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Supposed endogenous endophthalmitis caused by *Serratia marcescens* in a cat

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Abstract

An 8-year-old male neutered domestic shorthair cat was presented for evaluation of acute respiratory distress. Respiratory auscultation revealed a diffuse and symmetric increase in bronchovesicular sounds. Thoracic radiographs showed a diffuse unstructured interstitial pulmonary pattern with multifocal alveolar foci. Despite an aggressive treatment with supportive care, including oxygenotherapy and systemic antibiotics, progressive respiratory distress increased. Three days after the presentation, acute anterior uveitis was noticed on left eye. Ophthalmic examination and ocular ultrasonography revealed unilateral panuveitis with ocular hypertension. The right eye examination was unremarkable. Cytological examination of aqueous humor revealed a suppurative inflammation. *Serratia marcescens* was identified from aqueous humor culture. Primary pulmonary infection was suspected but was not confirmed as owners declined bronchoalveolar lavage. Active uveitis resolved and cat's pulmonary status improved after appropriate systemic antibacterial therapy. Vision loss was permanent due to secondary mature cataract. To the best of authors' knowledge, this is the first report of endogenous bacterial endophthalmitis secondary to *S. marcescens* infection in a cat.

Keywords: Cat, Cataract, Endogenous, Endophthalmitis, *Serratia marcescens*.

Introduction

The term endophthalmitis refers to any inflammation involving all intraocular structures, but in clinical practice, it most usually refers to intraocular bacterial or fungal infection (Jackson *et al.*, 2014). Endophthalmitis is divided into two types, exogenous and endogenous, depending on the route of the infection. In veterinary medicine, most cases are of exogenous origin when microorganisms are directly inoculated into the eye, after intraocular surgery, by penetrating injury or from retained foreign bodies. Endogenous endophthalmitis is rarely described. It occurs when organisms reach the eye *via* the blood stream, and then cross the blood–ocular barrier (Jackson *et al.*, 2014). This report describes a case of endogenous bacterial endophthalmitis (EBE) secondary to *S. marcescens* infection in a cat.

Case Details

An 8-year-old male neutered indoor/outdoor domestic shorthair cat was presented to the National Veterinary School of Alfort for evaluation of acute onset of respiratory distress. The cat has a history of respiratory disease with spontaneous resolution under supportive care. Vaccination against feline viral rhinotracheitis, calicivirus, and panleukopenia virus occurred within the previous year.

On the day of the presentation, the cat was reported to have open-mouth breathing.

On presentation to the Emergency Unit, the cat was assessed as weak with respiratory distress and hypothermia (35.4°C). Increased bronchovesicular sounds were present bilaterally although no murmur, crackles, or wheezes were ausculted. Venous blood gas analysis showed a combined respiratory acidosis (pH = 7.296; reference range 7.31–7.4), hypercapnia (pCO₂ = 47.6 mm Hg, reference range 40–44 mm Hg), and normal bicarbonate (21.5 mmol/L, reference range 20–24 mmol/L). The cat was placed in an oxygen cage with the fraction of inspired oxygen set at 60% and supplemental heat. Further testing was not performed given the cat's fragile condition. The next morning (day 2), serum chemistry profile, thoracic radiographs, and echocardiography were obtained. The serum chemistry panel was unremarkable. Thoracic radiographs showed a moderate, diffuse bronchial, and hazy interstitial patterns with alveolar changes in the cranial pulmonary lobes (Fig. 1). Echocardiography showed signs of hypovolemia and excluded primary cardiac disease as cause of the lung abnormalities. The preliminary clinical diagnosis was pneumonia and radiographic findings were consistent with a bacterial infection. Therapy was initiated with amoxicillin/

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Fig. 1. Ventrodorsal thoracic radiograph. Note the moderate interstitial and patchy alveolar lung pattern bilaterally (arrow).

clavulanic acid 15 mg/kg intravenously (IV) q12h (Augmentin; GlaxoSmithKline, Rueil-Malmaison, France) and intravenous fluids (lactated Ringer's solution at 3 mL/kg/h).

On day 4, the cat's clinical condition continued to decline. Anisocoria was noted and a presumptive diagnosis of anterior uveitis of the left eye (OS) was made. 0.1% dexamethasone/ polymyxin B/neomycin q8h OS (Maxidrol; Alcon, Rueil-Malmaison, France) and 1% atropine q8h OS (Atropine 1%; Alcon) were prescribed.

