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Complications of the Ultrasound-Guided Needle Biopsy of the Kidney in Dogs

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Abstarct: Percutaneous needle biopsy of the kidney may be helpful in formulating prognoses and treatment plans for some disease of kidney. Ultrasound guidance for renal biopsy improves the efficacy of the procedure. Complications of renal biopsy include hematuria, hemorrhage, infection, local peritonitis and severe circulatory dysfunction. The purpose of this study was to evaluate the accuracy of the technique and the possible complications of biochemical, hematological, radiological, ultrasonographical and pathological changes after ultrasound-guided needle biopsy of the kidney. Ten adult dogs were used, an 18 gauge Vim Tru Cut biopsy needle was introduced into the cranial pole of the right kidney using sonographic guidance. Clinical, ultrasonography and radiology, hemathological, biochemical and pathological changes were evaluated after biopsy procedure. All the biopsy samples contained renal tissue. Clinical evaluations showed that changes were all within normal reference ranges. Ultrasonographically and radiologicallly evaluations showed that no changes in kidney sizes. The results of hematological and biochemical evaluations showed that no statistically significant difference ($p>0.05$) between blood samples performed pre-biopsy and post-biopsy was found during the study. The results of this study indicate that the ultrasound-guided renal biopsy can be safely obtained from healthy dogs using 18-gauge Vim Tru Cut biopsy needle. Our study suggests that ultrasound-guided renal needle biopsy procedure has a minimal complication in dogs.

Key words: Ultrasound-guided, needle biopsy, infection, kidney disease

INTRODUCTION

The percutaneous needle biopsy of the kidney is a useful method for evaluating renal disease in dogs (Osborne *et al*., 1996; Groman *et al*., 2004). Renal biopsies play a valuable part in determining specific causes of primary kidney disease (Osborne *et al*., 1969; Jeraj *et al*., 1982; Osborne *et al*., 1996; Drost *et al*., 2000). By detecting the underlying cause for the renal dysfunction, a specific therapy can be formulated (Osborne *et al*., 1969; Osborne *et al*., 1996; Lulich *et al*., 1992; Drost *et al*., 2000). Information obtained by renal biopsy may confirm, support or eliminate diagnostic probabilities formulated on the basis of the history, physical examination, laboratory data and radiographic or ultrasonographic evaluation. Results of biopsy may be helpful in formulating prognoses and treatment plans for some diseases. In cases where renal biopsy permits establishment of a specific diagnosis, knowledge of the etiology facilitates formulation of specific therapy designed to eliminate or control the underlying causes of renal disease. Since, first introduced into veterinary practice nearly 40 years ago, current methods employ improved needle biopsy devices and less invasive methods of accurately directing the biopsy needle into the target tissue (Osborne *et al*., 1996; Groman *et al*., 2004). Several methods for obtaining biopsy samples of kidney in small animals have been described, including blind percutaneous biopsy, the keyhole technique, biopsy during laparatomy or laparascopy and endoscopic biopsies (Grauer *et al*., 1983; Osborne *et al*., 1996; De Rycke *et al*., 1999; Wise *et al*., 2002; Groman *et al*., 2004).

In recent years, ultrasound-guided biopsy of organs such as the liver, kidney, spleen, pancreas, stomach, intestine and prostate became very popular. By direct and constant visualization of the biopsy needle and the target organ, accuracy and safety are improved (Hager *et al*., 1985; De Rycke *et al*., 1999). Moreover, this technique is inexpensive, rapid, minimally invasive and it requires no general anesthesia (Reading *et al*., 1988; De Rycke *et al*., 1999).

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Two types of percutaneous biopsy samples can be obtained from kidney. Aspiration biopsy with needles ranging in size from 18-22 gauge yields cytologic samples. The term fine-needle aspiration biopsy is reserved for the use of needles smaller than 20 gauge. Penetrating kidney with needles of this caliber causes minimal risk of sepsis or extensive bleeding. Disadvantages of this type of needle are its flexibility and its small diameter which make ultrasonographic visualization more difficult (Hager *et al*., 1985; De Rycke *et al*., 1999). Tissue-core biopsy, using larger (usually 14-18 gauge) needles, yields tissue plugs for histopathologic examination (Saitoh, 1984; De Rycke *et al*., 1999).

