ADAPTIVE BIOPLASTIC DISORDERS OF THE KIDNEY IN DOGS – REVIEW

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Within this category of kidney lesions, we will talk about tissular growth disorders and topographical anomalies.

Most of these lesions are hereditary and congenital, but they can also be acquired during the life of the animal.

Hypoplasia, the most frequent renal dysplasia, represents the underdevelopment of the organ during its period of growth. The lesion is described especially in very young dogs, with the term of immature or fetal kidney and can be uni- or bilateral.

Macroscopically, the kidneys are smaller than normal, firm, pale and with a wrinkly, pseudo-lobulated aspect. The underdevelopment of the kidneys may be accompanied by the morphofunctional immaturity of the liver and thymus, the later being identifiable upon microscopical examination. In the unilateral form, usually affecting the left side, the kidney appears small, firm, with a thick, adherent capsule, and on the sectioned surface we may notice striations located in the cortical corresponding to fibrous tissue and hypoplasic interlobular areas.

Microscopically, in the cortex, we will be able to observe a reduction in the number of glomeruli and tubular hypertrophy. In the medullar area the collector tubes are reduced in numbers, uniformly dilated, with a flattened epithelium, surrounded by immature connective tissue without a tendency towards maturation into inflammatory cell infiltrated collagen (lymphocytes, plasma cells). Although many times it may have a normal aspect, the nephron can be functionally incompetent (Schulze and col., 1998).

Generally, hypoplasia is associated with compensatory hypertrophy of the congener kidney.

Renal dysplasia is a structural organization disorder that follows an abnormal differentiation during the period of nephrogenesis. The lesion may be uni- or bilateral, generalized or focalized. Histologically, dysplasia is highlighted through:

- non-synchronous differentiation of the nephrons, not corresponding to age;
- the persistency of primitive mesenchyme represented by a myxomatous type connective tissue;
- the persistency of metanephritic ducts;
- adenomatoid looking atypical tubular epithelium;
- the presence of osseous or cartilaginous tissue islands.

Renal dysplasia is a familial nephropathy seen in the following breeds: Chow-Chow, Samoyed, Doberman, Pincher, Norwegian Elkhound, Bull Terrier, Cocker Spaniel, Lhasa Apsos, Shih Tzu and Standard Poodle. In the youth of these breeds, the nephropathy with an autosomal dominant, autosomal recessive or sex-linked transmission represents the major cause for chronic renal insufficiency (Jansen and col., 1986; Brown and col., 1990; Picut and Lewis, 1987; Darrigrand and col., 2006).

Secondary to the renal dysplasia we can see interstitial fibrosis, renal cysts, glomerular hypercellularity (compensatory phenomena) (Zachary and McGavin, 2012).

The welding of the kidneys occurs during the nephrogenesis period being accomplished at one of the two poles (cranial or caudal) through a bridge formed by parenchyma that may or may not embody the bassinets, the ureters remaining separate. Thus, through fusion, we will see the formation of a structure with the appearance of a single, large kidney (horseshoe kidney), with two ureters, and with a normal histological structure and function (Zachary and McGavin, 2012).

Atrophy represents the reduction in the volume of the kidney that has reached its full morphofunctional maturity, following the diminishing of trophicity. It is secondary to vascular lesions, hydronephrosis, compression exercised by large tumors, retention or parasitic cysts. The atrophy of the epithelium of the nephrons is accompanied by the thickening of the basal membranes and is characteristic for chronic tubular lesions.

Macroscopically, the kidney is slightly smaller and with increased consistency.

Histologically, tubular atrophy was observed gradually, beginning with the shrinking of the tubular lumen from the medullar area following the direction of the compression force, the flattening and progressive atrophy of the epithelium down to its disappearance, the curling and considerable thickening of the tubular basal membranes. Finally, the uriniferous tubules will be replaced with connective tissue.

Agenesis represents the uni- or bi-lateral absence of the kidneys. Sometimes the kidney may be represented by only an embryonic vascular-connective bundle.

Aplasia, it is rare, and it represents the partial development of the kidney. Unilateral aplasia affects mostly the left kidney; it evolves associated or not with the hypoplasia or absence of the ureter, the hypoplasia of the opposite kidney or even other anomalies.

Hypertrophy represents the development of the kidney above the normal limits. It may be **compensatory**, in which case it is installed following the agenesis, aplasia, hypoplasia or surgical ablation of the opposite kidney. The healthy kidney does not undergo hypertrophy through nephron neoformation, but **cellular over-dimension** of the existing ones. In the case of total functional impairment of a kidney, the congener organ increases its size up to the normal wight of both kidneys in young animals, and up to 70% of their weight in adult ones (Coman and col., 1996).

