Ultrasound diagnosis of cystic cystitis with von Brunn's nest in two cats

Morgane Moreau[1] [ID], **Philippe Haudiquet[1]**, **Clémence Monton[2]**, **Fabien Arnault[3]** **and Renaud Jossier[1]**

Abstract

Case series summary Two cats were initially evaluated for recurrent dysuria and haematuria, which were unresponsive to antibiotic and anti-inflammatory treatments. An abdominal ultrasound revealed focal wall thickening with a severe hypoechoic multicystic parietal lesion at the bladder apex. Surgical excision of the lesion (apical cystectomy) led to complete resolution of the clinical signs in both cases. The histological findings were consistent with large cystic von Brunn's nest hyperplasia, along with foci of small glandular metaplasia. Urine and tissue cultures were negative. Cystitis cystica was diagnosed. No recurrence was reported within 2 years of surgery in both cases.

Relevance and novel information This case series illustrates the occurrence and ultrasonographic features of a type of cystitis rarely described in animals: cystic cystitis with von Brunn's nest hyperplasia. These lesions result from chronic irritation and can lead to recurrent cystitis if not excised. Cystic cystitis has previously been described histologically in cats. To the authors' knowledge, this is the first report of macroscopic apical cystic cystitis with pre-treatment ultrasound diagnosis. Surgical resection of the hyperplastic von Brunn's nests appeared to be curative in both cases.

Keywords: Von Brunn's nests; cystic cystitis; ultrasound; glandular cystitis

Introduction

Von Brunn's nests are defined as groups of urothelial cells derived from an invagination of the hyperplastic bladder surface into the superficial lamina propria.[1,2] This histological variation of the urothelium occurs not only in humans, but also in cats and dogs.[1,3] Macroscopically, these lesions are associated with cystic cystitis (minor form) and glandular cystitis (major form). Both are benign inflammatory conditions affecting the bladder. Cystic cystitis is characterised by bladder mucosa modifications connected to the development of degenerative cysts inside von Brunn's nests. Glandular forms are associated with epithelial metaplasia at the edge of the cysts, resulting in mucus production.[4] These macroscopic manifestations are seldom seen in cats, with only two previously documented cases of cystic and glandular cystitis.[1,5] Both forms are commonly identified in humans.[4,6] Here we describe two cases of cystitis with von Brunn's nest hyperplasia and the preoperative ultrasound findings.

Case series description

Case 1

A 10-year-old male castrated Turkish Angora cat was initially presented to a primary care veterinarian with a

[1]VetRef ANICURA, Beaucouzé, France
[2]Orciane, Vandoeuvre-lès-Nancy, France
[3]LorraineVet ANICURA, Ludres, France
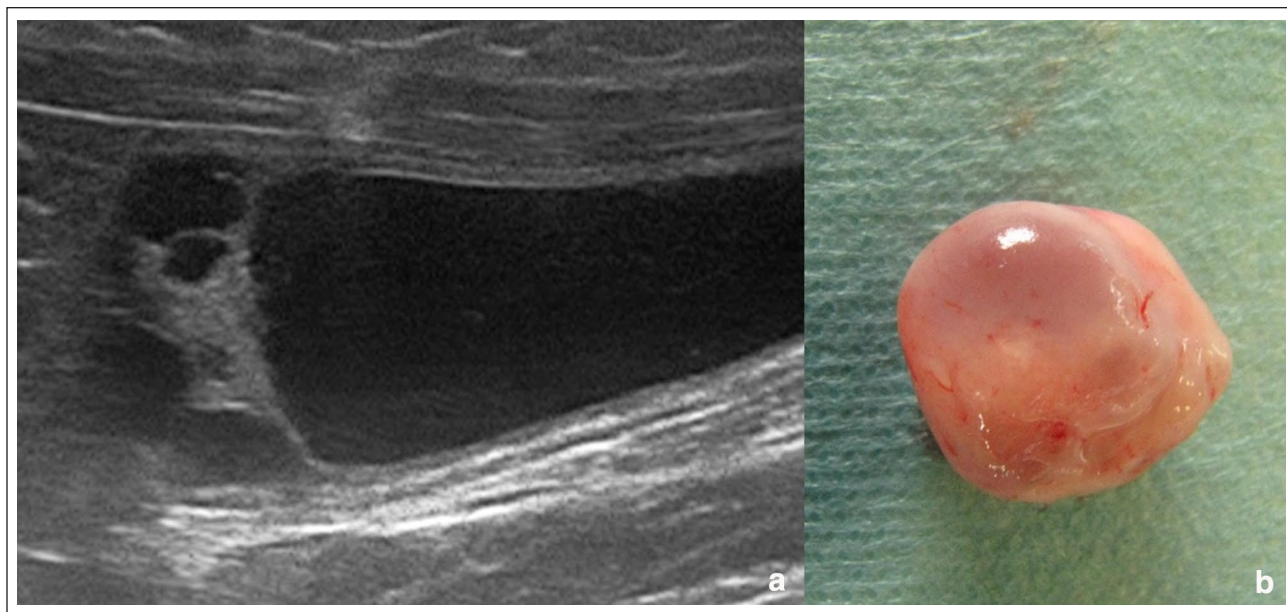
Corresponding author:
Morgane Moreau DVM, Clinique Vetref, 7 rue James Watt, 49070 Beaucouzé, France
Email: vet.moreau@gmail.com