Available biopsy needles have evolved from the types operated manually with 2 hands (e.g., Franklin-modified Vim-Silverman needles), to the types operated manually with one hand (e.g., Tru-cut® needles) and finally to the automated, spring-loaded types (e.g., Monopty® needles) operated by activating a trigger when the needle is properly positioned.

Ultrasound guidance for renal biopsy improves the efficacy of the procedure (Hager *et al*., 1985; Hoppe *et al*., 1986; Drost *et al*., 2000). Direct detection of the kidney and biopsy needle allows retrieval of a higher quality sample and decreases the severity of complication (Hager *et al*., 1985; Hoppe *et al*., 1986; Nyman *et al*., 1997; Drost *et al*., 2000). Even with ultrasound-guided biopsy performed by experienced individuals, biopsy of the kidneys has the potential to cause further renal damage. In addition to mechanical trauma directly caused by the advancement of the needle through the renal parenchyma, varying degrees of ischemia and infarction also occur secondary to disruption of perfusion of blood through vessels damaged by biopsy needles. Because renal arteries are end-arteries without collateral blood supply, sudden occlusion or transection of any portion of the arterial tree will be followed by ischemia and infarction of parenchyma distal to the site deprived of perfusion. This mechanism (ischemia and infarction) may result in a significantly greater quantity of damage to nephrons than mechanical tissue damage directly caused by the needle. Complications are decreased since, the operator can observe and avoid important structure (Hager *et al*., 1985; Hoppe *et al*., 1986; Nyman *et al*., 1997; Drost *et al*., 2000). Unfortunately, renal biopsies are not without complications. Complications of renal biopsy include hematuria, hemorrhage, an inadequate biopsy sample, infection and arteriovenous fistulas (Osborne *et al*., 1996; Drost *et al*., 2000). The other complications reported following renal biopsy in dogs include local peritonitis and hydronephrosis. Still, the frequency of severe complications is low (Livraghi *et al*., 1983; De Rycke *et al*., 1999). The most important contraindications for renal biopsy are hemorrhagic tendencies and severe circulatory dysfunction.

In this study, we described the technique and results of the ultrasound-guided needle biopsy of the kidney in ten normal dogs. The purpose of this study was to evaluate the accuracy of the technique (presence of targeted tissue regardless of its diagnostic value), the histologic quality of the samples and the possible complications of biochemical, hematological, radiological, ultrasonographical and pathological changes after ultrasound-guided needle biopsy of the kidney.

MATERIALS AND METHODS

Ten healthy male mixed-breed, adult dogs were used. Each dog used in this study, weighed between 20 and 25 kg. All the dogs were raised with a conventional protocol for feeding and husbandry, as well as socialization and routine health care. Ultrasound guided biopsies were performed using a 7.5 MHz mechanical, annular array, transducer (Tanco, sonoline, ESAOTE, Pie Medical, Netherlands). The biopsies were taken with a manual Vim Tru Cut 18-gauge (Gallini, Italy, 1.2×150 mm) disposable tissue-core biopsy needle (Fig. 1). Before biopsy, each dog was examined and weighed and samples of blood were obtained for hematologic and biochemical examinations. A sample of urine was collected of each dog for urine analysis. A lateral radiograph of the abdomen was made to examine the size of the kidney.

