Histopathological Studies on Renal, Prostate and Urinary Bladder Diseases in Dogs

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Abstract: Histologic evaluation of biopsy and cytology provides an accurate diagnosis, facilitates prognostication and helps in determining the specific cause of a disease to alter patient management through additional therapeutic measures specific for the primary disease. Therefore this study was conducted on ultrasound guided needle biopsy of the kidney, fine needle aspiration cytology of the prostate gland and surgical biopsy urinary bladder diseases with objective to show the importance of technique and to determine confirmatory diagnosis. Consequently, ultrasound guided needle biopsy sample was taken from seven dogs using 18 gauge Bard Max core disposable biopsy gun, ultrasound guided fine needle aspiration biopsy was taken from five dogs using a standard five or ten milliliter syringe and 22 or 23-gauge needle and full thickness incisional biopsy of urinary bladder tissues was taken from 15 dogs during cystotomy. Accordingly, the histopathological examination of ultrasound guided biopsy sample of renal tissue distinguished acute and chronic renal failure while ultrasound guided fine needle aspiration cytology differentiated benign prostatic hyperplasia (BPH) from prostatitis. However, diagnostic sample was obtained in only 42.9% (3/7) of renal biopsy samples and 60% (3/5) of fine needle aspiration samples of the prostate. Histopathological diagnosis of the urinary bladder of all dogs with urocystolithiasis had also chronic cystitis and/or metaplasia of varying degree, which was detected in only 26.7% (4/15) of the cases evaluated ultrasonographically. Biopsy and cytological evaluation of the kidney, prostate and urinary bladder are highly valuable tools to make better treatment decisions.

Key words: Diagnosis • Ultrasonography • Biopsy • Cytology

INTRODUCTION

Obtaining an accurate histological diagnosis is one of the most important steps in successful management of the dogs with renal disease as the presence of reversible kidney lesions throughout all stages of chronic kidney disease was reported, while irreversible lesions were more prevalent in later stages [1, 2]. Therefore, it is mandatory to obtain diagnostic biopsy sample for identification of underlying etiology at an early stage so that medical interventions can take place prior to the development of end stage renal disease. No doubt that surgical biopsy has been used as diagnostic tool for confirming disease. Ultrasonography is also found to be useful in guiding fine needle aspiration or biopsy of lesions. At present, ultrasound-guided biopsy is the most commonly used technique of kidney biopsy in dogs and cats [3]. Technical ease, less invasiveness and reduction in the incidence and severity of post-biopsy complications such as hemorrhage is considered as advantage of ultrasound guided localization of biopsy site as compared to blind methods such as localization of the lesion by palpation and keyhole technique [4]. Histopathological diagnosis of organ disease remains the gold standard because of the capability to assess tissue architecture as well as cell detail, but cytology has several advantages over histopathology for the investigation of prostatic disease. For example, cytology is a less invasive technique and most often does not require general anesthesia. In addition, the thin monolayer obtained with cytological
smears gives better assessment of cell detail and the identification of the possible etiologic agents [5]. However, as compared to surgical biopsy techniques, the ultrasound guided biopsy is under-exploited. Therefore the study was conducted on renal, prostate and urinary bladder diseases with objective to show the importance of technique and to determine confirmatory diagnosis.

MATERIALS AND METHODS

Ultrasound Guided Needle Biopsy: Ultrasound guided needle biopsy of the kidney was done using Bard Max core disposable biopsy instrument (C.R Bard, Inc. UK,) which had 18 gauge and was 16 cm in length (Fig. 1). The needle had sample notch length of 1.8cm and depth of penetration of 22mm. The patient is placed in left or right lateral recumbency for biopsy of the right or left kidney, respectively. The hair over the biopsy site is removed, the skin is aseptically prepared and sterile coupling gel is applied. The kidneys are scanned for general examination of the renal architecture and for selection of the biopsy site. Once the site of entry for the biopsy needle is determined, the tip of the needle was introduced adjacent to the transducer in the same plane as the sound beam at a skin entrance angle of approximately 45°. After the needle tip was put in caudal pole of the kidney (Fig. 2), a cutting cannula was fired by pressing a button on the gun to obtain the sample. Two biopsy samples were taken from each dog. The procured sample was preserved in 10% formalin until it was processed for histopathological examination.