Figure 1 Case 1. (a) Urinary bladder longitudinal ultrasound image. Focal interruption of the continuity of the bladder mucosa was noted at the cranial pole by anechoic polycystic deformation of the bladder apex. Beside the lesion, the bladder wall appears normal. (b) Bladder apex excision

2-week history of haematuria and pollakiuria. The cat had a history of recurrent cystitis, experiencing an average of two episodes per year in the past 9 years. Typically, clinical improvement occurred with antibiotic (amoxicillin–clavulanic acid 12.5 mg/kg PO q12h) and non-steroidal anti-inflammatory drugs (meloxicam 0.05 mg/kg q24h). Nutritional management and multimodal environmental enrichment using an anti-anxiety pheromone (Feliway; CEVA) and nutritional supplements (Cysticat PO; Sogeval) were initiated in an attempt to reduce recurrence but ultimately proved unsuccessful. A 5-day course of marbofloxacin (1.9 mg/kg PO q24h) and meloxicam (0.05 mg/kg PO q24h) was prescribed; however, no significant improvement was reported.

The cat was referred for further imaging. Clinical examination revealed caudal abdominal discomfort. A chemistry panel and a complete blood cell count were unremarkable.

Abdominal ultrasonography revealed a parietal apical bladder polycystic anechoic deformity, approximately 1.5 cm in diameter, with no tissue neoformation. A focal interruption of the continuity of the bladder mucosa was noted at the cranial pole (Figure 1). No additional abnormalities were observed, including the urethra, ureters and local lymph nodes. We hypothesise that these changes were consistent with an intramural urachal remnant and diverticulum with an atypical local inflammatory complication, given the presumed chronicity of the diverticula and the multiple episodes of cystitis. Urinalysis revealed haematuria and a urine culture was negative. Crystals were not identified.

