ORIGINAL PAPER

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

Etio-pathogenic and morphological correlations in congenital hydronephrosis

MĂDĂLINA BOŞOTEANU[1,2)], C. BOŞOTEANU[2)], MARIANA DEACU[1,2)], MARIANA AŞCHIE[1,2)], P. BORDEI[3)]

[1)]*Department of Pathology, Faculty of Medicine, "Ovidius" University, Constanta*
[2)]*Service of Pathology, Emergency County Hospital, Constanta*
[3)]*Department of Anatomy, Faculty of Medicine, "Ovidius" University, Constanta*

Abstract

Hydronephrosis, "distension in varying degrees of pelvis and calyces, accompanied by progressive atrophy of renal parenchyma due to obstruction in urinary flow", is an apparently simple reno-urinary disease, but, in reality, by association of its own characters with those conferred by causative lesions, becomes of a significant complexity. The purpose of this paper is to demonstrate the plurivalent character of this entity on a batch of cases with congenital hydronephrosis, by identification of lesional features correlated with cause of disease. The etiology of hydronephrosis in analyzed cases was characterized by heterogeneity: polar inferior artery, horseshoe kidney, extrarenal pelvis, transverse valves of pelviureteral junction (PUJ), adhesion of ureter to PUJ, intrinsic stenosis of PUJ, vesico-ureteral reflux, posterior urethral valves, stenosis of urethral meatus. The way of intervention of urinary obstruction and the uni- or bilateral character of damage were definitory for the macroscopical appearance of the hydronephrotic kidney, renal pelvis demonstrating its role of expansion room for kidney protection. In analyzed cases of congenital hydronephrosis, correlation specific cause–pelvic lesion evidenced histopathological differences related to etiology. Anatomical preparations obtained by injection followed by corrosion have revealed that renal vessels appear elongated, distanced from each other and even reduced in density, which explains the appearance of ischemia accompanying pathogenetic changes of obstructive uropathy. Regardless of etiology, all cases of congenital hydronephrosis were characterized by varying degrees of fibrosis in chorion of renal pelvis, accompanied by active chronic inflammation, observation that support the idea of connection between the two pathological changes.

Keywords: congenital hydronephrosis, polar artery, horseshoe kidney, extrarenal pelvis, pelviureteral junction dysectasia.

Introduction

Hydronephrosis, "distension in varying degrees of pelvis and calyces, accompanied by progressive atrophy of renal parenchyma due to obstruction in urinary flow", is an apparently simple reno-urinary disease, but, in reality, by association of its own characters with those conferred by causative lesions, becomes of a significant complexity.

The purpose of this paper is to demonstrate the plurivalent character of this entity on a batch of cases with congenital hydronephrosis, by identification of lesional features correlated with cause of disease.

Multifactorial etiology of primary (congenital) hydronephrosis can be systematized as follows:

Intrinsic factors

Obstruction (dysectasia) of pelviureteral junction

Obstruction (dysectasia) of pelviureteral junction (PUJ) is one of the most common congenital upper urinary tract malformation, due to the following causes: atresia of pyelo-ureteral junction; abnormal valves with effect of dysectasia if only their disposition is one in front to the other; congenital hypertrophy of the muscle fibers of the pyelo-ureteral junction (abnormal disposition of the muscular ureteral layers in uretero-pelvic region) [1]. Pelviureteral junction obstruction is present in 10–40% of cases of congenital hydronephrosis, affects mostly males (2:1); is mainly found on the left side and may have familial aggregation [2].

Ureteral obstruction

Ureteral obstruction can be caused by ureteral atresia (absence of lumen); strictures (frequent at both extremities of the ureter) or by congenital ureteral valves (single or multiple transversal folds) [3].

Pyelo-ureteral dilation associated to vesico-ureteral reflux

Vesico-ureteral reflux (VUR) represents the effect of a developmental abnormality at vesico-ureteral junction level; normally, ureter joins bladder at a sharp angle and has an oblique trajectory through the muscle layers of the bladder wall over a distance of 5–18 mm, depending on age; shortening of the intravesical segment and opening at an obtuse angle are the main causes of VUR [4].

Campbell MF and Harrison JH [3] classified the main causes of VUR:

1. Uretero-trigonal muscle hypotonia (majority of cases);

2. Ureteral abnormalities (complete duplication, ectopic orifice, ureterocele);

3. Intense bladder trabeculation (spastic neurogenic bladder, severe obstruction of the bladder neck, cystitis);

4. "Triad" syndrome (congenital absence of abdominal muscles, obstructive uropathy, cryptorhidia).

Usually, VUR resolves spontaneously, due to restore of normal anatomical relations at vesico-ureteral junction level with growth, but persistent organic etiological factors require surgical correction.

Posterior urethral valves

Posterior urethral valves (PUV) affect usually male gender, with an incidence of 1:5000–1:8000. Their appearance is due to the presence of congenital mucous folds in posterior urethra, at *veru montanum* level, leading to upstream dilation of urinary tract; the aspect is of asymmetrical hydronephrosis, often associated with renal dysmorphism / dysplasia, closely correlated with presence of VUR [5].

