Case Report

A case report: colonic and urethral infectious granuloma associated with fungal pathogen and extended-spectrum beta-lactamases-producing *Escherichia coli* in a Thai Bangkeaw dog

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Abstract

A 4-year-old, neutered male Thai Bangkeaw dog presented with clinical signs of diarrhea, pollakiuria and a mass-like lesion between the bulbus glandis and testicular sac 2 weeks after castration. Ultrasound (U/S) revealed a mass-like lesion from the urethra expanded to the colon. A computerized tomography (CT) scan indicated that the mass had invaded the colon and nearby lymph node. Bacterial culture from the lesion identified infection caused by extended-spectrum beta-lactamases-producing *Escherichia coli* (ESBL-producing *E. coli*). Using fine needle aspiration (FNA) of the mass-like lesion, cytology showed irregular, negatively stained hyphal structures. Given the very large size of the lesion, surgical excision could not be performed. A combination of itraconazole, terbinafine and carprofen was prescribed for medical treatment. Additionally, amikacin was given following antimicrobial susceptibility testing. However, there was no improvement after medical treatment. Ultimately, euthanasia was selected. The gross findings revealed an area of swelling primarily located at the caudoventral abdomen due to marked edema and hemorrhage with a focal tract lesion from the focus of the hair skin defect through the urethra. Regionally, the descending colon was markedly thickened. Microscopically, the intestinal wall was obliterated by nodular and coalescing aggregates of granulomas surrounding many indiscernible hyphae with non-parallel walls, non-dichotomous branching and rare septations. Organisms were negatively stained with Periodic Acid Schiff (PAS) but strongly highlighted by Grocott's methenamine silver (GMS) staining. The findings were consistent with intestinal pythiosis. However, macerate tissue culture for fungi and oomycetes was negative.

Keywords: Granuloma, fungal infection, colitis, urethral obstruction, ESBL-producing *E. coli*

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Introduction

A granuloma is a type of chronic inflammation defined by organized aggregates of mononuclear cells such as macrophages indicating a histiocytic inflammation. A cluster of epithelioid histiocytes accumulate around the site of the inflammation or necrotic area. This inflammation develops in various organs, inside or outside, if there are agglomerations of inflammation-like tumors called granulomas (de Brito and Franco, 1994; Shah *et al*., 2017). The etiologies of granulomatous disorders can include bacterial, fungal or parasitic infections, as well as autoimmune diseases and certain toxins or irritants (Amarnath *et al*., 2021).

Canine fungal granulomas can develop in a variety of organs including the brain, gastrointestinal tract and urogenital tract. They are most commonly found in dogs living in outdoor settings with water resources (i.e. lake, river, lagoon or marsh). The common fungal organisms that induce granuloma in the gastrointestinal tract are oomycetes, including genus *Pythium* and *Lagenidium* (Grooters *et al*., 2003; Jaeger *et al*., 2002; Reagan *et al*., 2019). These infectious granulomas induce obstructive symptoms including chronic diarrhea, hematochezia, tenesmus, weight loss and cachexia. The most effective treatment is mass removal surgery combined with medicinal therapy. Nevertheless, euthanasia may be considered in uncontrolled cases (Grooters *et al*., 2003). Herein, we describe an uncommon granulomatous disease in a Thai Bangkeaw dog with a mixed bacterial-fungal infection in Thailand. This granuloma caused a progressive lesion by invading the gastrointestinal and urinary systems. A multidrug-resistant bacteria was identified, however, the fungal culture method revealed a negative result.

Clinical description

A 4-year-old male, Thai Bangkeaw dog weighing 12.5 kg presented to Prasu-arthorn Animal Hospital, Faculty of Veterinary Science, Mahidol University, with a history of diarrhea, pollakiuria and 3 cm mass-like lesion on the penis. The dog was fed a home-cooked diet. It spent time outdoors and swam freely in a pond. This dog received a necessary health program consisting of vaccination, de-worming and ectoparasite control. Physical examination showed that the dog had normal vital signs. Palpation revealed a firm, irregular mass-like lesion cranially to the castration wound and caudally to the bulbus glandis with smooth preputial mucosa. Abdominal palpation found a tubular mass-like structure at the caudo-dorsal abdomen. Urinary catheterization indicated urethral stenosis at the level of a mass-like lesion. Rectal palpation discovered a smooth rectal mucosa with a mass-like lesion underneath.

