Pyelonephritis in small animals

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INTRODUCTION

Pyelonephritis refers to inflammation of both the renal pelvis and parenchyma, whereas pyelitis reflects inflammation of the renal pelvis only. Whilst most cases of pyelonephritis originate from ascending infection of the lower urinary tract (LUT), less commonly cases may arise from haematogenous dissemination of infection. Ascending urinary tract infection (UTI) probably occurs more commonly than is clinically suspected in dogs and cats since many patients are asymptomatic or have only signs of lower urinary tract infection (LUTI). The condition may be acute or chronic, and unilateral or bilateral, although many cases are bilateral.

CAUSES

Ascending UTI and pyelonephritis are usually caused by aerobic bacterial organisms, most commonly *Escherichia coli* and *Staphylococcus* sp., and less commonly with species of *Proteus*, *Streptococcus*, *Klebsiella*, *Enterobacter*, and *Pseudomonas aeruginosa*. The risk of ascending UTI is increased by vesicoureteral reflux (VUR), congenital renal dysplasia, diabetes mellitus, hyperadrenocorticism and renal failure. Exogenous corticosteroid administration, urethral catheterisation, urine retention, uroliths and urinary tract neoplasia are additional predisposing factors.

Although uncommon, pyelonephritis can result from descending or haematogenous infection from a bacterial infection elsewhere (e.g. endocarditis), and infrequent systemic mycobacterial infections may result in a granulomatous nephritis. Other infectious agents rarely associated with pyelonephritis include fungi and algae, e.g. *Blastomyces*, *Aspergillus*, *Cryptococcus*, *Fusarium*, *Candida* and *Prototheca* species in countries where these agents are endemic. Although rare causes, these agents deserve some consideration due to increased intercontinental pet travel.

PATHOGENESIS

The normal urinary tract is inherently resistant to ascending infection, with natural host defence mechanisms including its mucosal defence barriers, vesicoureteral valves, ureteral peristalsis and an extensive renal blood supply. Hence, any underlying impairment in these defences will predispose to ascending UTI. Abnormalities that increase the risk for secondary bacterial UTI include decreased urine concentration, altered urine composition, VUR, urolithiasis, poor urine flow in the renal pelvis or ureter, abnormalities of local urothelial mucosal defence mechanisms, and impaired immune responses.

Normally the vesicoureteral valve maintains unidirectional urine flow from the upper to the lower tract. VUR involves abnormal reflux of urine from the urinary bladder to the kidney. Although minimal VUR occurs during micturition, it occurs to a greater degree under conditions of increased intracystic pressure, such as with obstructive lesions of the urinary tract lumen (e.g. neoplasia, calculi). Urine stasis associated with obstructive lesions or neurogenic urinary bladder dysfunction following spinal cord injury increases the risk of ascending UTI. Similarly, endotoxin produced by gram negative bacteria infecting the urinary tract, inhibits ureteral peristalsis, enhancing VUR. Structural anomalies (e.g. ectopic ureters, vestibulovaginal stenosis, recessed vulva and pelvic bladder) have also been implicated as causal factors in dogs with lower urinary tract disease. Renal failure predisposes to UTI due to reduced urine concentration. Altered urine composition (in urolithiasis, metabolic disorders such as diabetes mellitus and polyuria) also predisposes to UTI.

The renal medulla is very susceptible to infection due to its relatively poor blood supply. Additionally its interstitium has a high osmolality that inhibits neutrophil function, and a high ammonia concentration that inhibits complement activation. Consequently, upon bacterial colonisation of the renal pelvis, the medulla is readily infected. Organisms ascend within the collecting duct system leading to tubular epithelial necrosis and inflammation that progressively extends throughout the tubular system and interstitium, radiating from pelvis to cortex.