Stenosis of urethral meatus

Stenosis of urethral meatus is a congenital anomaly that complicates hypospadias; represents incomplete canalization of urethral terminal ectoderm [5].

Extrinsic factors

Renal abnormalities in shape and fusion

The most frequent is horseshoe kidney, composed of two distinct renal masses, situated on both sides of the spine, fused to the upper or lower pole by a parenchymal mass or fibrous isthmus, crossing the midline; ureters are high inserted, are laterally distant, depending on the thickness of the isthmus; usually, it is associated with VUR or with PUJ obstruction [6].

PUJ compression by an inferior polar artery

Together with the corresponding vein, it produces a vascular clamp at the PUJ level or on upper third of the ureter [6].

Materials and Methods

In this study, we investigated a group of 11 cases of congenital hydronephrosis, composed of nephrectomy specimens and kidneys sampled during necroptic procedure, in the period 2007–2009 (Table 1).

Table 1 – ***Etiology of congenital hydronephrosis***

Etiology	No. of cases
PUJ compression by an inferior polar artery	2
Transverse valves of PUJ	1
Adhesion of ureter to PUJ	1
Horseshoe kidney	1
Intrinsic stenosis of PUJ	2
Extrarenal pelvis	1
Vesico-ureteral reflux	1
Posterior urethral valves	1
Stenosis of urethral meatus	1

Macroscopic and microscopic examination of hydronephrotic kidneys was performed in the Service of Pathology, Emergency County Hospital of Constanța. Anatomical preparations obtained in order to highlight variants of renal arteries and their branches were made in the Department of Anatomy, Faculty of Medicine, "Ovidius" University, Constanța. Age of patients ranged between 0 and 31 years, both sexes being affected. Pelvi-calyceal distension was noticed both unilaterally and bilaterally. Causes of this disease were characterized by heterogeneity.

Gross description of hydronephrotic kidneys comprised the description of several features:

- kidney dimensions;
- external renal surface;
- section surface;
- grade of hydronephrosis;
- aspect of restant parenchyma (thickness, color, cortico-medulary limit);
- aspect of pyelic and calyceal mucosa, with particular features;
- evaluation of PUJ permeability and estimation of stenosis grade; this was done by introducing a thin stylet, whose passage was difficult or, in some cases, impossible;
- description of ureter (proximal or entirely, depending on fragment harvested intraoperatively or intranecroptic): length, caliber, thickness of the wall, aspect of mucosa, presence of eventual lesions;
- characteristics of bladder: dimensions, external, internal and sectioned aspect of the wall;
- specific changes at urethral level.

Specimens of congenital hydronephrosis caused by inferior polar artery were obtained by dissection of kidney harvested with segments of abdominal aorta and inferior vena cava, by injection molding (Tehnovit), followed by corrosion with sodium hydroxide at a temperature of 70–80^{0}C.

For download of hydronephrotic kidney images, a Nikon Coolpix 4500 digital camera was used.

After macroscopic analysis of the specimens, they were processed to obtain microscopic preparations. Suggestive fragments were taken from the pelvis, calyces, parenchyma and ureter. For an optimal processing, harvested fragments were of 4–5 cm² maximal area and 3–5 mm thick. Successive operations were specific for conventional histological technique and used stains were of routine (Hematoxylin–Eosin) and special type (van Gieson, Masson) [7].

Visualization of histopathological preparations was performed using a Nikon Eclipse E600 microscope and capture of microscopic images was accomplished using Lucia image software.

Results

Polar inferior arteries

Case No. 1: male, 31-year-old, autopsy specimen

Gross description

Evisceration unit composed of renal segment of abdominal aorta and inferior vena cava, right kidney (13/6.5/5 cm) and left kidney (14/7/5.5 cm); external surface presents small scar depressions; on section, obvious dilation of collecting system; smooth surface

of pyelic mucosa, with punctiform hemorrhages. Renal parenchyma is reduced to a thickness of 0.7–1.5 cm, reddish, with cortico-medullary boundary attenuation (grade II hydronephrosis).

Origin of inferior polar artery with retroureteral trajectory is from aorta, above its terminal bifurcation, 2 cm over the origin of inferior mesenteric artery (Figure 1, left side); controlateral, an obvious compression over superior portion of ureter, exerted by the inferior polar branch with origin in renal artery, as its terminal branch and an impression on the lower portion of the renal pelvis made by inferior branch of prepyelic artery and inferior branch of renal vein, localized between the two aforementioned arteries (Figure 1, right side).