Hematological profiles revealed mild normocytic normochromic anemia, leukocytosis with neutrophilia and hyperproteinemia. Normal biochemistry and urinalysis profiles were observed. X-ray could not identify the margins of the mass-like structure (data not shown). Ultrasonography (Fig. 1) showed the descending colon thickening with a mass-like lesion and poorly-defined wall layer. Additionally, this lesion also involved the urethral tissue. A computerized tomography scan (CT scan) (Fig. 2) indicated a colonic wall mass with expansion to the urethra as well as distal urinary tract and penis, medial iliac, colic and superficial inguinal lymphadenopathy. Fine needle aspiration from the mass-like lesion on the penis showed severe suppurative inflammation with intralesional fungal/algal hyphae (Fig. 3). However, the fungal culture from the aspirated sample revealed only bacterial growth on Sabouraud dextrose agar with chloramphenicol (SDA^+) but no fungi were observed. The bacterial culture showed an extended-spectrum beta-lactamases-producing *Escherichia coli* (ESBL-producing *E. coli*) that was susceptible to imipenem, amikacin, gentamicin, neomycin, doxycycline and tetracycline. Because surgical intervention was not possible due to the progressive lesion, medical treatment was considered. The dog received a combination of itraconazole, terbinafine and amikacin together with symptomatic treatment. However, there was no improvement after medical treatment. Due to financial constraints, the intricacy of surgery and a lack of additional care time, the owner ultimately requested euthanasia. During gross examination, the haired skin over the caudoventral abdomen involving prepuce and scrotum was markedly edematous, resulting in regional, fairly well-demarcated, swelling approximately 20x15x5 cm in diameter with multiple areas of variably discrete dark red discoloration. At the base of the penis, the haired skin was disrupted and had an approximately 1.5x2 cm in diameter discrete hole circumferentially rimmed by a slightly indented white to dark red discolored area with an approximately 2 cm long track-like space extending deep into the urethra (Fig. 4A). The anus was markedly dilated and the corresponding rectal mucosa was bright red. In the section through the region of haired skin swelling, the subcutis was markedly expanded by edema with areas of yellow discoloration and dark red ecchymoses as well as associated accumulations of dark red transparent serosanguineous fluid and blood clot. There were small amounts of yellow-tinged watery fluid and white creamy material within the abdominal cavity. The descending colon measuring 20 cm in length was regionally dilated, the serosa was widely covered by thin mats of yellow fibrin and the colonic wall and the mucosa was diffusely thickened resulting in a corrugated mucosal surface with hundreds of variably discrete areas of brown to mottled dark red discoloration (Fig. 4B). The omentum was diffusely red with an increased number and prominence of vascular injections. The urinary bladder mucosa were variably red. The section through the swollen scrotum revealed multifocal areas of hemorrhage scattered throughout the cut surface of both testicles. Microscopically, the tunica muscularis of the large intestine was widely obliterated by densely cellular, transmural, nodular and coalescing aggregates of granulomas composed of predominant epithelioid macrophages with often-laden scant brown granular pigment and many multinucleated giant cells (Langerhans and foreign body type) intermixed with variable infiltrates of lymphocytes and plasma cells dissecting variably dense bands of granulation tissue and fibrosis. Within the nodular aggregates of

granulomas, there were central accumulations of eosinophilic cellular debris and high numbers of poorly discernible, 6-10 µm wide hyphae with non-parallel walls, non-dichotomous branching and rare septations. These organisms were highlighted by Grocott's methenamine silver (GMS) staining but negatively to faintly stained with Periodic Acid Schiff (PAS) staining (Fig. 5A and B). In addition, the previously-described mixed inflammatory cells with associated variably loose edematous bands of granulating fibrosis extended to and tracked along the intestinal serosa and obliterated the adjacent omental adipose tissue. The histomorphologic features described, combined with the results of special staining, were consistent with intestinal pythiosis. However, the macerate tissue culture of the large intestinal specimen for fungi and oomycetes yielded no growth. Fungal and oomycete culture from the macerated large intestinal specimen was negative.