Apical cystectomy was performed, confirming a macroscopic parietal inflammatory appearance, but failing to identify the suspected diverticulum (Figure 1). The cat was maintained on isoflurane after induction with morphine (0.2 mg/kg IV), midazolam (0.2 mg/kg IV) and alfaxolone (2 mg/kg IV). Bladder histology revealed marked hyperplasia of the urothelium with foci of glandular metaplasia, cysts and von Brunn's nests (Figure 2). Therefore, cystic cystitis with small glandular proliferation was diagnosed. The tissue sample bacteriology was negative.
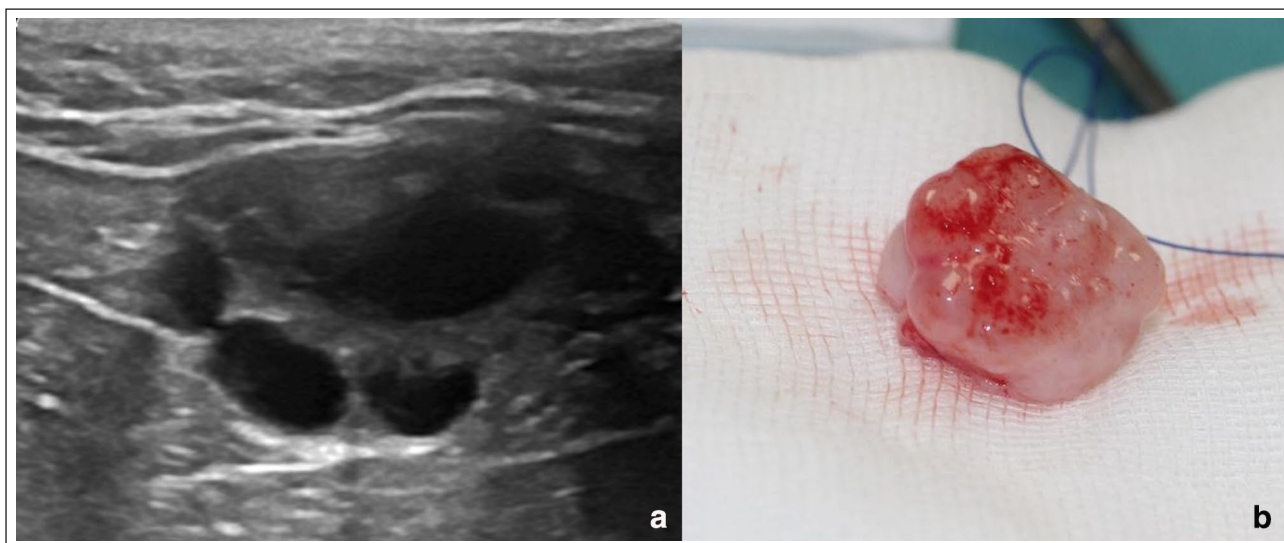
Pain was managed postoperatively with buprenorphine (0.02 mg/kg IV) for 8 h and meloxicam (0.05 mg/kg SC then PO q24h) for 6 days. Ultrasound follow-ups were performed, and a progressive normalisation of the bladder wall was observed. No postoperative complications were reported, and no recurrence was documented during the 2 years after the diagnosis.