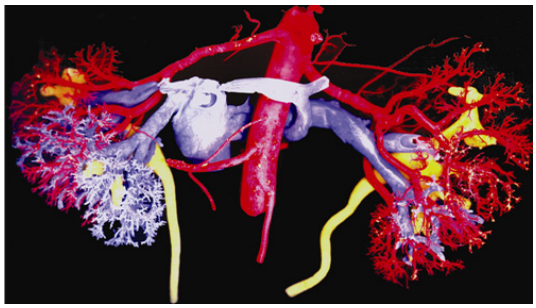

Figure 1 – ***Polar inferior arteries.***

Retroureteral inferior polar artery originating in the aorta describes a precaval horizontal trajectory, with a slight concave superior curvature (Figure 1, left side). Penetration of renal parenchyma by the arterial branch is at the medial border of the inferior pole, just below the hilum (Figure 1, left side) and terminal arterial branching occurs intrarenal. Crossing of the artery with ureter occurred at the pelvi-ureteral junction level (Figure 1, left side).

Microscopic description

Pyelic and pyelo-ureteral junction epithelium displayed papillomatous proliferation and moderate dysplasia; thinned aspect of tunica muscularis, due to atrophy and hyalinization of smooth muscle fibers, with loss of fascicular disposition; numeric decrease of elastic fibers.

Case No. 2: male, 30-year-old, autopsy specimen

Gross description

Right kidney of 12.5/7/5 cm, with slight boselated external surface; on section, extreme pyelo-calyceal dilatation, with hemorrhagic suffusions in renal pelvis; 0.5 cm thick renal parenchyma, with vague cortico-medullary limit (grade III hydronephrosis); fragment of ureter 10 cm length and 1 cm diameter, thin wall, bleeding suffusions in adventitia.

In this case, morphologic variant involved in genesis of hydronephrosis was inferior polar artery with retroureteral situation and with origin in retropyelic artery (Figure 2). Its trajectory was downward, obliquely infero-lateral, describing a slight curvature with supero-lateral concavity (Figure 2); renal sinus penetration was infero-medially, subhilar (Figure 2), and terminal branches were strictly intrarenal located. Intersection of the artery with ureter occurred at upper extremity of the latter (Figure 2).

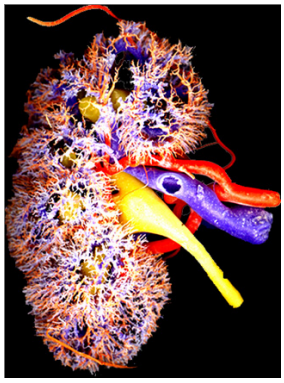

Figure 2 – ***Polar inferior artery.***

Microscopic description

Pelvic structure is modified by flattening of the urothelium with focal ulcerations and presence of large areas of fibrosis that extend to the medulla, causing the disappearance of tubular structures. Pyelo-ureteral junction had important folding of the epithelium, fibrosis of the chorion and of the muscular interstitium (Figure 3).

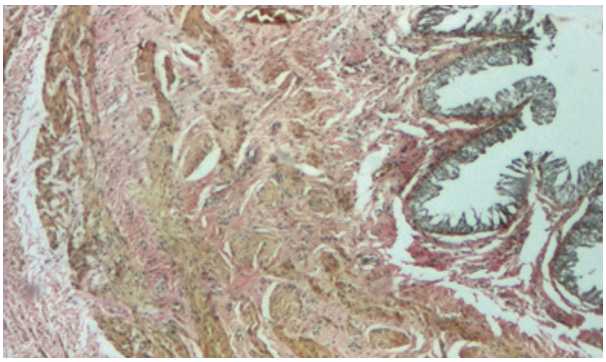

Figure 3 – ***Pyelo-ureteral junction: interfascicular fibrous proliferation (van Gieson stain, ×40).***

Ureter presented ulceration and partial atrophy of the transitional epithelium, massive hemorrhage and chronic inflammatory infiltrate in the underlying layers; in tunica media, come muscular fibers were dilacerated, the remainder having a predominantly longitudinal disposition, separated by connective fibers.

Horseshoe kidney

Male, 31-year-old, autopsy specimen

Gross description

Kidneys of 13/8/5 cm each, bound at inferior poles level by an isthmus of 5/3/2.5 cm (Figure 4).

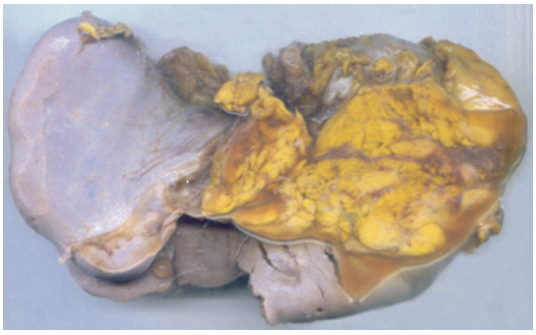

Figure 4 – ***Horseshoe kidney.***

Section surface evidenced collecting system dilatation and atrophy of the renal parenchyma to a thickness

of 2 cm; cortico-medullary boundary appeared blurred (grade II hydronephrosis).

Microscopic description

Renal capsule appeared thickened, mostly in isthmic region; capsular slastic tissue was segmented, interrupted, twisted; we noticed the presence of capillaries that dissect connective tissue, with agglutinated red blood cells in the lumen (aspect of passive hyperemia); also in the capsule, we observed tissue edema, in the form of optically empty vacuoles. Urothelium showed squamous metaplasia with focal areas of severe dysplasia: multilayered nuclei, karyomegaly, granular chromatin, prominent nucleoli. Stroma contained an important inflammatory infiltrate of lympho-granulocytic type.