Figure 1 Ultrasonography showed the large intestine thickened with a mass-like lesion, poor defined wall layer. This mass-like lesion entered the pelvic area and was involved entirely with urethral tissue from prostatic urethra up to the penile urethra (*arrow head*).

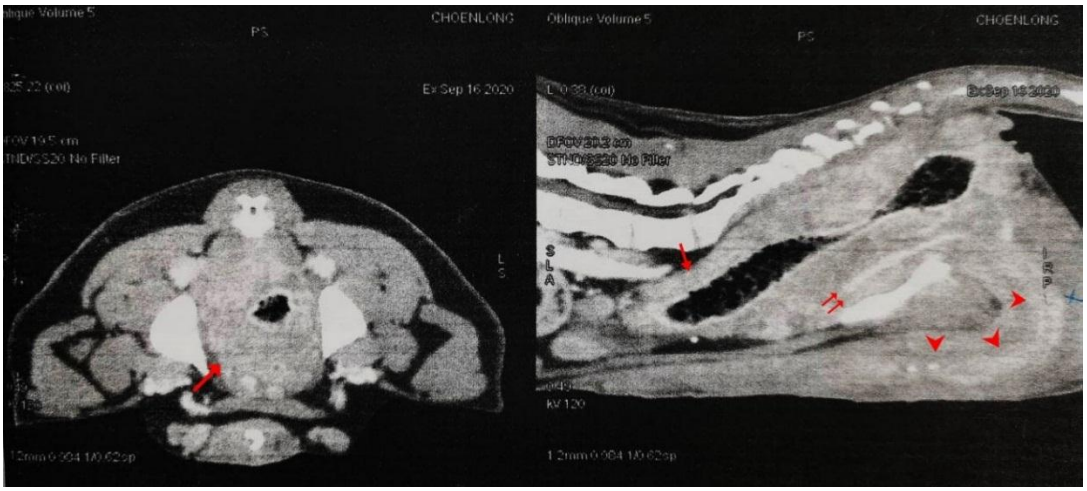

Figure 2 CT scan revealed marked thickening of colonic wall (*arrow tail*) with ventrally deviated urethra (*double arrow*) and penis (*arrow head*).

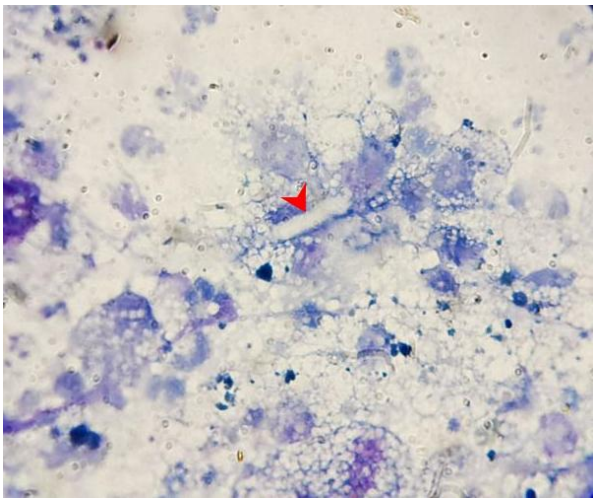

Figure 3 FNA mass shown as transparent slightly refractile hyphae (*arrow head*).

Figure 4 (A) a granuloma at prepuce until scrotal sac (*arrow head*) and a focal fistula track extending from an area of haired skin defect to the urethra noted immediately prior to the scrotum. (B) Colonic wall and the mucosa (*arrow*) were diffusely thickened resulting in a corrugated mucosal surface with hundreds of variably discrete areas of brown to mottled dark red discoloration.