Case 2
A 2-year-old female spayed cat aged approximately 2 years was presented with recurrent haematuria and pollakiuria that had improved after recent antibiotic treatment (amoxicillin–clavulanic acid, for 10 days, unknown dosage) and anti-inflammatory drugs (meloxicam 0.05 mg/kg q24h for 3 days). The animal's medical history was incomplete, owing to a former shelter stay. An ultrasound examination revealed a multicystic nodular deformity of the bladder apex, measuring 20 mm in diameter, with anechoic content and fine echogenic septa (Figure 3). No parietal thickening was noted. Based on
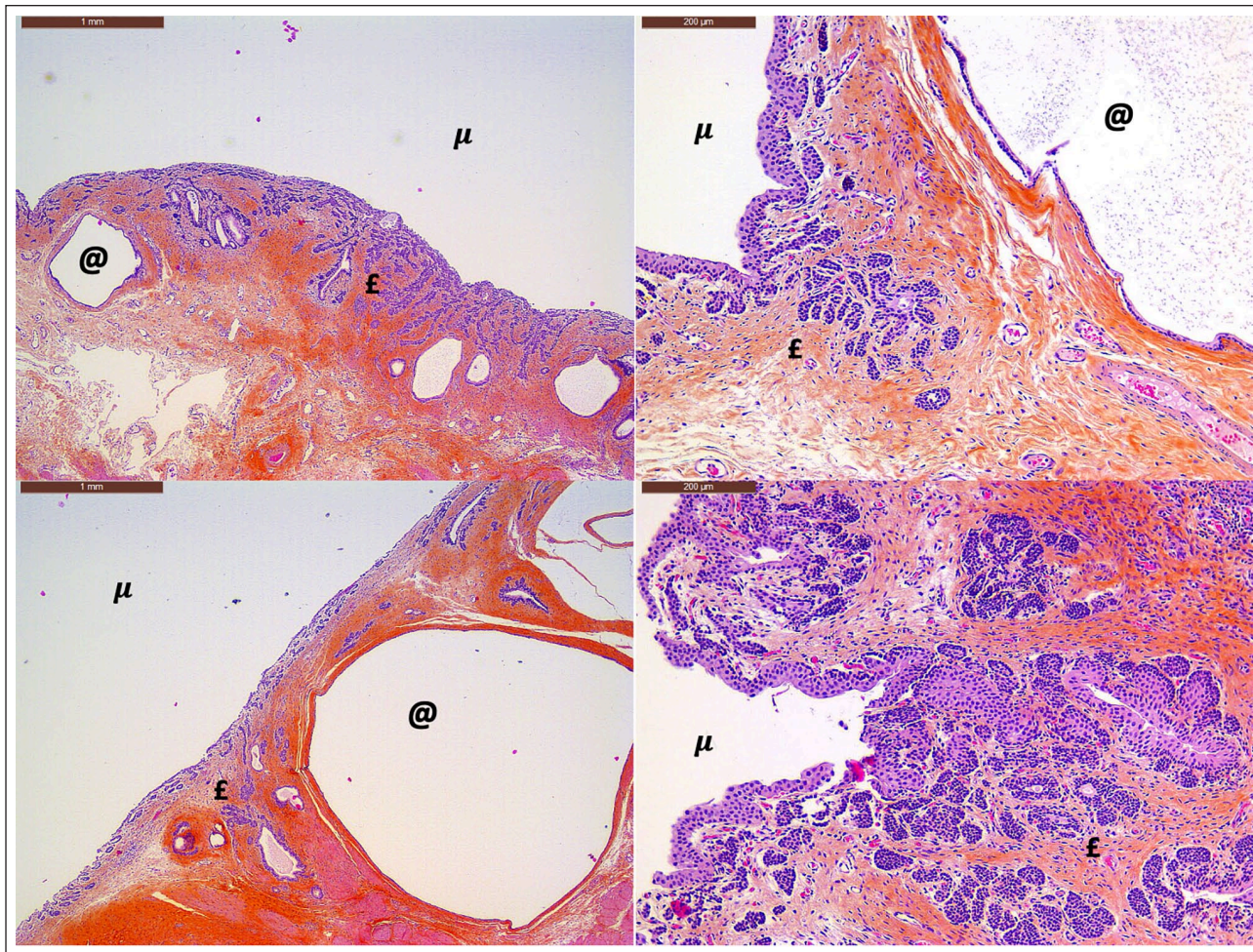
Figure 2 Case 1. Urinary bladder wall histology. @ = cystic dilatation of the lumen of von Brunn's glands; μ = bladder lumen; £ = von Brunn's gland hyperplasia. Image courtesy of Dr Murielle Hurion Vebio, Gentilly

Figure 3 Case 2. (a) Urinary bladder longitudinal ultrasound image. Anechoic polycystic deformation of the bladder apex. (b) Bladder apex excision

the experience of the previous case, cystic and/or glandular cystitis with von Brunn's nest hyperplasia was suspected. The cat was premedicated with morphine (0.2 mg/kg IV) and anaesthesia was induced with propofol (4 mg/kg IV) and diazepam (0.2 mg/kg IV). Anaesthesia was maintained with isoflurane, and partial cystectomy was performed. Pain was managed postoperatively with buprenorphine (0.02 mg/kg IV q8h) for 24 h and meloxicam (0.05 mg/kg SC then PO q24h) for 3 days.

The bacteriology results were negative. Histology confirmed a large cystic hyperplasia of von Brunn's nests with small foci of glandular metaplasia. No complications or recurrence were documented during the 2 years after the diagnosis.

Discussion

Von Brunn's nests have been reported in the urethra, ureters and renal pelvis of humans, dogs and cats.[6–9] They are considered a common histological variation, affecting up to 80% of normal canine bladders and 93% of normal human bladders.[6,9] The presence of these microscopic nests in bladders is known to be a possible cause of idiopathic cystitis or bladder pain in humans and cats.[10] A study revealed that von Brunn's nests were present in 40% of cats' bladders with idiopathic cystitis, compared with only 6% in a control population.[10] There appears to be a male predominance in humans and female in dogs. They can occur at any age, with a predisposition in older people.[3,11,12] In humans, a histological observation of microscopic von Brunn's nests has also been described at the periphery of urothelial carcinomas. There has been a debate about whether these nests represent pre-neoplastic changes;[1,13] however, evidence to support this hypothesis is lacking in the veterinary literature.[9]

