of the glomerular structures and secondly by alterative changes located in other renal structures (uriniferous tubules, vascular and connective stroma). To this date glomerulonephritis are a major concern in nephrology, affecting both humans and animals. The renal glomeruli may be damaged by the action of both specific pathogens and systemic diseases.
Key words*: glomerulonephritis, dog, morphology*

Introduction

The kidney is at often times the target of ilnesses of extra-renal origin. Its structure and functions make it susceptible to various pathologies that may affect the living organism.

The increased blood pressure in the glomerular capillaries, the ultrafiltration function and the glicoproteins with strong negative charge that are a part of the glomerular filtration barier are elements that plead in favour of the susceptibility to the potentially negative action of circulating endogenous or exogenous substances (Crespeau, 2003).

Based on the underlying pathogenetic mechanism, immune mediated glomerulonephritis may be divided into two categories:

1. glomerulonephritis caused by immune complexes precipitated inside the glomerulus;
2. glomerulonephritis caused by anti-basal membrane antibodies.

The studies on spontaneous and experimental glomerulonephritis have shown that the immunological mechanisms play an important role in glomerular pathology (Brostoff, 1991).

Acording to recent studies, in human pathology 70-80% of immune glomerulonephritis are produced by immune complexes precipitating and depositing inside the glomeruli. In veterinary pathology, 77% of cases with proteinuria in campanion carnivores are due to immune mediated glomerulonephritis (Jergens, 1987; McGavin, 2007).

The pathogenesis of glomerulonephritis caused by immune complexes has two possible mechanisms that may determine structural glomerular changes and both of them are based on type three hypersensitivity reactions:

A. through Atg-Atb circulating immune complexes (preformed);

B. through Atg-Atb immune complexes formed "in situ" (within the glomerulus).

As a general rule, immune mediated glomerulonephritis are characterized by the fact that immune complexes and fractions of the complement precipitate on the basal membranes and the mesangium as discontinuous and granular deposists that may be visualized through immunofluorescence and peroxydase methods (Dambach, 1997).

These granular, immunofluorescent deposits are the opposite of the smooth, linear and diffuse looking deposits seen in glomerulonephritis caused by anti-basal membrane antibodies.

The pathogenic action of these circulating immune complexes resides in the capacity they have to trigger a series of changes that will end with the altering of the basal membranes (membranous, proliferative-membranous glomerulonephritis) and the proliferation of the mesangial cells (proliferative glomerulonephritis) (McGavin, 2007).

Clinical simptoms are expressed mainly through severe proteinuria (Euzeby, 1989).

Results and discussions

Immune mediated glomerulonephritis were diagnosed mainly in adult dogs. The following types were observed:

- **membranous glomerulonephritis**, translated histologically throught the thickening (5-6 times) of the basal glomerular membranes, those of the peripheral glomerular capillaries (solitary) being especially distorted and with folded aspect (wire loop), accompanied by a slight proliferation of the mesangial cells and an increase in the mesangial matrix (Fig.1, 2).

The evolution is favourable, the lesions being reversible in the most part. Sometimes, a slow progressive evolution towards glomerular sclerosis may be observed, due to the obliteration of the capillaries.

The majority of the membranous glomerulonephritis evolve in a generalized form or globally, being idiopathic (the source of the circulating immune complexes could not be identified) and reflecting the presence of some pathological processes (infections, neoplastic processes, intoxications or autoimmune diseases) (Green, 2006; Jansen, 1986).

Membranous glomerulonephritis can also be an expression of old age (synthesis of membranous material), intoxication with heavy metals (gold, mercury), chronic septic diseases (pyometra in dogs), parasitic infestations, chronic interstitial nephritis (in dogs), systemic metabolical changes (diabetes, thyroiditis) or idiopathic (unidentified immune complexes) (Jubb, 2007).