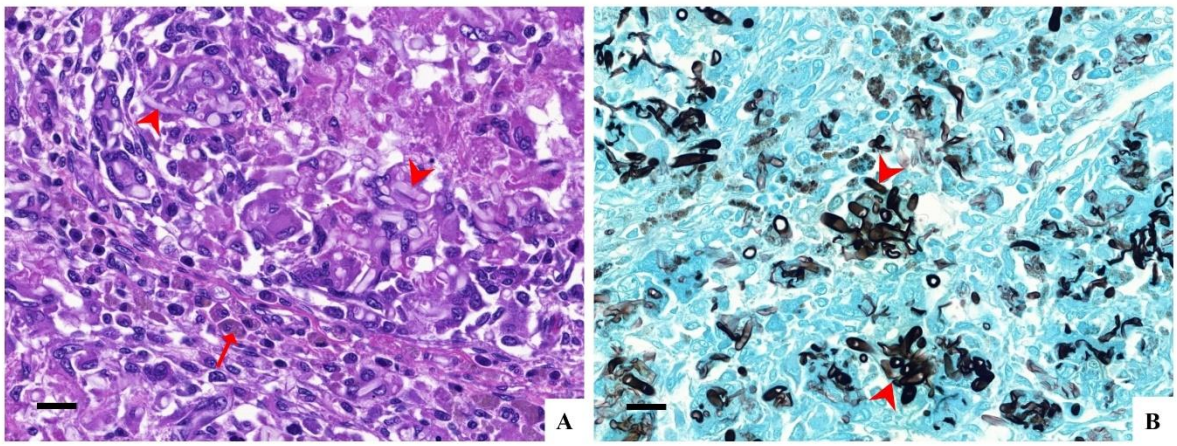

Figure 5 (A) H&E stain colon section 40x, 20 µm scale bar showed granulomatous with associated variable interstitial and perivascular infiltrates of lymphocytes and plasma cells. granulomas were composed of numerous epithelioid macrophages (*arrow*) and surrounding occasional central areas of devitalization and variable numbers of 4-15 um in diameter, extracellular and intrahistiocytic, poorly discernible hyphae (*arrow head*). These hyphae exhibit non-parallel, transparent, refractile walls with rare septation and had irregularly acute to right or non-dichotomous branching. (B) Additional sections of the above-described colon and soft tissue specimen specially stained with GMS stain 40x, 20 µm scale bar were examined. Many hyphae are highlighted by GMS (*arrow head*).

Discussion

Canine granuloma in the gastrointestinal (GI) tract can be described as a chronic localized inflammatory reaction to a persistent foreign entity, especially microorganisms. Bacterial infection-induced gastrointestinal granuloma has been documented as granulomatous colitis, which has previously been associated with the presence of invasive *E. coli* in Boxers and French Bulldogs (Manchester *et al*., 2012). In other breeds, infectious granuloma is frequently associated with fungi such as *Histoplasma* sp., *Candida* spp., and *Basidiobolus ranarum*, as well as oomycetes such as *Pythium insidiosum* and *Lagenidium* sp. Fungi can be identified using culture methods; however, accurate identification of oomycetes requires an immunodiagnostic, molecular or proteomic assay. Patients with endocrinopathies and immunodeficiency disorder are predisposed to fungal infection. Histoplasmosis has been reported to occur in the small and large intestines, while candidiasis has been commonly diagnosed in the small intestine. Additionally, both pathogens can be identified by cytology or histopathology in which the yeasts and fungal hyphae infiltration are observed using modified Wright–Giemsa stain and H&E staining (Duchaussoy *et al.,* 2015; Berle *et al.,* 2020). Gastrointestinal basidiobolomycosis has been identified as a rare fungal disease in immunocompetent hosts. One study reported that *Basidiobolus ranarum* infected the colon of a Shiba dog, causing granulomatous inflammation. H&E staining revealed numerous fungal hyphae varying in size up to 30 µm in diameter within the granuloma. GMS also revealed the visibility of the fungal hyphae and spore-like structures (Okada *et al*. 2015). *Pythium insidiosum* and *Lagenidium* sp. are oomycetes or fungal-like microbes that cause granuloma with intralesional hyphae in the GI tract. However, their histological staining abilities are distinct. In *Lagenidium* sp., thick-walled hyphae of varying diameters (7-25 µm) with occasional septate can be observed in H&E, PAS, and GMS stained sections. Besides that, vascular encroachment by hyphal organisms has been noticed. On the other hand,