![Fig. 1: Bard disposable biopsy gun used for renal biopsy (A = the whole needle, B = the sample notch)](image1.png)

![Fig. 2: Area in the caudal pole of the kidney (Arrow) targeted for ultrasound-guided needle biopsy](image2.png)

![Fig. 3: Kidney showing chronic interstitial-and glomerulo-nephritis, along with metastatic (m) calcification and replacement of parenchyma with mature fibrous CT (HE x 100)](image3.png)
Fig. 4A: Kidney showing marked chronic interstitial- and glomerulo- nephritis along with dystrophic (d) and metastatic (m) calcification (HE X 40)

Fig. 4B: Kidney showing marked tubular degeneration and necrosis, marked necrosis and disruption of glomerular tuft along with metastatic calcification in Bowman’s capsule (HE X 100).

Ultrasound Guided Fine Needle Aspiration: Fine needle aspiration was performed in dogs suspected with prostatomegaly using a standard syringe (5 or 10 mL) and needle (22 and 23-gauge) with ultrasound guidance. Little amount of air was drawn into the syringe and the needle was moved into the prostate quickly and negative pressure was applied for few times and the needle was withdrawn. The material collected was then expelled on clean glass microscope slides. Squash preparation was made by squeezing and rotating the aspirate between two microscopic slides. The smears were allowed to dry quickly using artificial heat and stained with Wright-Giemsa stain for microscopical examination.

Surgical Biopsy: About one inch cystotomy incision was made on the dorsal aspect of bladder wall in the least vascular area after taking all aseptic precautions in anesthetized dogs. Incisional full thickness biopsy of urinary bladder wall was collected and preserved in 10% formalin solution for histopathological examination (Fig. 3, Fig. 4A and Fig. 4B).

Tissue Processing for Histopathological Study: Formalin fixed tissue samples were washed overnight in running tap water, then dehydrated through ascending grades of alcohol and cleared with acetone and benzene. The tissues were further processed routinely for paraffin embedding and 5-6 micron thick sections were cut. These sections were stained by routine haematoxyline and eosin stain [6] and evaluated by a pathologist with expertise in nephropathology.

RESULTS AND DISCUSSION

Histopathology of Ultrasound Guided Needle Biopsy of Renal Tissue: Ultrasound guided needle biopsy of renal tissue was sampled from 7 dogs presented with intrinsic renal failure with significant changes in BUN (Mean ± SE = 207.7 ± 33.5 mg/dl) and creatinine (Mean ± SE = 9.97 ± 2.27 mg/dl) values and/or in those cases in which renal parenchyma had been significantly altered in size, echotexture and cortico-medullary demarcation on ultrasonogram. Postmortem kidney tissue was taken from
Fig. 5A: Kidney showing diffuse tubular necrosis (nephrosis) indicative of acute renal failure (HE x 40)

Fig. 5B: Higher magnification of Fig. 5 A showing diffuse tubular degeneration and necrosis along with congestion, more clearly (HE x 100)