Renal biopsy: The dogs were refrained from eating for 12 h before the biopsy procedure. They were sedated with Acepromazine (Neurotrong, Alfasan 1%, Woerden-Holland, 0.1 mg kg^{-1}, IM) and Xylazine (Xylazine 2%, Alfasan, Worden-Holland, 1.1 mgkg^{-1}, IM). After sedation, each animal was placed in left lateral

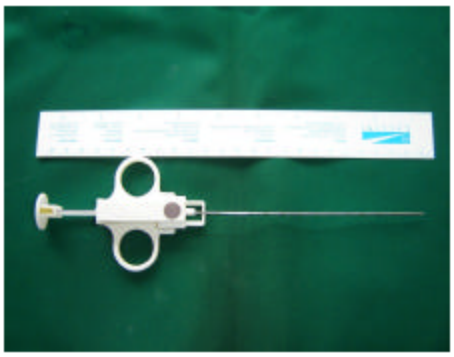

Fig. 1: Manual Vim Tru Cut 18-gauge (1.2×150 mm) disposable tissue-core biopsy needle

recumbency and the biopsy area was clipped and the skin over the right kidney was aseptically prepared. Sterile gel was used to maintain contact between the transducer and the skin.

The biopsy procedure was performed by 2 examinators, one handling the ultrasound transducer and the other the biopsy needle. A small skin incision was made over the cranial pole of the right kidney using a scalpel blade. A pre-biopsy scan of the right kidney was made. An 18 gauge Vim Tru Cut biopsy needle was introduced into the skin hole and advanced into the cranial pole of the right kidney using sonographic guidance. Biopsy from the kidney was made when the examinators could see a clear image of both the needle tip and the target kidney. For the biopsy procedure, the end of outer cannula was inserted 1-2 mm through the renal capsule, while the inner obturator was retracted. Then, it was directed parallel or perpendicular to longitudinal axis of the kidney. Later, with the handle of outer cannula held in position, we advanced the inner obturator into the kidney; after that, we advanced outer cannula into the kidney by pushing the obturator all the way until the spring-loaded trigger fired and then we pulled the needle directly out of the kidney and skin and passed it to the assistant. The sample was placed in 10% buffered formalin. Immediately upon completion of the biopsy procedure, the kidney was examined sonographically for evidence of hemorrhage. Following the procedure, the dogs were observed continuously until they were able to support themselves in the sternal position. Thereafter, they were observed every 10-15 min until they could stand and appeared sufficiently recovered to be fed. The patients were given Penicillin Procaine (20000 Iu kg^{-1}, IM) for 3 days after the biopsy procedure.

Histology: Thin sections of each fixed sample were placed on a microscope slide. Each slide was stained using an H and E stain. Any abnormalities associated with the renal tissue were noted and only animals with normal renal tissue were included in the remainder of the study.

Clinical examination: For the next 24 h post-biopsy, days 2 and 3 after biopsy procedure and every week, the dogs were observed clinically for signs of hemorrhage or hypotension by monitoring mucosal membrane color, capillary refill time, pulse and respiratory rates.

Ultrasonography and radiology examination: Fifteen minuets after the biopsy; days 1, 2 and 3 after biopsy procedure and every week, the sampling site was observed ultrasonographically for any fluid accumulation suggestive of hemorrhage. The next 24 h after the biopsy and also every week after the biopsy procedure, a lateral radiograph of the abdomen was made to examine the size of the kidney.

Hemathological and biochemical examination: Blood from all the 10 dogs for hematology, microscopic evaluation and biochemical examinations were drawn on days 1, 3, 7, 14 and 28 post-biopsy. Blood samples were collected in plastic tubes with no anticoagulant and the serum was separated by centrifugation 2 h after the blood was drawn. The following parameters were determined: urea, keratin, uric acid and total protein. Blood for hematology was collected in plastic tubes containing EDTA. Hematological assays were performed within 2 h of blood collection with an automated cell counter calibrated for canine blood. The following parameters were determined: hematocrit, hemoglobin concentration, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red blood cell (RBC) count, white blood cell (WBC) count and total white blood cell count.

Urinalysis examination: The analysis of urine was performed on days 1, 3, 7, 14 and 28 after the biopsy procedure. Urine samples were collected by sterile catheterization before meals. Urine was collected into clean and preferably sterile containers. The analysis of urine was determined by Dip-stick testing including Glucose, Bilirubin, Ketones, Specific gravity, Blood, PH, Protein, Urobilinogen, Nitrite, Leucocytes and Urine physical characteristics including Colour, Turbidity and Odour.