non-parallel walls and rare septate hyphae of *P. insidiosum* are not stained by basic dye and PAS reaction positive hyphae are identified by GMS stain with diameters ~3–10 μm (Grooter *et al.*, 2003; Firmino *et al.*, 2017; Reagan *et al.,* 2019; Shmalberg *et al.,* 2020; Hummel *et al.,* 2011).

A lower urinary tract infection presented with the following frequencies: bacterial urinary tract, infection micturition disorders, urolithiasis, prostatic disease and traumatic problems (Mendóza-López *et al.,* 2017). *Candida* spp., *Aspergillus* spp., *Blastomycosis* spp., and *Cryptococcus* spp. have been reported in fungal infections of the lower urinary tract. *Candida albicans* was the most commonly detected by microscopic examination of urine sediment and isolated by urine culture. However, granulomatous inflammation was not developed (Jin and Lin, 2005; Olin and Bartges, 2015). Fungal granuloma in the urinary tract has been reported with *Penicillium* sp., *Curvularia* sp., and *Scedosporium apiospermum* inducing urinary tract obstruction. The fungal elements of these organisms were observed in H&E stained sections (Soonthornsit *et al.,* 2013; Kochenburger *et al.,* 2016; Herbert *et al.,* 2019). One report showed the lower urinary tract obstruction was caused by prostatic pythiosis. Postmortem examination revealed that the prostate gland was enlarged and adhered dorsally to the serosa of the descending colon within the pelvic canal. GMS-positive hyphae were detected in histopathology (Jaeger *et al.,* 2002).

In this report, the original margin of the granuloma was vaguely delineated by the gross lesion, which indicated a mass-like lesion involving the descending colon and urethra. Microscopically, the intestinal wall was obliterated by nodular and coalescing aggregates of granulomas surrounding many indiscernible hyphae with non-parallel walls, non-dichotomous branching and rare septations. The hyphal structure was stained negatively with PAS but was strongly highlighted by GMS staining, suggesting that *Pythium* sp. was the most likely pathogen in this dog. Additionally, the infection was referred to as immunocompromised because the first lesion was found to be of a surgical size. More reports contributed to postoperative immunosuppression and increased susceptibility to septic complications (Dąbrowska and Słotwiński, 2014).

Pythium is a waterborne fungus-like organism or parafungus belonging to the kingdom Stramenopila, class Oomycetes. This pathogen causes skin, GI tract, reproductive tract and ocular infection in humans and animals. In dogs, *Pythium insidiosum* commonly causes progressive gastrointestinal and skin granuloma which are formed mass like lesions in infected tissue and penetrate to nearby organs (Jaeger *et al.,* 2002; Fernandes *et al.,* 2012; Chindamporn *et al.,* 2020; Chitasombat *et al.,* 2020). Identifying the organism is challenging, as a H&E stain poorly stains the *P. insidiosum* hyphae while GMS can reveal the fungal elements with typically ~3–10 μm wide, thick walls, few septa and close to right-angle branches. Detection of anti-*P. insidiosum* antibody using serological assays have high sensitivity and high specificity using enzyme-linked immunosorbent assay (ELISA) or immunocPhromatography (ICT). On the other hand, an immunodiffusion test (ID) is insensitive for diagnosis. The serodiagnostic test is also limited due to the multi-step procedures involved and complexity, and we should be aware of false-negative results especially in ocular pythiosis. Using a culture method, *P. insidiosum* grows well on standard agar types, such as SDA, that a creamy or colorless-to-white flat colony can be observed in a few days. However, temperature control is necessary to ensure viability and the failure to isolate (Chareonsirisuthigul *et al.,* 2013; Chitasombat *et al.,* 2020). The gold standard for identifying *P. insidiosum* is molecular analysis, particularly real-time PCR, which has 100% sensitivity and 100% specificity (Keeratijarut *et al.,* 2015). Additionally, using nested PCR improves the sensitivity of detecting *P. insidiosum* DNA in formalin-fixed, paraffin-embedded tissue sections in dogs (Elshafie *et al.,* 2022). In this report, the morphology of hyphae in tissue sections was consistent with oomycetes, particularly *Pythium* sp. However, the pathogen could not be isolated using culture methods. Because the serological assay was not available in our hospital, we attempted to extract pathogen DNA from paraffin-embedded tissue sections; however, the quality of the DNA was insufficient for PCR testing.