two dogs which succumbed to death during the course of treatment. Three chronic renal failures and one acute renal failure were diagnosed based on three ultrasound guided needle biopsy and two post mortem renal necropsy samples. Out of the seven needle biopsy samples, four were processed and three (75%) were found to be diagnostic. Three (42.9%) samples could not be processed due to fragmentation. Authors that compared diagnostic quality of specimens obtained with 14- versus 18-gauge biopsy needles, concluded that excellent-quality renal biopsy specimens with large numbers of glomeruli can be obtained with 14-gauge, double-spring-activated biopsy needles whereas renal biopsy specimens obtained with 18-gauge biopsy needles frequently had few glomeruli and often were crushed or fragmented, increasing the difficulty in making an accurate diagnosis [7]. In this study out of the three biopsy samples found to be diagnostic two revealed chronic renal failures (Fig. 3, Fig. 4A and Fig. 4B) while one showed acute renal failure (Fig. 5A and 5B). The chronic renal failure in one case was characterized by marked chronic interstitial nephritis and glomerulitis with loss of corticomedulary junction while in the other it was evidenced with chronic interstitial nephritis and glomerulonephritis. The acute renal failure was characterized by congestion, tubular degeneration and necrosis with acute glomerulitis and interstitial nephritis. Out of the two post mortem renal tissue samples, one confirmed the acute renal failure diagnosed based on ultrasound guided needle biopsy where as the other one diagnosed chronic renal failure for which ultrasound guided needle biopsy was insufficient for processing. Jeraj et al. [8] reported necropsy diagnosis match with needle biopsy diagnosis in 80 of 82 dogs necropsied. The postmortem renal tissue necropsy which diagnosed chronic renal failure in this study was taken from a dog with end-stage renal failure associated with calcium oxalate renal calculi and the histopathology revealed advanced chronic interstitial nephritis with glomerulitis and glomerulosclerosis, calcification around the bowman’s capsule and thickening of the kidney capsule (Fig. 3). Jeong et al. [9] microscopically examined necropsy samples of kidney tissue from three dogs died of nephrolithiasis and elucidated necrosis of the proximal convoluted tubules and severe calcification in the tubules of the cortex and in the basement membrane.
Table 1: Histopathological lesions of urinary bladder wall of dogs affected with urolithiasis

<table>
<thead>
<tr>
<th>Pathologic lesions observed</th>
<th>Incidence</th>
</tr>
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<tbody>
<tr>
<td>Severe chronic cystitis</td>
<td>4 (26.7%)</td>
</tr>
<tr>
<td>Mild chronic cystitis</td>
<td>5 (33.3%)</td>
</tr>
<tr>
<td>Moderate cystitis</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Fibropapilloma</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Transitional cell papilloma</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Carcinoma in situ</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Thickening with haemorrhage and sloughing of epithelium</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Haemorrhage with loss of epithelium</td>
<td>1 (6.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>15 (100%)</td>
</tr>
</tbody>
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Fig. 6: Fine needle aspiration biopsy of the prostate showing benign prostatic hyperplasia (BPH) characterized by honeycomb-like cells of uniform morphology in a monolayer with coarse cytoplasmic granules (Wright-Giemsa x 100)

Post biopsy complication observed in this study was gross haematuria in one dog which was operated for pyometra and had died during recovery. Another dog with end stage renal disease was euthanized on owner’s request due to poor prognosis. Post mortem evaluation revealed haematoma just caudal to the sampled kidneys in both dogs. In one dog blood clot was also seen in the renal pelvis and urinary bladder. It was reported that small perirenal hematomas are common after renal biopsy [2]. Perirenal hematomas were also reported to occur in about 9% of sampled dogs [3]. Jeraj et al. [8] also biopsied 163 dogs and reported post biopsy complications that included gross haematuria in four dogs, microscopic haematuria in 41 of 53 cases in which urine analysis was performed within 48 hours, hydronephrosis in 3 of 82 dogs necropsied, two severe post biopsy haemorrhages and one death as a direct consequence of biopsy induced haemorrhage.

Ultrasound Guided Fine Needle Aspiration Cytology of Prostate Gland: Ultrasound guided fine needle aspiration biopsy sample was collected from dogs (n=5) suspected of having prostate gland enlargement. Out of the five cases of fine needle aspiration samples, only three (60%) were diagnostic. Of the three cases two were diagnosed with benign prostatic hyperplasia (BPH) (Fig. 6) whereas one case was neutrophilic prostatitis. Mahajan [10] diagnosed eight dogs with ultrasound guided fine needle aspiration biopsy and reported benign prostatic hyperplasia (BPH) and prostatitis in five and one dog, respectively. Parry [11] opined that BPH was the most common canine prostatic disorder and it was present either grossly or microscopically in almost 100% of sexually intact adult male dogs over the age of seven years. Krawiec [12] reported bacterial prostatitis as the second most common prostate disorder in sexually intact male dogs.