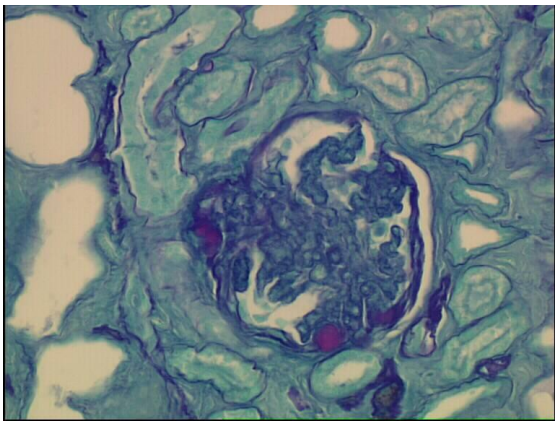

Fig. 1 Membranous glomerulonephritis. Hematoxylin-Eosin-Green trichrome light stain, x200

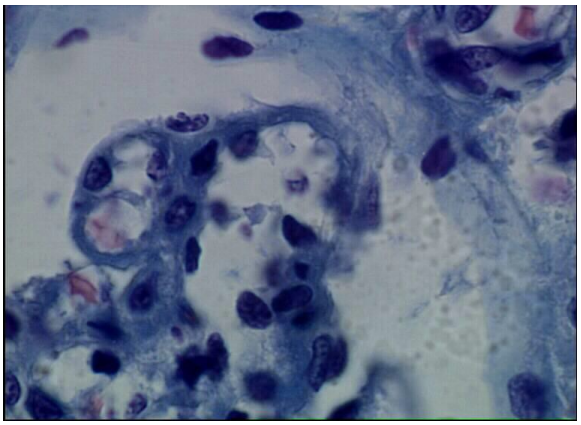

Fig. 2 Membranous glomerulonephritis. Masson's trichrome stain, x1600

- **proliferative mesangial glomerulonephritis** are histologically dominated by cellular proliferations that lead to a multicellularity aspect or polynucleosis of the Malpighi corpuscle.

This type of immune glomerulonephritis was the most frequently diagnosed form in our cases, being characterized by cellular and matrix changes of the glomerular mesangium, translated

morphologically through an increase in the number of cells within its structure, as a consequence of the mesangial and endothelial cell proliferation associated with the presence of inflammatory cells (polynucleated, mononucleated cells), an increase of the mesangial matrix and accumulation of mesangial deposits (Fig. 3, 4, 5, 6).

Hyperplasic phenomena within the structure of the glomeruli (glomerular polynucleosis) produced a remarkable decrease of glomerular capillaries through external compression, all the way to complete stenosis, resulting in a decreased glomerular blood perfusion and finally sclerosis.

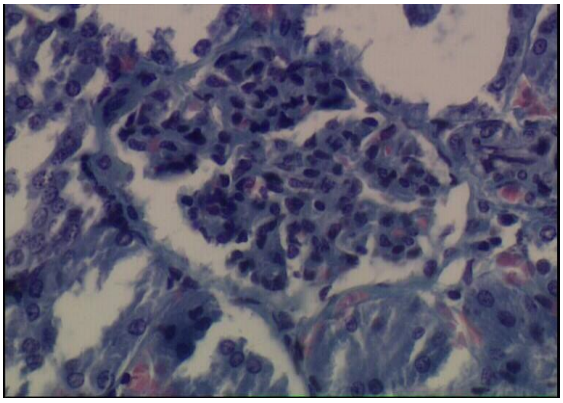

Fig. 3 Proliferative mesangial glomerulonephritis. Masson's Trichrome stain, x400

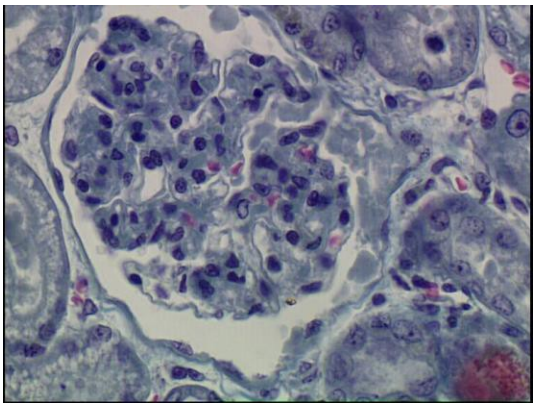

Fig. 4 Proliferative mesangial glomerulonephritis. Masson's Trichrome stain, x400