Extrarenal pelvis

Male, 26-year-old, nephrectomy specimen

Gross description

Left nephrectomy specimen of 12/7/3 cm, presenting on section surface dilated collecting system with secondary thinning of renal parenchyma – 0.5–2 cm (grade II hydronephrosis); renal pelvis of 5/3/2 cm, located exterior to the renal sinus and continuous with an ureteral fragment of 5 cm length, with elastic wall (Figure 5).

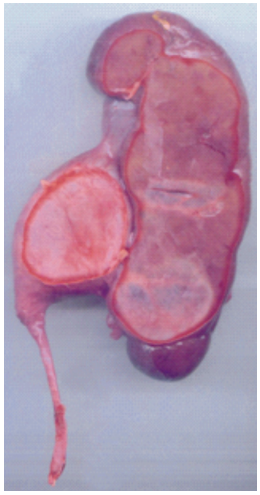

Figure 5 – ***Extrarenal pelvis.***

Microscopic description

Pelvic urothelium evidenced lesions of moderate dysplasia, with ulcerations and associated intra- and subepithelial lympho-granulocytic inflammation; chorion with fibrosis; hyaline degeneration of numerically reduced smooth muscle fibers. Pyelo-ureteral junction evidenced papillomatous proliferation alternating with focal ulcerations of transitional epithelium; smooth muscle fibers of all parietal layers are dissected by fibrous septa. At ureteral level, we observed moderate epithelial dysplasia, atrophy and hyalinization of parietal myocytes.

Transverse valves of PUJ

Female, 9-year-old, nephrectomy specimen

Gross description

Right nephrectomy specimen of 7/5/3 cm, bosselated external surface, gray-reddish with bleeding points; on section, thinned renal parenchyma (0.5 cm), dilated pyelo-calyceal system, with smooth white-yellowish internal surface (grade III hydronephrosis). PUJ presented two intraluminal folds with transverse disposition, of 0.4/0.2 cm each, with gray smooth surface and elastic consistency. Ureteral length was 10 cm and its walls were thin.

Microscopic description

Renal pelvis presented squamous metaplasia of urothelium; in chorion, hemorrhage and chronic inflammatory infiltrate; in muscularis, marked hypertrophy and hyperplasia of smooth muscle fibers. At PUJ level, we noticed papillomatous epithelial proliferations, sustained by a well-developed fibro-muscular core (Figure 6).

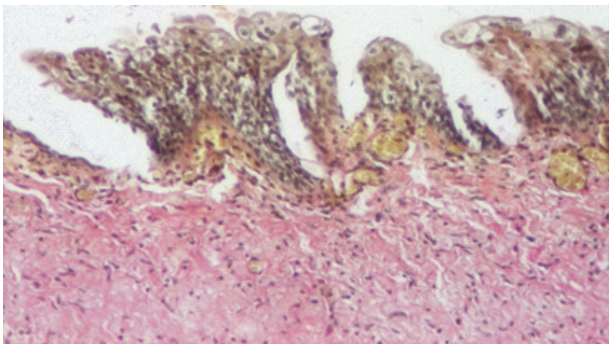

Figure 6 – ***Transverse valves of PUJ: papillomatous proliferation of urothelium (van Gieson stain, ×100).***

Ureter evidenced focal papillomatous change of transitional epithelium; subepithelial, discrete fibrosis and chronic inflammatory infiltrate; slight hypertrophy of muscularis; serosal hyperemia.

Adhesion of ureter to PUJ

Male, 5-month-old, autopsy specimen

Gross description

Right kidney of 8/6/4 cm, with mild pelvic distension and renal parenchyma of 2.5 cm thick (grade I hydronephrosis). Sharp angulation and adhesion of the ureter against the lower portion of the pelvis were obvious in this case of PUJ obstruction, giving the appearance of a high insertion of the ureter into the pelvis.

Microscopic description

Changes of basinetal epithelium consisted in atrophy alternating with foci of papillomatous proliferation; lamina propria with edema and discrete lymphomonocitary inflammation; well-represented smooth muscle and elastic fibers.

Intrinsic stenosis of PUJ

Case No. 1: male, 6-year-old, nephrectomy specimen

Gross description

Left unilateral nephrectomy specimen of 7/4/2.5 cm, with hemorrhagic areas on external surface; on section, extremely dilated calyces and pelvis with loss of pyelocalyceal demarcation; thinned parenchyma (0.2–0.8 cm) and effacement of pyramids (grade III hydronephrosis). PUJ appeared narrowed, allowing the passage of the stylet with difficulty.

Microscopic description

Atrophy of pelvic urothelium, associated with ulcerations and neutrophilic infiltrate localized intra- and subepithelial; in chorion, hyperemia-hemorrhage; hypertrophy and hyperplasia of smooth muscle fibers (Figure 7).