ESBL-producing *E. coli* has been recognized as a multidrug-resistant bacteria which produces a group of enzymes that mediate resistance to most β-lactam antibiotics, including extended-spectrum cephalosporins and monobactams. ESBL-producing *E. coli* was isolated from the gastrointestinal tract in healthy dogs with prevalence of 25.84% (Thepmanee *et al.,* 2018; Huang *et al.,* 2020). Additionally, a high prevalence was also reported in hospitalized patients, livestock wastewater and the environment (Runcharoen *et al.,* 2017). This pathogen frequently causes urinary tract, reproductive tract and skin infections. MDR *E. coli*-associated granulomatous colitis has been noticed in Boxers and French Bulldogs. Pathogens typically are observed in clusters within macrophages (Manchester *et al.,* 2021). In this report, Thai Bangkeaw did not have a breed predisposition to granuloma and antibiotic treatment did not reduce the size of the lesion. Therefore, the secondary infection of ESBL-producing *E. coli* in this case might have been caused by the environment or feces after contamination of the skin wound. Antibiotic susceptibility testing revealed that ESBL-producing *E. coli* was susceptible to imipenem, meropenem, amikacin, gentamicin and nitrofurantoin (Huang *et al.,* 2020, Gharavi *et al.,* 2021). Similar to our report, amikacin could be used for the treatment of ESBL-producing *E. coli* infection. *E. coli* has been recognized as a soluble fungicidal factor-producing bacteria inhibiting *C. albicans* growth *in vitro* (Cabrel *et al.,* 2018). Additionally, an antifungal protein isolated from *E. coli* BL21 (PPEBL21) completely inhibited the expression of a 16 kDa protein in *Aspergillus fumigatus* (Yadav *et al.,* 2010). Because ESBL-producing *E. coli* may inhibit the growth of fungi or oomycetes on SDA^{+} agar, this could be one of the reasons why the fungal or oomycete pathogen was not detected using the fungal culture technique in this dog. Other possibilities were that 1) the fungus in the tissue was not viable at the time of

sampling, 2) the tissue was collected from two locations, with one sample passing to microbiology and the other to pathology (Guarner and Brandt, 2011). However, all processes and outcomes were meticulously reviewed again by the authors and the results showed that everything had been done appropriately. Taken together, we suggest that a PCR assay may be useful for fungal identification when cultures are negative or due to bacterial contamination.

Here, we reported on granuloma with an uncommon lesion caused by fungi or oomycete infection with secondary infection of ESBL-producing *E. coli* involving the descending colon and lower urinary tract. Unfortunately, no fungal or oomycete species were identified using the culture method, while a bacterial colony was observed in SDA^{+}, implying that a negative fungal culture result could not rule out fungal or oomycete infection. Therefore, even if the fungal culture is negative, antifungal therapy should be considered if the lesion and cytology suggest a fungal disease. The possible routes of infection were considered to be 1) infection from the GI tract with penetration to the urethra, 2) infection from the urethra with penetration to the large intestine, 3) infection at the surgical site and penetration to the urethra, intestine, and abdominal wall. According to the treatment, using antifungal drugs alone could not inhibit the progression of the disease. Therefore, surgical intervention combined with antifungal drugs should be considered and the pathogen species should be ascertained in this case.