Urinary bacterial load alone does not always correlate with

the degree of inflammation or signs and extent of pyuria. Causative bacteria may possess specific virulence factors (VF's) that enhance their ability to adhere to and colonise the urothelium. *Escherichia coli*, the most common cause of cystitis and acute pyelonephritis in dogs and cats, produces VFs important to the development of pyelonephritis, and isolates associated with UTI possess more than those from healthy animals. Factors known to be more specific to the pathogenesis of pyelonephritis include: haemolysin, various adhesins, pyelonephritis-associated pili, cytotoxic necrotising factor-1, aerobactin and secreted autotransported toxin.
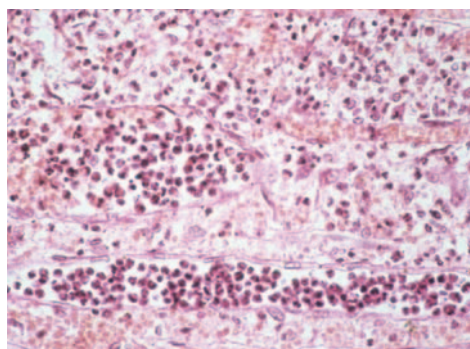
Fig. 1: *Microscopic changes of acute pyelonephritis: Tubule epithelial cells are lost or attenuated, and dilated lumina are filled with neutrophils that extend into the adjacent haemorrhagic parenchyma. Photograph courtesy of Professor Michael H Goldschmidt .*
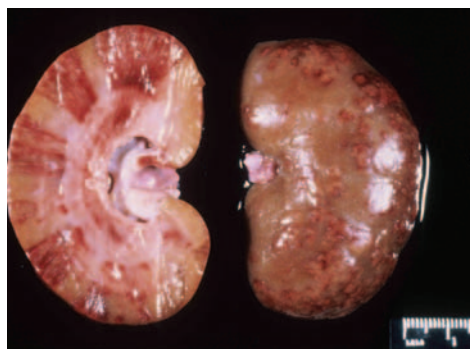
Fig. 2: *Gross changes of acute pyelonephritis: on cut surface, irregular radiating streaks of cortical haemorrhage are seen, and the pelvis is mildly dilated. On the external capsular surface, irregular small purulent foci have a narrow peripheral zone of haemorrhage. Photograph courtesy of Professor Michael H Goldschmidt .*

Impaired cellular and humoral immune responses are important in the pathogenesis of pyelonephritis by predisposing the animal to infection. Cushingoid patients, or those receiving parenteral corticosteroids or cytotoxic drugs, can be immunocompromised, and immune-mediated diseases such as systemic lupus erythematosus (SLE) predispose to secondary pyelonephritis especially in advanced stages of the condition. Feline leukaemia virus or feline immunodeficiency virus are additional important causes of immunosuppression to consider. Impaired immune competence is considered important in development of disseminated conditions such as systemic aspergillosis, mycobacteriosis and algal infections.

CLINICAL FINDINGS

Clinical signs of pyelonephritis are variable with no abnormalities found on physical examination in some cases. Often signs progress unrecognised until renal failure ensues, and although acute renal failure may occur, pyelonephritis is more commonly associated with chronic renal failure (CRF). Acute pyelonephritis can be associated with depression, anorexia, pyrexia, vomiting, and lumbar or abdominal pain especially during renal palpation. Chronic pyelonephritis may be sub-clinical or associated with intermittent pyrexia, anorexia and depression, or result in uraemia in cases of extensive renal parenchymal destruction. Polydypsia and polyuria may occur due to reduced urine concentrating ability through interference with the renal medullary countercurrent mechanism, with bacterial endotoxin also implicated in this. Signs of LUTI such as dysuria, pollakiuria, stranguria, haematuria, and malodorous or discoloured urine may be evident. Absence of urinary changes does not rule out pyelonephritis as infection can localise to the renal parenchyma, producing no abnormalities on urinalysis and negative urine cultures.

DIAGNOSIS

Attaining a definitive diagnosis of pyelonephritis can be difficult. Although history and clinical findings may be suggestive of acute pyelonephritis, they are often not helpful in chronic cases. Consequently clinical diagnosis is often presumptive and based on results from haematology, serum chemistry, urinalysis, urine culture and imaging procedures.