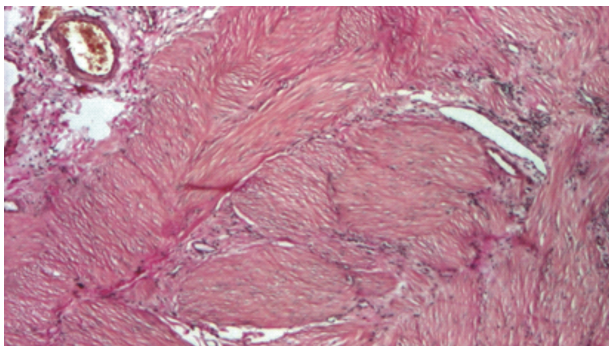

Figure 7 – ***Intrinsic stenosis of PUJ: hypertrophy and hyperplasia of myocytes of tunica muscularis (van Gieson stain, ×40).***

At PUJ level, extensive fibrosis with intra- and interfascicular disposition, leading to the replacement of some myocytes with collagen fibers.

Case No. 2: female, 1-year-old, autopsy specimen

Gross description

Right kidney of 10/6/4 cm with granular external surface; on section, blunting of the medullary pyramids, renal parenchyma of 2.5 cm thick, dilated collecting system with diffuse bleeding spots (grade I hydronephrosis). PUJ stricture was obvious and the proximal ureter appeared thin walled and narrowed.

Microscopic description

Histopathological examination of renal pelvis evidenced the atrophy of transitional epithelium and hyalinization of muscular wall, with loss of layered architecture, accompanied by decreased amount of elastic tissue. PUJ evidenced focal epithelial ulcerations and variations in the normal helical disposition of smooth muscle fibers, due to interspersed hypocellular fibrosis. Ureteral stenotic segment was characterized by an increased amount of connective tissue associated with mild inflammatory infiltrate.

Vesicoureteral reflux

Male, 1-year-old, nephrectomy specimen

Gross description

Left nephrectomy specimen of 4/2.5/1.5 cm, with irregular blackish surface; section surface revealed dilatation of pyelo-calyceal apparatus and renal parenchyma of 1 cm thick (grade II hydronephrosis). Ureter was 7 cm long and 1.2 cm in diameter, with thickened rigid wall and flattened mucosal folds.

Microscopic description

Histopathological changes consisted in atrophy of basinetal epithelium, associated with collagenization of lamina propria extended to renal interstitium; a particular feature was represented by sliding of renal tubules in areas of fibrosis at basinetal level (Figure 8); we also observed flattening of ureteral transitional epithelium, with subjacent intense proliferation of collagen fibers, subsequent smooth muscle atrophy and lymph-monocytary inflammatory reaction dispersed in all layers of the wall.

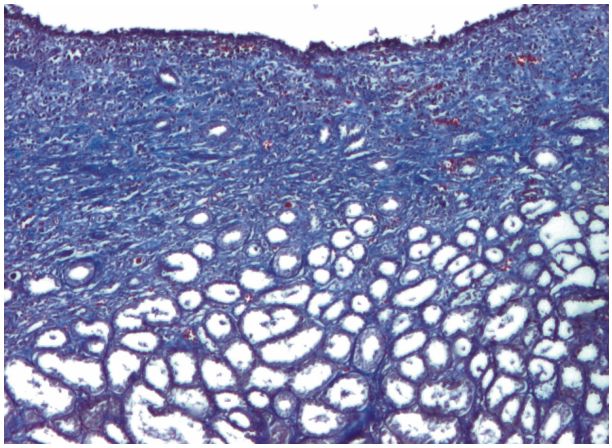

Figure 8 – ***Vesico-ureteral reflux: sliding of tubular structures in pyelic wall (Masson stain, ×100).***

Posterior urethral valves

Male, 5-month-old, autopsy specimen

Gross description

Kidneys of 4/3/2 cm and 5/3.5/3 cm, respectively, revealed on section moderate distension of collecting system and parenchymal narrowing to 1 cm thick (grade II hydronephrosis); both ureters appeared dilated and in urethral lumen we observed a pair of reddish, elastic, anteriorly fused valves.

Microscopic description

Basinetal and ureteral epithelium evidenced moderate atrophy and stromal fibrosis, associated with loss of elastic fibers. Urethral valves were composed of transitional epithelium supported by a well-represented fibrovascular axis.

Meatal stenosis

Male, 18-year-old, necroptic specimen

Gross description

Both kidneys were of 12/6/3 cm, with marked dilation of pyelo-calyceal system, lined by a fine granular, gray surface; restant renal parenchyma with a maximal thickness of 0.8 cm (grade III hydronephrosis); dilated ureters, about 1.5 cm diameter, white wall; intense trabeculation of bladder wall; stenosis of urethral meatus associated to hypospadias.