Pathology examination: Thrity days after the biopsy procedure, the dogs were euthanized by an intravenous injection of an overdose of Barbiturate. Immediately thereafter, the right kidney was removed from the abdomen. The renal capsular surface was examined for evidence of gross scarring and then each kidney was cut transversely into a series of 0.5 cm thick slices. The cut surface of each slice was then examined for gross lesions. Slices were fixed in 10% buffered formalin and each slice was stained using an H and E stain.

Statistical analysis: Statistical analysis was performed with the SPSS software. Test for significant differences in hemathological and biochemical parameters between control and biopsy samples was performed with a Wilcoxon matched-pairs signed rank test. A $p<0.05$ was considered to indicate a statistically significant difference.

RESULTS

Histology: All the tissue samples, including those taken with the needle had sharp-cut edges. All the biopsy samples contained renal tissue (Fig. 2). The histologic quality of the section was good and allowed a detailed study of the glomeruli and differentiation between proximal and distal contorted tubuli. Hisopathologically, the biopsy samples from the kidney were normal.

Clinical examination: Clinically, no signs of pain or discomfort were seen in any of the animals. Clinical evaluation in days 1, 2, 3, 7, 14 and 28 post-biopsy showed that the body temperature, pulse and respiratory rates were all within normal reference ranges. Mucosal membrane color, capillary refill time and their appetite were also normal in all animals. However, no macroscopic hematuria following the biopsy was noticed.

Ultrasonography and radiology examination: Ultrasonographically, through evaluations in different points of time i.e., 15 min after the biopsy; days 1, 2, 3, 7, 14 and 28, no hemorrhage in the biopsy sites was detected, but such bleeding was judged to be clinically inconsequential in one dog immediately after biopsy. Lateral radiographs performed days 1, 7, 14 and 28 showed that no changes in kidney sizes occurred and no renal calculi was detected in graphs.

Hemathological and biochemical examination: The results of hematological and serum biochemical performed before biopsy and days 1, 3, 7, 14 and 28 post-biopsy were within normal reference ranges (Table 1 and 2).

No statistically significant difference ($p>0.05$) between blood samples performed pre-biopsy and post-biopsy was found at any time during the study. The biochemical and hematological values were within normal limits for each dog at every time point throughout the study.

Urinalysis examination: The analysis of urine pre-biopsy and post-biopsy showed that Bilirubin, Ketones, Specific gravity, PH, Protein, Urobilinogen, Nitrite, Leucocytes were normal but in days 1 and 3 after the biopsy procedure a little blood in urine was detected in all cases and in 2 cases there was a little blood in urine at day 7 post-biopsy. Urine physical characteristics including Colour, Turbidity and Odour in all cases were normal after biopsy procedures.

Pathology examination: At necropsy, the inspection of the capsular surfaces of the kidneys showed that before they were sectioned in all dogs, they were normally shaped and symmetric. Grossly evident capsular lesions were limited to small focal scars on the surfaces of the biopsied kidneys. After the kidneys were sectioned, grossly visible biopsy tracts were detected on the cut surface of at least one slice of biopsied kidneys. Light

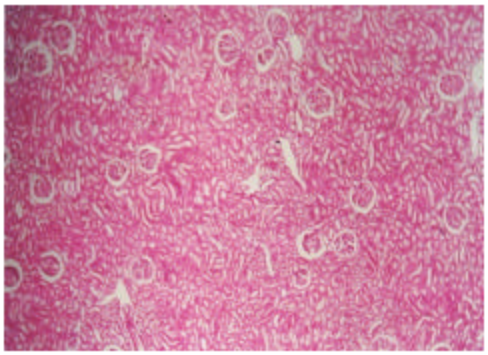

Fig. 2: Photomicrograph of a renal biopsy specimen (Hematoxylin-Eosin ×150)