Histopathology of Urinary Bladder: Urinary bladder tissue was taken during surgery from 15 dogs operated for cystotomy and various histopathological lesions were recorded (Table 1). All the dogs were affected with urolith except one, which was misdiagnosed as urolithiasis since ultrasound showed acoustic shadowing (Fig. 8) whereas it was found to be tumor during surgery (Fig. 7). Histopathological diagnosis revealed four (26.7%) severe chronic cystitis, five (33.3%) mild chronic cystitis, one (6.7%) moderate cystitis, one (6.7%) fibropapilloma, one (6.7%) transitional cell papilloma, one (6.7%) carcinoma in situ (Fig. 9A, 9B and 9C), one (6.7%) thickening of bladder wall with haemorrhage and sloughing of epithelium and one (6.7%) haemorrhage with loss of epithelium. Among the four severe chronic cystitis cases two had metaplastic changes (Fig. 10A and 10B), one had both metaplastic and hyperplastic changes while one had hyperplasia. Two of the mild chronic cystitis cases had hyperplastic changes while the other one had also cystic cavitation in the bladder wall (Fig. 11). Haemorrhage was observed in seven (46.7%) cases. Waldron [13] reported that the mucosa of urinary bladder responds to chronic inflammation or urinary tract infection by hyperplasia and hypertrophy, which causes thickening of the wall.
Fig. 7: Gross appearance of the carcinoma in situ during cystotomy

Fig. 8: Sonogram of carcinoma in situ showing hyperechoic structure (Arrow) with distal acoustic shadowing (AS) (3.5 MHz microconvex transducer)

Fig. 9A: Histopathology of carcinoma in situ showing highly proliferative epithelial cells (EP) along with marked infiltration of lymphomononuclear cells (L) in the sub epithelial region (HE X 40)

Fig. 9B: Higher magnification of the carcinoma in situ (EP in Fig. 9A) showing multiple layers of dysplastic epithelial cell proliferation (HE x 100)

Fig. 9C: Higher magnification of the lymphoid follicle (L in Fig. 9A) associated with carcinoma in situ showing lymphomononuclear cell aggregation/infiltration (HE x 100)

Fig. 10A: Urinary bladder showing mild chronic cystitis along with marked squamous metaplasia of epithelium and focal haemorrhage (H) (HE x 100)
Ultrasonographic scanning showed cystitis with wall thickness (Fig. 12) in only four (26.7%) of the urolithiasis cases while in one case it had shown carcinoma in situ as hyperechoic mass with acoustic shadowing (Fig. 8). This study is in agreement with the findings of Singh [14] who examined nine dogs with urolithiasis and noted mild to chronic cystitis in most of the cases. It was also reported that mild chronic cystitis was characterized by hyperplastic and/or necrotic changes in the transitional epithelium along with fibroplasias and mild to moderate infiltration of lymphomononuclear cells whereas chronic cystitis was evidenced with marked necrotic/hyperplastic/metaplastic changes in the transitional epithelium along with marked fibroplasias and marked infiltration of lymphomononuclear cells extending down to the tunica muscularis of urinary bladder [14].

CONCLUSION

Ultrasound guided biopsy of renal tissue was helpful in distinguishing between acute and chronic renal failure while ultrasound guided fine needle aspiration cytology was important to distinguish among prostatic affections such as BPH and prostatitis leading to a well informed best patient management. Most dogs with urocrystolithiasis, had also chronic cystitis of varying degree with or without metaplastic changes on histopathological diagnosis, which may not be detected by ultrasonographic evaluation.

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REFERENCES