The presence of urinary leucocyte casts is consistent with renal inflammation. Positive bacterial culture from urine obtained by cystocentesis is yielded in most acute cases, although in chronic cases cultures are often negative, and multiple cultures may be required to confirm UTI. Unfortunately, the leucocytosis may resolve with chronicity, making chronic pyelonephritis difficult to diagnose. Similarly serum chemistry profile is usually normal unless CRF develops.

Radiography, intravenous urography (IVU) and ultrasonography are helpful diagnostic techniques, and all may demonstrate renomegaly in acute pyelonephritis and small, irregularly contoured kidneys in chronic cases. IVU may additionally demonstrate dilated, blunted calices or dilated, tortuous ureters. In addition to providing an estimate of renal size, ultrasound examination of the

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kidney can allow assessment of the renal parenchyma. Non-specific changes such as hyperechogenicity of the renal cortex, decreased corticomedullary demarcation (Fig. 3) and dilation of the renal pelvis may be evident, and compressive or obstructive lesions such as neoplasia may also be identified. Due to lack of specificity, however, ultrasonography is of limited diagnostic value alone, and must therefore be used to complement rather than replace other diagnostic tests.
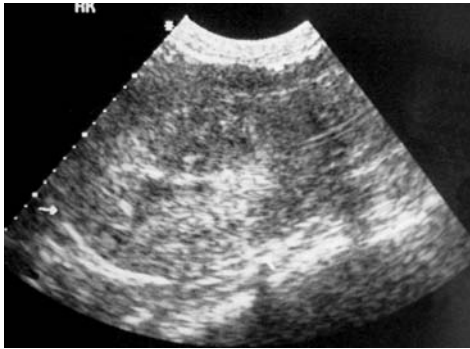
Fig. 3: *Renal ultrasonographic changes in a cat with pyelonephritis: loss of corticomedullary definition is evident. Photograph courtesy of Martha Cannon.*

Although dilation of the renal pelvis and proximal ureter is common, their absence does not completely exclude pyelonephritis. Similarly, these changes are not pathognomonic for pyelonephritis, since ultrasonographic features of hydronephrosis can be similar.

Definitive diagnosis requires either a positive culture of renal pelvic fluid, or renal histopathology and thus necessitates the use of invasive procedures. Nephro–pyelocentesis involves renal pelvic fluid aspiration, and can be performed percutaneously using ultrasound guidance or during exploratory surgery. Cytologic examination and bacteriologic culture (aerobic, anaerobic, and fungal) of this fluid can identify pyelonephritis. Fluid samples should ideally originate from the renal pelvis and not the urinary bladder, since urine in these regions may contain different microorganisms with different antimicrobial sensitivities. Occasionally, urinary bladder contents may even be sterile, despite the presence of bacteria in the renal pelvis.

For histopathology, the renal biopsy specimen should comprise both the renal cortex and medulla; however, such biopsies procedures are technically problematic due to the risk of severe haemorrhage from the arcuate vessels and the potential for infarct. Microscopic lesions of pyelonephritis are usually most severe in the inner medulla, and necrosis and loss of the transitional urothelium may be associated with interspersed fibrin, neutrophils, necrotic debris and bacterial colonies. Renal tubular epithelium is also necrotic

and lumina contain neutrophil casts and bacteria. Neutrophils infiltrate the adjacent interstitium which may be haemorrhagic and oedematous. Renal papillary necrosis may also be present, and inflammation eventually progresses to involve the cortex. With lesion chronicity, neutrophil numbers are reduced, with increasing numbers of lymphocytes and plasma cells, and eventual fibrosis.

TREATMENT OPTIONS

Broad-spectrum parenteral antibiotic treatment (four to six weeks' minimum duration) should be initiated, and purulent material removed from the renal collecting system as soon as possible. The latter will decrease intrarenal pressure to improve renal function and perfusion, and facilitates tissue antibiotic penetration. Antibiotic choice should be based on results of renal pelvic urine culture and sensitivity testing, should achieve good serum and urine concentrations and preferably not be nephrotoxic.