Table 1: The mean of hematological parameters value in pre-biopsy and post-biopsy

	Pre-biopsy	Day 1	Day 3	Day 7	Day 14	Day 28
Urea (mg dL^{-1})	19.0	20.6	22.1	24.7	26.6	25.2
Keratin (mg dL^{-1})	1.21	1.25	1.31	1.2	1.4	1.27
Uric acid (mg dL^{-1})	1.56	1.5	1.44	1.26	0.97	0.85
Total protein (mg dL^{-1})	5.88	5.75	5.66	5.93	6.3	6.51

Table 2: The mean of biochemical parameters value in pre-biopsy and post-biopsy

	Pre-biopsy	Day 1	Day 3	Day 7	Day 14	Day 28
Hematocrit	47	44.6	44.1	41.6	41.2	42
Hemoglobin	15.82	14.4	14.85	14.02	14.03	14.31
MCV	72.6	71.5	72.3	71.9	72.1	71.4
MCHC	33.67	33.6	33.74	33.8	34.06	34.03
RBC×10^6	6.46	6.1	6.08	5.78	5.72	5.9
WBC	12210	12420	12340	12520	13300	12840
Neu.	8144.4	8390	8387	8682.4	9027.6	9043.4
Lym.	2672.6	2568.7	2444.6	2643.6	2829.4	2701.3
Mon.	709.2	707.4	708.6	546.6	619.6	750.8
Eos.	683.8	691	700	647.4	789.4	680.2

Table 3: Microscopically evaluation of biopsy sites

Case	Inflammatory cells	Proliferation of collagenous connective tissue	Fibrin	Healing process
1	+	+	-	+
2	+	few	-	+
3	+	+	-	+
4	+	+	few	+
5	few	few	-	+
6	+	+	few	+
7	+	+	-	+
8	+	+	-	+
9	+	+	few	+
10	+	+	few	+

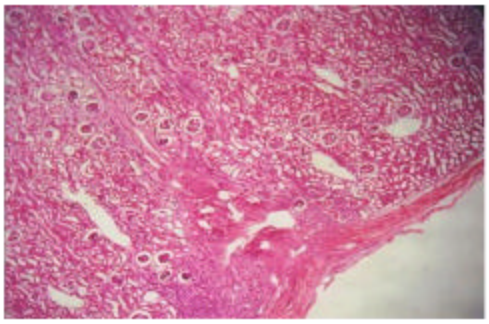

Fig. 3: Photomicrograph wherein a typical lesion caused by needle biopsy is visible (H and E×40)

microscopic lesions were observed only in sections from the biopsied kidney in each dog (Fig. 3).

When lesions were identified, they were focal and characterized by effacement of cortical architecture with tubular atrophy, interstitial proliferation of collagenous connective tissue and infiltrates of mixed mononuclear inflammatory cells (Table 3).

DISCUSSION

Percutaneous needle biopsy of the kidney is a useful method for evaluating renal disease in dogs. Complications of renal biopsy include hematuria, hemorrhage, an inadequate biopsy sample and arteriovenous fistulas. In a study of 86 dogs and 9 cats, almost all animals had self-limiting microscopic hematuria following a renal biopsy which was performed through a keyhole or blind, percutaneous approach (Osborne, 1971). In another study of 181 animals, 120 cats and 61 dogs, all 181 animals had microscopic hematuria following renal biopsy was related more to the biopsy technique and the experience of the person performing the biopsy than to the renal disease affecting the patient (Osborne, 1971; Jeraj *et al*., 1982; Minkus *et al*., 1994).

Studies of the renal response to needle biopsy in dogs and cats generally have not evaluated the biopsy methods most commonly used in veterinary practice and morphologic effects of the biopsy procedure. In this study, we evaluated the complications of clinical, urinalysis, hematological, biochemical, radiological, ultrasonographical and pathological changes of the routinely ultrasound-guided needle biopsy through a Vim Tru Cut with 18-gauge device on the kidneys of healthy dogs.