Cytomegaly or renal megalocytosis is characterized through nuclear-cytoplasmic gigantism of the nephrocytes and is located inside the proximal contort tubules. It is caused by aflatoxin, nitrosamine and pyrrolizidine alkaloids from plants belonging to *Senecio, Cynoglossum, Echium, Crolalaria* genera, etc. (Coţofan O., 1992; Pop I., 2004).

Hydronephrosis, congenital or acquired, represents the dilation of the internal space of the kidney associated with the progressive compression atrophy of the renal parenchyma. Ureteral obstructions cause uni-lateral lesions, those affecting the urethra, bi-lateral lesions. In dogs, the most frequent causes for hydronephrosis are the decrease of the urinary transit following congenital malformations, urinary calculi, chronic urocystitis, urinary bladder or prostate neoplasia (Zachary and McGavin, 2012)**.** The glomerular filtration that continues even when there is an obstacle present in the extrarenal urinary tract will lead to the progressive accumulation of urine in the distal segments of the nephron, the atrophy of the papillae, of the pyramids and later of the cortex and the replacement of the normal morphofunctional elements with neoformed connective tissue. Finally, the kidney will appear as an immense, irregular sack, delimited at the periphery by a thin remanence of atrophied renal parenchyma

Osseous metaplasia can be seen in the hydronephrotic kidney, the transition cell epithelium simulating the transformation of mesenchymal cells into osteoblasts (Jubb and col., 2007).

Renal cysts are cavitary formations present in the renal parenchyma.

The shape and volume of the kidneys are dependent by the number and size of the cysts, which may be **congenital** or **acquired**. We hence feel the need to mention several aspects:

- the single renal cyst - affects a lobe. The volume of the cysts, although variable, may be greater than the one of the remaining kidney. The wall is thin, smooth, fibrous, lined on the inside with a shinny epithelium, the cavity containing a watery, colourless, odourless liquid, without urine smell.

- the polycystic kidney is usually bilateral. The cortical area is deformed by numerous cysts, creating the resemblance to a grape. We will find multiple cavities, of variable sizes, with a diameter of about 2-6 mm, separated by fibrous tissue of debris of atrophied parenchyma. When the cysts are numerous, the kidneys are very enlarged, pale and with a spongy aspect. This disorder appears to result from an anastomosis defect between the secretory and the excretory segments of the tubes, with the accumulation of urine and cystic distension of the proximal parts of the nephron. Congenital renal cysts can develop along with cysts inside other organs as well.

Histologically, we will observe the wall of the cysts, formed of densified collagen fibres and lined with a flattened epithelium, and around the cyst, the renal parenchyma will be compressed and fibrotic.

Polycystic kidney disease (PKD), being a **dominant autosomal hereditary disease** has been observed in dogs belonging to Cairn Terrier, West Highland White Terrier and Collie breeds, up to 6 months of age, as well as in Persian cats. Along with this lesion bi-lateral cysts were also observed. In the majority of cases, the abdomen was enlarged following the enlargement of the liver and kidneys (Gough and Thomas, 2004; Sellers and Richie, 1978).

The causes of this disease appear to be the dysfunctions of proteins *polycystin-1* and *polycystin-2* as a result of mutations in genes PKD-1 or PKD-2, involved in the synthesis of these proteins. The formation of tubular cysts is owed to mutations located on both alleles of these genes, PKD-1 and PKD-2 (Carone and col., 1994, Angus K.W., 1990).

Polycystin-1 is involved in the normal proliferation of cells and the mechanism of apoptosis. Also, this protein has a very important role in cellular adhesion, being a main component of desmosomes. Its absence or the formation of a mutant protein would lead to a faulty differentiation of tubular epithelial cells with the loss of polarity and an abnormal arrangement of cells within the structure of the uriniferous tubules, decreasing tubular absorption and determining the distension of the uriniferous tubules with the formation of tubular cysts (Schultze and col., 1998).

Polycystin-2 is located inside the Ca^{2+} canals of the cytoplasmic membranes.

In Bull Terriers, besides the polycystic kidney, nodular thickening of the mitral and aortic valves could be observed. Patients with ages between 6–15 months presented with hematuria and severe cardiac insufficiency (Gough and Thomas, 2004).

Acquired renal cysts are generally small and numerous. The aetiology also includes hypokalemia. The differential diagnosis should include hydatidosis. In dogs, the lesion may be bi-lateral.

Histologically, we may observe both glomeruli and uriniferous tubules distended and filled with a homogenous, clear material (sometimes basophilic), which, through progressive accumulation, leads to the atrophy and disappearance of the glomerular vascular bundle and the tubular epithelium. We may also observe the thickening of the basal membranes of both the glomerular capsule and the uriniferous tubules through the formation of connective tissue with laminar aspect and concentric arrangement. Glomerular and tubular cysts may also develop following extensive cortico-medullary fibrosis.

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