Microscopic description

Pyelic urothelium was characterized by atrophy and foci of severe dysplasia, as an effect of associated chronic active inflammation; ureteral epithelium evidenced advanced atrophy; both structures presented dissecting paucicellular fibrosis through muscular fascicles of tunica media and diminution of elastic fibers. An interesting finding was represented by entrapment of tubules in fibrotic chorion of renal pelvis.

At vesical level, marked hyperplasia and hypertrophy of smooth muscle fibers in all three tunics of the muscle layer were obvious.

Discussion

On our batch of study, males were more often affected by congenital hydronephrosis, age group 0–1 year being predominantly interested.

Sex distribution of unilateral hydronephrosis showed predominance of right renal disease for females and of left kidney damage for males, results consistent with data from literature [8]. Bilateral hydronephrosis interested exclusively male population, because of its correlation with specific urethral pathology (posterior urethral valves, urethral meatus stenosis).

The way of intervention of urinary obstruction and the uni- or bilateral character of damage were definitory for the macroscopic appearance of the hydronephrotic kidney. In case of unilateral, acute and complete obstruction, glomerular filtration was early compromised; consequently, renal function has got insufficient before pelvi-calyceal expansion became important, so, collecting system was moderately dilated, but the atrophy of renal parenchyma seldom appeared, as in our second case of PUJ stenosis. When the unilateral obstruction was subtotal or intermittent, glomerular filtration was not suppressed and progressive dilatation of urinary tract appeared, associated with renal parenchymal atrophy, due to its direct compression by dilated pyelo-calyceal system and prolonged renal ischemia. In addition, macroscopic appearance of the kidney was dependent on the location of the obstacle. In the situation of intrarenal obstruction, especially at pelvic level, damage had a rapid onset with significant effect on calyces and parenchyma (intrinsic stenosis of PUJ, transverse valves of PUJ). In case of an extrarenal obstacle, pelvis tends to relax more and calyces, less, with more distant in time consequences, renal pelvis playing the role of expansion room for kidney protection (inferior polar arteries, adhesion of ureter to PUJ) [9].

Bilateral obliterations slowly installed caused asymmetric damage to both kidneys (urethral meatus stenosis, posterior urethral valves, vesico-ureteral reflux).

In analyzed cases of congenital hydronephrosis, correlation specific cause–pelvic lesion revealed histopathological differences related to etiology.

The study of anatomical variants of retroureteral arteries in our two cases of congenital hydronephrosis produced by vascular clamp revealed their different origin: aorta or retropyelic artery. Horizontal or oblique-descending trajectory of retroureteral arteries determined compression of ureter that is crossed at its upper extremity or at pelvi-ureteral junction level, leaving impressions influencing urinary drainage.

In case of double renal arteries, their pre- and retropyelic arrangement resulted in the formation of a strong forceps compressing over the pelvi-ureteral junction.

Supranumerary vessels occur frequently, unilaterally, on the left side and in males; this abnormal relationship between polar vessels and the upper end of ureter is rarely the unique etiologic factor of hydronephrosis, usually being associated with other malformations of junction and causing aggravation of obstruction. This trajectory variant of renal artery, of its collateral or terminal branches is driven by a variety of other morphological features of kidney, of vascular distribution or of pyelo-calyceal system: upward-located renal hilum, extrarenal short pelvis or completely intrarenal pelvis, the penetration level of polar artery into the renal parenchyma, the presence of inferior polar arteries originating in the aorta or common iliac artery (ectopic renal arteries).

Mechanisms by which vascular clamp leads to hydronephrosis are various: in its trajectory, polar artery crosses pyelo-ureteral junction on one side, causing obstruction [9]; other authors consider that, initially, renal ptosis appears, resulting in angulation of ureter over renal vessels and in subsequent urinary stasis; it was also hypothesized that pulsations of supranumerary arteries inhibit ureteral peristalsis at the level where vessels cross the ureter, either by rhythmic mechanical irritation or by abnormal currents of action, initially causing a permanent localized spasm (stage of functional or dynamic dysectasia), and subsequently trophic alterations consecutive to persistent spasm (edema, sclerosis) [6]; if extrinsic stenosis of the ureter by the inferior polar artery produces hydronephrosis, there is a reciprocal action, consisting of compression exerted by the ureter over the renal arteries, which leads to decreased volume of urine excreted by the affected kidney [9].

Anatomical preparations obtained by injection followed by corrosion have revealed that, in case of hydronephrotic kidneys, renal vessels appeared elongated, distanced from each other and even reduced in density, which explains the appearance of ischemia accompanying pathogenetic changes of this condition.

Dysectasia of pyelo-ureteral junction produced by the inferior polar arteries showed microscopic lesions dominated by papillomatous transformation with dysplasia of urothelium and extensive fibrosis of pelvic wall, causing muscle atrophy and loss of layered architecture; elastic fibers of stroma and muscular interstitium, severely diminished.