A variety of needles differing in caliber, length, needle tip configuration and mechanism of sample acquisition is available for percutaneous biopsies. Biopsy needles can be classified as small-caliber (20-25 gauge) or large-caliber (14-20 gauge) needles and also as aspiration or cutting needles. In this study, we used a Vim Tru Cut tissue-core biopsy needle with 18-gauge. We presume this needle provide high-quality histopathologic specimens, reduce the number of passes needed to obtain adequate tissue for diagnosis and decrease the procedural time without increasing the complication rate. All renal biopsy specimens that were examined by light microscopy contained renal parenchyma. Other studies have reported obtaining renal tissue from dogs in 40-97% of percutaneous ultrasound-guided biopsy attempts (Hager *et al*., 1985; Hoppe *et al*., 1986; Yamamoto *et al*., 1991; Leveille *et al*., 1993; De Rycke *et al*., 1999). This difference might be ascribed to various factors including the equipment used, different criteria for adequacy, the positioning of the animal and the increased experience of the operators.

Our study suggests that ultrasound-guided renal needle biopsy procedure has a minimal complication in normal dogs. Needle biopsies of kidneys invariably cause some degree of subcapsular or perirenal hemorrhage (Nash *et al*., 1983; Hoppe *et al*., 1986; Yamamoto *et al*., 1991; De Rycke *et al*., 1999), but in this study, no hemorrhage by ultrasonography 15 min after the biopsy procedure was detected and ultrasonographical examinations in days 1, 2 and 3 after the biopsy procedures showed that no hemorrahage in the biopsy sites occurred.

In addition, in this study, the renal ultrasound-guided biopsy technique minimized the risk of damage to large renal vessels and renal pelvis, but in patients with a hemorrhagic tendency or hypertension should not be biopsied unless these abnormalities can first be adequately controlled. Also, renal size should be considered when evaluating the risks of needle biopsy of the kidney. Reduction in the thickness of renal cortex as a consequence of chronic progressive renal disease increases the likelihood of needle damage to larger intrarenal vessels such as the arcuate arteries. Radiological evaluations showed that in all cases the kidney sizes were normal and no renal calculi or clots were detected. Evidence of gross hematuria was not observed following biopsy in any dog, but other researchers have reported that gross hematuria has sometimes been observed after ultrasound-guided needle biopsies have been obtained from kidneys of healthy dogs (Yamamoto *et al*., 1991; De Rycke *et al*., 1999). In biochemical and hematological evaluations, we did not find any significant statistical results ($p>0.05$). Urinalysis showed a little blood in urine in days 1, 3 and 7 after the biopsy procedure and it was normal because renal tissue was damage by the biopsy needle. Grossly and

macroscopically, biopsied kidneys were otherwise healthy and only a few small discrete scars could be identified. Light microscopic changes observed within the confines of the focal lesions that were induced by the renal biopsies were healing in the kidney tissue.

The results of this study indicate that the ultrasound-guided renal biopsy can be safely obtained from healthy dogs using 18-gauge Vim Tru Cut core biopsy needles that generate minor renal lesions and no detectable changes of clinical, biochemical, hematological, radiological, ultrasonographical, pathological and urinalysis in biopsied kidneys. Overall, this study showed that the ultrasound-guided biopsy of the kidney through 18-gauge Vim Tru Cut needle appears to be a rapid and safe technique. Orientation of the tissue samples during sectioning appeared to significantly influence the quality of the histologic sections.

By way of summation, we suggest that the following recommendations be taken into account in all renal biopsy patients:

- In pre-biopsy, a full biochemical and hematological work-up including a coagulation profile with bleeding time is advisable.
- During biopsy, appropriate intravenous fluid therapy is required in order to maintain production and to also reduce the risk of obstruction from any pelvic blood clots.
- In post-biopsy, it is recommended to evaluate for evidence of internal bleeding for up to 24 h post biopsy and an appropriate course of antibiotics can be given prior to or immediately after biopsy.

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