References

Amarnath S, Deeb L, Philipose J, Zheng X, Gumaste V 2021. A Comprehensive Review of Infectious Granulomatous Diseases of the Gastrointestinal Tract. Gastroenterol Res Pract. 2021, 8167149.

Cabral DJ, Penumutchu S, Norris C, Morones-Ramirez JR, Belenky P 2018. Microbial competition between Escherichia coli and Candida albicans reveals a soluble fungicidal factor. Microb Cell. 5:249-255.

Chareonsirisuthigul T, Khositnithikul R, Intaramat A, Inkomlue R, Sriwanichrak K, Piromsontikorn S, Kitiwanwanich S, Lowhnoo T, Yingyong W, Chaiprasert A, Banyong R, Ratanabanangkoon K, Brandhorst TT, Krajaejun T 2013. Performance comparison of immunodiffusion, enzyme-linked immunosorbent assay, immunochromatography and hemagglutination for serodiagnosis of human pythiosis. Diagn Microbiol Infect Dis.,14(1).

Chávez-Peón Berle E, KuKanich K, Biller D 2021. Ultrasonographic findings of gastrointestinal histoplasmosis in dogs. Vet Radiol Ultrasound. 62: 108– 115.

Chindamporn A, Kammarnjessadakul P, Kesdangsakonwut S, Banlunara W, 2020. A case of canine cutaneous pythiosis in Thailand. Access Microbiol 2, acmi000109.

Chitasombat MN, Jongkhajornpong P, Lekhanont K, Krajaejun T 2020. Recent update in diagnosis and treatment of human pythiosis. PeerJ. 8:e8555.

Dąbrowska AM, Słotwiński R 2014. The immune response to surgery and infection. Cent Eur J Immunol 39:532-537.

Duchaussoy AC, Rose A, Talbot JJ, Barrs VR 2015. Gastrointestinal granuloma due to Candida albicans in an immunocompetent cat. Med Mycol Case Rep. 10:14–17.

Elshafie NO, Hanlon J, Malkawi M, Sayedahmed EE, Guptill LF, Jones-Hall YL, Santos AP 2022. Nested PCR Detection of *Pythium* sp. from Formalin-Fixed, Paraffin-Embedded Canine Tissue Sections. Vet Sci. 9(8):444.

Fernandes CPM, Giordani C, Grecco FB, Sallis ESV, Stainki DR, Gaspar LFJ, Garcez Ribeiro CL, Nobre MO 2012. Gastric pythiosis in a dog. Revista Iberoamericana de Micología. 29:235-237.

Firmino M, Frade M, Alves RC, Maia L, Olinda R, Ximenes RG, Souza AP, Dantas AFM 2017. Intestinal intussusception secondary to enteritis caused by *Pythium insidiosum* in a bitch: Case report. Arq Med Vet Zootec. 69:623-626.

Gharavi MJ, Zarei J, Roshani-Asl P, Yazdanyar Z, Sharif M, Rashidi N 2021. Comprehensive study of antimicrobial susceptibility pattern and extended spectrum beta-lactamase (ESBL) prevalence in bacteria isolated from urine samples. Sci Rep. 11: 578.

Grooters AM, Hodgin EC, Bauer RW, Detrisac CJ, Znajda NR, Thomas RC 2003. Clinicopathologic findings associated with *Lagenidium* sp. infection in 6 dogs: initial description of an emerging oomycosis. J Vet Intern Med. 17:637-646.

Guarner J, Brandt ME 2011. Histopathologic diagnosis of fungal infections in the 21st century. Clin Microbiol Rev. 24:247-80.

Herbert J, Chong D, Spielman D, Krockenberger M, Wildner J, Bishop R. 2019. Unusual presentation and urinary tract obstruction due to disseminated intra-abdominal *eumycetomas* caused by *Curvularia* species in a dog. Med Mycol Case Rep. 26:28-31.

Huang YH, Kuan NL, Yeh KS 2020. Characteristics of Extended-Spectrum β-Lactamase–Producing *Escherichia coli* From Dogs and Cats Admitted to a Veterinary Teaching Hospital in Taipei, Taiwan From 2014 to 2017. Front Vet Sci. 7:35.