Intrinsic stenosis of PUJ caused complex changes in the pyelic wall: epithelial atrophy with multiple ulcerations and associated chronic inflammatory infiltrate; in muscular layer, hypertrophy and hyperplasia of myocytes with predominantly longitudinal arrangement, separated by an inter- and intrafascicular collagen proliferation, with elastic tissue loss (which in normal kidney contribute to pelvic distension). These observations justify the rigidity and the difficulty in adaptation of junctional caliber at diuresis variations, being in consensus with Murnaghan's law [6]: "Where there is only longitudinal musculature, there is no peristalsis" (Figure 9).

In cases of congenital hydronephrosis caused by transverse valves and by adhesion of ureter to PUJ, parietal alterations were of lower intensity, characterized by flattening / papillomatous proliferation of epithelium, variable collagen proliferation in chorion, well represented musculo-elastic component.

Vesico-ureteric reflux and extrarenal pelvis produced pathological changes at pyelic level, correlated with inflammatory infiltrate invariably present in these situations: urothelial dysplasia, lympho-granulocytic inflammation, intense paucicellular fibrosis in chorion and in tunica media, with almost entire replacement of muscular structures, loss of elastic fibers and inclusion, in some cases, of renal tubules in fibrotic areas. Similar microscopic lesions were noted in cases of urethral obstruction (posterior urethral valves, urethral meatus stenosis), possible effect due to association between inflammation and urinary stagnation in the urinary system [10].

The presence of metaplastic changes in urothelium of horseshoe kidney was illustrative for wide potential of differentiation and also for non-specificity of germ-layers evolution. This phenomenon was triggered by urine stasis and by associated inflammation and represents a favorable state for development of subsequent carcinoma [11].

Regardless of etiology, all cases of congenital hydronephrosis were characterized by varying degrees of fibrosis in chorion of renal pelvis, accompanied by active chronic inflammation and, sometimes, by hyperemia/hemorrhage. Fibrosis is more intense in cases associated with marked inflammation, observation that supports the idea of connection between the two pathological changes (Figure 10).

Our findings, which are similar to those of Zhang PL *et al.* [12], describe a significant inflammatory component present in the lamina propria of collecting system, as a possible effect of high urinary pressure, that determine a primary epithelial break, responsible for spread of urine inside renal pelvis wall. Inflammatory cells that subsequently appear at this level release cytokines, which induce prolonged muscular spasm, leading to increase of the intrapelvic pressure and so causing enlargement of the epithelial break. A connective tissue reaction of the pyelic wall would thus occur, which should be considered a secondary event related to the presence of inflammation, so a vicious circle is established, supported by the local cytokine environment and progressing to a self-amplifying process of fibrosis, typical for chronic inflammatory tissue.

The presence of collagen proliferation at pyelic level supports the idea that lack of chorion elasticity causes inextensibility of collecting system, having thus a central role in the maintenance and aggravation of dysectasia [13]. Coexistence of collagenization of musculo-elastic wall induces lesional aggravation.

In specific cases, compressive effect of pyelo-caliceal dilation determined tubular structures to slide in the muscular layer of renal pelvis, certifying the influence of raised basinetal pressure over renal components (Figure 11) [14].

It is well known that tunica muscularis of renal collecting system consists of two types of smooth muscle cells, distinct from morphological and histochemical point of view: typical myocytes and particular myocytes, the latter acting as pacemakers with role in the initiation and control of peristaltic contractions [15, 16]. Loss of layered disposition of smooth muscle fibers due to their replacement by fibrous tissue interferes both with peristaltic activity and with distensibility of renal pelvis.

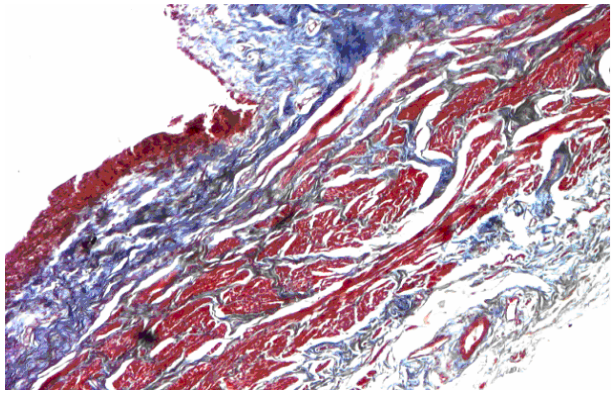

Figure 9 – ***Renal pelvis: urothelial atrophy, predominance of longitudinal muscular fibers and collagen proliferation in tunica media (Masson stain, ×40).***

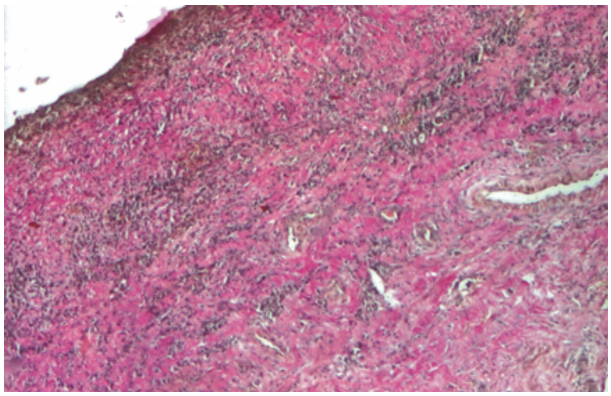

Figure 10 – ***Renal pelvis: urothelial atrophy, intense inflammation and fibrosis of the wall, architectural disorganization (van Gieson stain, ×40).***