The proliferation of von Brunn's nests can rarely lead to macroscopic cystitis, known as cystic and/or glandular cystitis (CGC). The pathogenesis is poorly understood, and two theories have been put forward in humans. Some authors suggest that classical CGC is a metaplastic transformation of the epithelium in response to chronic irritation. The urothelium proliferates into von Brunn's nests in connective tissue, which then degenerate into mucin-secreting cysts. Irritating factors may include stones, prolonged urinary stasis, urinary tract infection and repeated urinary catheterisation.[7] Pelvic lipomatosis due to intrapelvic overgrowth of mature fatty tissue has been suggested as a predisposing factor in humans, favouring urinary stasis and inflammation.[11]

Other authors have presumed that intestinal germ cells migrate into the urinary tract when it separates from the rectum during the fifth week of embryonic development. Colonic glandular cells are then located within the urinary chorion and, after inflammatory stimulation, may proliferate in a pseudotumorous cluster, known as the florid form.[4] Intestinal-type CGC has not yet been reported in animals, and it was absent in these two cases, thus supporting the first metaplastic hypothesis.

The two cats with cystic cystitis reported here were presented with non-specific signs, including stranguria, haematuria and pollakiuria. In humans, lesions are often located in or around the trigone and neck of the bladder and they can become large enough to cause obstructive urinary signs or hydronephrosis.[2] Two case reports of CGC in cats identified ureterovesical junction obstruction,[5,7] leading to hydronephrosis. As in the first case described in cats,[1] our two cases presented apical bladder locations, thus reducing the risk of urinary obstruction.

Ultrasonography is routinely used to investigate urinary tract signs. It is a non-invasive and reliable option to explore recurrent lower urinary diseases and a useful tool in the diagnosis of cystitis. It also provides further information regarding the kidneys and ureters. In human medicine, minor cystic forms are usually characterised by well-demarcated nodular anechogenic parietal lesions, mostly smaller than 5 mm in diameter, with an intact urothelial surface.[14] A case of cystic cystitis characterised by a large cyst measuring 5.8 cm in diameter has been described in humans.[14] Such cysts are commonly seen during ultrasound examinations in humans, but to date, have not been described in animals. Previous cases of CGC with a predominant cystic form in dogs and cats were surgical discoveries or only histological diagnoses. The two cases reported here are the first ultrasonographic descriptions of cystic cystitis in cats. Based on the ultrasound features, a benign origin of the lesions was first suspected, given the low proliferative component and large cavitary lesions.

In case of major glandular cystitis, ultrasound reveals tissue proliferation. Such proliferative lesions complicate the diagnosis, as they mimic bladder neoplasia in imaging studies. Differential diagnoses include tumours, such as urothelial carcinomas, papillomas and adenomas with a cystic component.[7,15] Such differentiation can be critical, as urothelial carcinoma is an aggressive malignancy. The coexistence of glandular cystitis and malignant bladder tumours is estimated to be in the range of 10–42% in humans.[12] According to a recent study carried out on a large cohort of cats, the trigone appears to be the most common location for bladder neoplasia.[16] Although some apical tumours have been described, the apical location of the lesion supports our hypothesis of a benign process in our two cats.

Other imaging modalities are less useful in animals for the diagnosis of CGC. Radiographs can be useful in the diagnosis of some urolithiasis, but their diagnostic value remains limited. CT can be used to assess for local and distant invasion in case of suspected neoplasia. The cystoscopic features are non-specific and can vary from an inflammatory unremarkable appearance to a large

bladder cyst or mass. A definitive diagnosis requires histopathological examination in all cases, because CGC typically has inconclusive cystoscopic and ultrasound features. The value of cystoscopic biopsy has not been established, with some authors favouring direct complete excision,[7] particularly in cats, whose small size makes sampling difficult. Given the cystic feature of the lesion, a more challenging histological diagnosis on a partial sample than a complete lesion can be assumed.