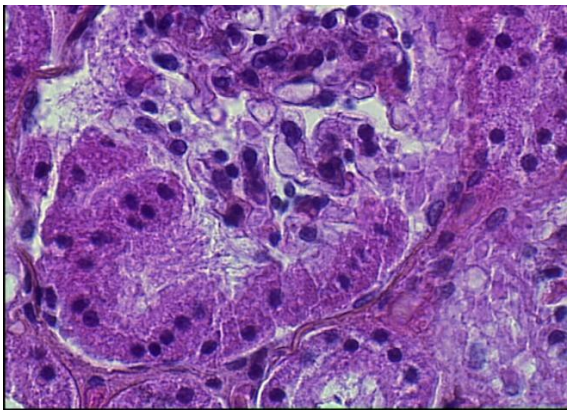

Fig. 5 Proliferative mesangial glomerulonephritis. Hematoxylin - Eosin – Saffron Trichrome stain, x1000

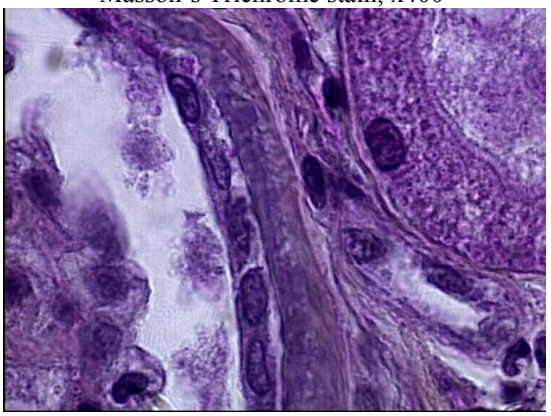

Fig. 6 Proliferative mesangial glomerulonephritis. Proliferation of the parietal cells. Hematoxylin - Eosin – Saffron Trichrome stain, x1000

- membrane - proliferative glomerulonephritis (Fig. 7, 8) called also capillary - mesangial glomerulonephritis 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, thus presenting with both aspects of the membranous and mesangio-proliferative glomerulonephritis (McGavin, 2007; Crespeau, 2003).

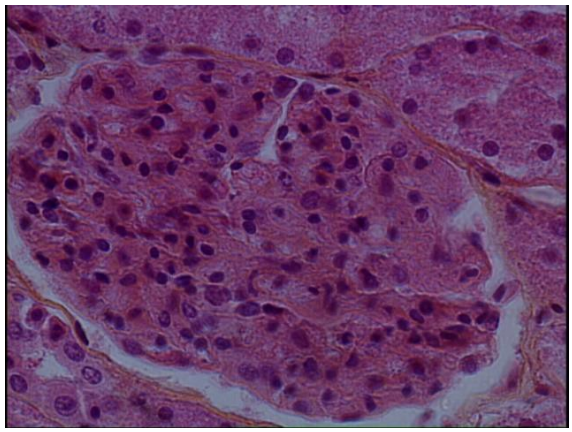

Fig. 7 Membrane-proliferative glomerulonephritis. Hematoxylin - Eosin – Saffron Trichrome stain, X 1000

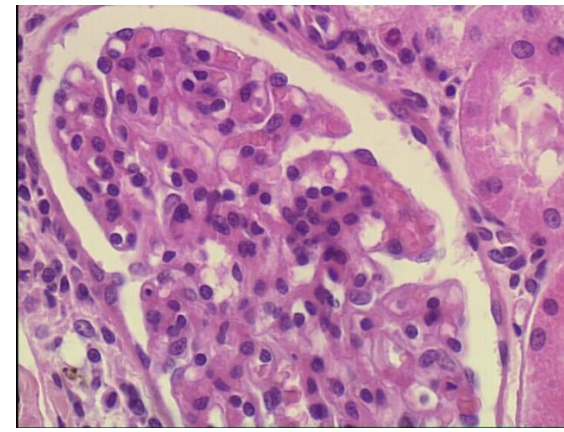

Fig. 8 Proliferative glomerulonephritis. Hematoxylin - Eosin – Saffron Trichrome stain, x 1000

Conclusions

The sum of inflammatory phenomena caused by the circulating immune complexes deposits or after their "*in situ*" formation, from various causes, is perpetuated continuously, thus affecting the integrity and permeability of the glomerular basal membrane.

All that being said, the response generated by the glomeruli towards these agressions is somewhat constant, being characterized by the thickening of the glomerular basal membrane, cell proliferation and sclerosis.

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