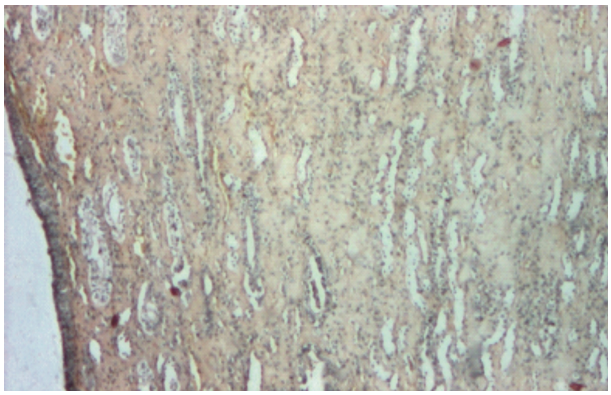

Figure 11 – ***Renal pelvis: subepithelial hypocellular fibrosis including tubular structures (van Gieson stain, ×100).***

Conclusions

Interdependence between different causes of hydronephrosis and pyelic lesions is correlated primarily with mode of installation and action of urinary drainage obstruction. Main histopathological changes that influence the structure and function of renal pelvis consist in fibrosis correlated with variable degrees of inflammatory infiltrate and in changes in smooth muscle fibers distribution, leading to impaired urinary drainage and to disease aggravation.

References

[1] Keeling JW (ed), *Fetal and neonatal pathology*, Springer-Verlag, New York, 1987, 412–414.

[2] Badea RI, Dudea SM, Mircea PA, Stamatian F, *Tratat de ultrasonografie clinică*, Ed. Medicală, Bucureşti, 2000, 460–467.

[3] Campbell MF, Harrison JH, *Urology*, vol. II, 3rd edition, W.B. Saunders Co., Philadelphia–London–Toronto, 1970, 1472–1484.

[4] Mevorach RA, *Obstructed megaureter*, eMedicine, Last updated: April 22, 2009, http://emedicine.medscape.com/article/441734-overview.

[5] Bernstein J, Churg J (eds), *Urinary tract pathology: an illustrated practical guide to diagnosis*, Raven Press, New York, 1992, 5–9.

[6] Conley SB, *Congenital kidney diseases*, http://cybernephrology.ualberta.ca/nephkids/congdiseases.htm, 2010.

[7] Mogoantă L, Georgescu CV, Popescu CF, Bădulescu A, Mehedinți-Hâncu M, *Ghid de tehnici de histologie, citologie şi imunohistochimie*, Ed. Medicală Universitară, Craiova, 2003, 66–70.

[8] Fogo AB, Bruijn JA, Cohen AH, Colvin RB, Jennette JC (eds), *Fundamentals of renal pathology*, Springer–Verlag, New York, 2006, 149–153.

[9] Cameron S, Davison AM, Grünfeld JP, Kerr D, Ritz E (eds), *Oxford textbook of clinical nephrology*, vol. 3, Oxford University Press, London, 1988, 2031–2035.

[10] Rosai J (ed), *Rosai and Ackerman's surgical pathology*, 9th edition, Mosby, 2004, 1226–1227.

[11] Tavora F, Fajardo DA, Lee TK, Lotan T, Miller JS, Miyamoto H, Epstein JI, *Small endoscopic biopsies of the ureter and renal pelvis: pathologic pitfalls*, Am J Surg Pathol, 2009, 33(10):1540–1546.

[12] Zhang PL, Peters CA, Rosen S, *Ureteropelvic junction obstruction: morphological and clinical studies*, Pediatr Nephrol, 2000, 14(8–9):820–826.

[13] Weidner N, Cote RJ, Suster S, Weiss LM (eds), *Modern surgical pathology*, 2nd edition, Saunders, 2009, 896–912.

[14] Bijol V, Mendez GP, Hurwitz S, Rennke HG, Nosé V, *Evaluation of the nonneoplastic pathology in nephrectomy specimens: predicting the risk of progressive renal failure*, Am J Surg Pathol, 2006, 30(5):575–584.

[15] Mehedinți T, *Histologie*, vol. II, "Ovidius" University Press, Constanța, 1998, 214–230.

[16] Raica M, Mederle O, Căruntu ID, Pintea A, Chindris AM, *Histologie teoretică şi practică*, Ed. Brumar, Timişoara, 2004, 210–211.

Corresponding author

Mădălina Boşoteanu, Lecturer, MD, PhD, Department of Pathology, Faculty of Medicine, "Ovidius" University, Constanța; Service of Pathology, Emergency County Hospital, 145 Tomis Avenue, 900591 Constanța, Romania; Phone +40745–146 803, e-mail: mbosoteanu@yahoo.com

Received: May 3rd, 2010

Accepted: January 8th, 2011