Jaeger, GH, Rotstein DS, Law JM 2002. Prostatic pythiosis in a dog. J Vet Intern Med. 16:598-602.

Jin Y, Lin D 2005. Fungal urinary tract infections in the dog and cat: a retrospective study (2001-2004). J Am Anim Hosp Assoc. 41:373-381.

Keeratijarut A, Lohnoo T, Yingyong W, Rujirawat T, Srichunrusami C, Onpeaw P, Chongtrakool P, Brandhorst TT, Krajaejun T 2015. Detection of the oomycete Pythium insidiosum by real-time PCR targeting the gene coding for exo-1, 3-β-glucanase. Journal of Medical Microbiology. 64(9):971–977.

Kochenburger J, Eriksson C, Greenberg M, Hoyt L 2019. Ultrasonography of a ureteral and bladder fungal granuloma caused by *Scedosporium apiospermum* in a basset hound. Vet Radiol Ultrasound. 60:E6-E9.

Manchester AC, Dogan B, Guo Y, Simpson KW 2021. *Escherichia coli*-associated granulomatous colitis in dogs treated according to antimicrobial susceptibility profiling. J Vet Intern Med. 1:150-161.

Manchester AC, Hill S, Sabatino B, Armentano R, Carroll M, Kessler B, Miller M, Dogan B,

McDonough SP, Simpson KW 2013. Association between granulomatous colitis in French Bulldogs and invasive *Escherichia coli* and response to fluoroquinolone antimicrobials. J Vet Intern Med. 27:56–61.

Mendóza-López CI, Del-Angel-Caraza J, Alejandro I, Hernández Q, Barbosa-Mireles MA 2017. Analysis of lower urinary tract disease of dogs. Pesq Vet Bras. 37: 1275-1280.

Okada K, Amano S, Kawamura Y, Kagawa Y 2015. Gastrointestinal basidiobolomycosis in a dog. J Vet Med Sci. 77: 1311–1313.

Olin SJ, Bartges JW 2015. Urinary tract infections: treatment/comparative therapeutics. Vet Clin North Am Small Anim Pract. 45:721-746.

Peleg A, Hogan D, Mylonakis E 2010. Medically important bacterial–fungal interactions. Nat Rev Microbiol. 8:340–349.

Pereira DI, Botton SA, Azevedo MI, Motta MA, Lobo RR, Soares MP, Fonseca AO, Jesus FP, Alves SH, Santurio JM 2013. Canine gastrointestinal pythiosis treatment by combined antifungal and immunotherapy and review of published studies. Mycopathologia. 176:309-15.

Reagan KL, Marks SL, Pesavento PA, Della Maggiore A, Zhu BY, Grooters AM 2019. Successful management of 3 dogs with colonic pythiosis using itraconzaole, terbinafine, and prednisone. J Vet Intern Med. 33:1434-1439.

Runcharoen C, Raven KE, Reuter S, Kallonen T, Paksanont S, Thammachote J, Anun S, Blane B, Parkhill J, Peacock SJ and Chantratita N 2017. Whole genome sequencing of ESBL-producing *Escherichia coli* isolated from patients, farm waste and canals in Thailand. Genome Med. 9(1):81.

Shmalberg J, Moyle PS, Craft WF, Walton SA. Severe meningoencephalitis secondary to calvarial invasion of *Lagenidium giganteum* forma caninum in a dog 2020. Open Vet J. 10:31-38.

Soonthornsit J, Banlunara W, Niyomthum W, Pusoonthornthum R 2013. *Penicillium* species-induced granuloma in a cat resulting in chronic lower urinary tract disease. J Feline Med Surg. 15:1154-1159.

Thepmanee J, Rodroo J, Awaiwanont N, Intanon M, Na Lampang K, Thitaram N, Thongkorn, K 2018. Prevalence and antibiotic resistance of extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* in healthy dogs in Chiang Mai Jirapa. Veterinary Integrative Sciences. 16:233–245.