Unfortunately since there is often poor antibiotic penetration into the renal medullary parenchyma, chronic pyelonephritis may be difficult to treat. A urine sample may be cultured seven to ten days after treatment initiation, and then repeated one week post-antibiotic therapy, and monthly thereafter until three consecutive negative cultures are obtained.

Fig. 4: *An engorged ureter in a case of pyelonephritis. Photograph courtesy of Carl Gorman.*

Percutaneous ultrasound-guided pyelocentesis has been described as a therapeutic option in addition to its diagnostic use. Nephrectomy remains a relatively common treatment for chronic pyelonephritis, especially in cases where the affected kidney is non-functional secondary to urine outflow obstruction.

Animals with renal failure require appropriate therapy, and cases of chronic or recurrent infection require investigation for predisposing causes.

CONCLUSION

Many dogs lack specific signs attributable to pyelonephritis, and any animal with UTI could be affected. Consequently, consider pyelonephritis as a differential diagnosis for any animal with fever of unknown origin, polydipsia/polyuria, CRF, or lumbar/abdominal pain. Haematuria, pyuria, proteinuria, a positive urine culture, cylindruria, a dilated renal pelvis, leucocytosis with a left shift and pyrexia provide supportive evidence of pyelonephritis, but are not always present. Since unresolved chronic cases may lead to CRF, and recurrent cases may be asymptomatic, diagnostic follow–up is important to ensure complete resolution of the pyelonephritis. Although primary pyelonephritis can occur, most cases are secondary, and hence an underlying aetiology should be investigated when this condition is confirmed. Overall the prognosis for patients with pyelonephritis is fair to good, and many return to normal health unless there is uncorrected underlying cause for UTI.

TABLE 1: Predisposing factors for pyelonephritis in small animals

DISEASE CATEGORY	CONDITIONS
Congenital/Hereditary	Ectopic ureters Renal dysplasia
Infectious	Bacterial UTI Systemic bacterial, mycobacterial, fungal or algal infections FeLV or FIV infection
Inflammatory	Inflammation secondary to uroliths or urethral catheters
Immune compromise	Immune-mediated disease (SLE) Corticosteroid therapy Cushing's disease FeLV or FIV infection
Metabolic	Endocrinopathies (Cushing's disease, diabetes mellitus) Renal failure (Any condition leading to polyuria)
Iatrogenic	Exogenous corticosteroid therapy Urethral catheterisation
Obstructive	Urinary tract neoplasia Calculi Inflammatory foci
Trauma/Degenerative	Spinal trauma with neurogenic urinary bladder dysfunction

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These multiple choice questions are based on the above text. Readers are invited to answer the questions as part of the RCVS CPD remote learning program. Answers appear on page 99. In the editorial panel's view, the percentage scored, should reflect the appropriate proportion of the total time spent reading the article, which can then be recorded on the RCVS CPD recording form.

1. The most common cause of ascending urinary tract infection in small animals is:

   a. *Klebsiella* sp.
   b. *Escherichia coli*
   c. *Prototheca zopfii*
   d. *Aspergillus terreus*
   e. *Pseudomonas aeruginosa*

2. Which of the following is true?

   a. Renal pelvic dilation is pathognomonic for pyelonephritis
   b. Most cases of chronic pyelonephritis resolve spontaneously
   c. Clinical signs are often lacking in animals with pyelonephritis
   d. Pyelonephritis is always associated with a positive urinary culture
   e. Pyelonephritis is more commonly associated with acute renal failure

3. All are true except:

   a. All animals with pyelonephritis are azotaemic
   b. Pyelonephritis reflects inflammation of the renal pelvis and parenchyma
   c. Any condition causing polyuria may predispose to urinary tract infection
   d. Haematogenous dissemination of infection is an uncommon cause of pyelonephritis
   e. Bacterial load alone does not always correlate with degree of urinary tract inflammation.