Surgery is the treatment of choice in humans, and this option was curative in our two cases. Removal of the aggravating factor, along with concurrent antibiotics and chemoprophylaxis, can result in resolution of the cystic inflammation.[2,11] In most cases, as in these two cases, no underlying inflammatory cause was identified. In the absence of aetiological factor identification or response to medical treatment, surgical intervention is necessary.[11,12] A previous case of glandular cystitis has been described in a cat, secondary to a chronic foreign body. Severe hyperplasia of the epithelium formed a heterogeneous, discretely cavitated mass with a urethral catheter at the centre. Removal of the foreign body resulted in complete resolution of the clinical signs.[5] After treatment, it is recommended that patients with CGC are monitored for recurrence through clinical examination, urinalysis and ultrasound. In humans, a follow-up of approximately 2 years is recommended.

Conclusions

Our cases provide the first preoperative ultrasound descriptions of cystic cystitis with von Brunn's nest hyperplasia. It should be considered in cats with recurrent lower urinary tract signs and an apical cystic bladder mass observed on abdominal ultrasound. The prognosis after medical treatment and surgical management is good.

ORCID iD Morgane Moreau https://orcid.org/0009-0001-5575-5158

References

1 Zachary JF. **Cystitis cystica, cystitis glandularis, and Brunn's nests in a feline urinary bladder.** *Vet Pathol* 1981; 18: 113–116.

2 Zhu JXG, Gabril MY and Sener A. **A rare case of recurrent urinary obstruction and acute renal failure from cystitis cystica et glandularis.** *Can Urol Assoc J* 2012; 6: 72–74.

3 Gelberg HB. **Urinary bladder mass in a dog.** *Vet Pathol* 2010; 47: 181–184.

4 Zhang T, Yin SF, Feng WB, et al. **Florid cystitis glandularis (intestinal type) with mucus extravasation: two case reports and literature review.** *Front Surg* 2023; 10. DOI: 10.3389/fsurg.2023.1048119.

5 Agut A, Carrillo JD, Soler M, et al. **Cystitis glandularis in a cat.** *J Feline Med Surg* 2014; 16: 363–365.

6 Wiener DP, Koss LG, Sablay B, et al. **The prevalence and significance of Brunn's nests, cystitis cystica and squamous metaplasia in normal bladders.** *J Urol* 1979; 122: 317–321.

7 Militerno G, Bassi P, Bettini G, et al. **Von Brunn's nests in the ureter of two cats.** *Open J Vet Med* 2017; 7: 162–167.

8 Ahmad A, Imbisat MZ, Ranjan N, et al. **Cystitis glandularis – rare cause of urinary bladder mass: case report and literature review.** *Afr J Urol* 2022; 28: 11.

9 Lage AL, Gillett NA, Gerlach RF, et al. **The prevalence and distribution of proliferative and metaplastic changes in normal appearing canine bladders.** *J Urol* 1989; 141: 993–997.

10 Kullmann FA, McDonnell BM, Wolf-Johnston AS, et al. **Inflammation and tissue remodeling in the bladder and urethra in feline interstitial cystitis.** *Front Syst Neurosci* 2018; 12: 13. DOI: 10.3389/fnsys.2018.00013.

11 Wong-You-Cheong JJ, Woodward PJ, Manning MA, et al. **From the archives of the AFIP – inflammatory and non-neoplastic bladder masses: radiologic-pathologic correlation.** *Radiographics* 2006; 26: 1847–1868.

12 Harrison S, Lamchahab H, Djamal J, et al. **Cystitis glandularis: a rare benign condition presenting as bladder tumor.** *Open J Urol* 2018; 8: 336–343.

13 Jones E, Palmieri C, Thompson M, et al. **Feline idiopathic cystitis: pathogenesis, histopathology and comparative potential.** *J Comp Pathol* 2021; 185: 18–29.

14 Potts S and Calleary J. **Cystitis cystica as a large solitary bladder cyst.** *J Endourol Case Rep* 2017; 3: 34–38.

15 Manini C, Angulo JC and López JI. **Mimickers of urothelial carcinoma and the approach to differential diagnosis.** *Clin Pract* 2021; 11: 110–123.

16 Griffin MA, Culp WTN, Giuffrida MA, et al. **Lower urinary tract transitional cell carcinoma in cats: clinical findings, treatments, and outcomes in 118 cases.** *J Vet Intern Med* 2020; 34: 274–282.