A complete ophthalmic exam was performed on day 5. Moderate blepharospasm with moderate serous discharge was noted OS. Menace response was present in the right eye (OD) and absent in the left eye. A moderate mydriasis OS was noted. The direct and consensual pupillary light reflexes (PLR) were absent OS; direct PLR OD was normal and consensual PLR OD was absent.

Slit-lamp examination (SL-17 Portable Slit Lamp; Kowa Company, Tokyo, Japan) revealed diffuse mild corneal edema, aqueous flare (4+), hypopyon, a large fibrin clot within the anterior chamber and iridal hyperemia and hemorrhages OS (Fig. 2). Funduscopic examination OS was precluded by anterior segment opacity. Ophthalmic examination OD with slit-lamp biomicroscope and indirect ophthalmoscope (Heine Video Omega 2C; Heine Instruments, Herrsching, Germany) was unremarkable. Intraocular pressure measurements obtained by rebound tonometry (Tonovet; Tiolat, Helsinki, Finland) was within reference limits OD (12 mm Hg) but abnormally high OS (45 mm Hg).

The left posterior segment examined by ocular ultrasound (MyLabOne; Esaote, Saint-Germain-en-Laye, France) was filled with diffuse heterogeneous hyperechoic material (Fig. 3). The conclusion of the ophthalmic examination was acute panuveitis OS associated with ocular hypertension. Several potential causes were considered: infectious diseases, neoplasia,

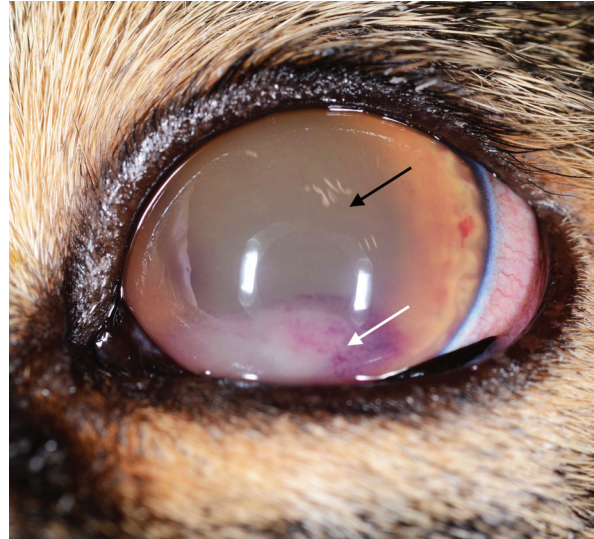


Fig. 2. Left eye at the initial presentation. Note the conjunctival hyperemia, diffuse corneal edema, hypopyon (white arrow), large fibrin clot (black arrow), moderate mydriasis, and iridal hyperemia and hemorrhages.

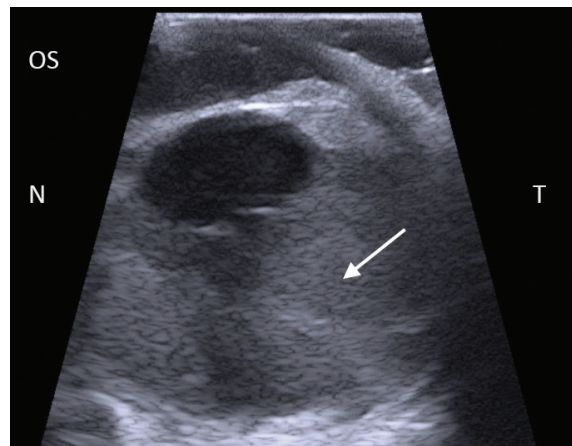


Fig. 3. Ultrasonography findings of the left eye (OS) at initial presentation. Note the diffuse heterogeneous hyperechoic material in the posterior segment (arrow). Linear transducer (18 MHz). (N): Nasal; (T): Temporal.

and idiopathic uveitis. A test for feline leukemia and immunodeficiency viruses was negative. Tests for other common pathogens were recommended but were declined by the owner.

A sample of aqueous humor OS was collected by fine needle paracentesis under brief propofol sedation and was followed by an intracameral injection of tissue plasminogen activator (tPA) 25 µg (Actilyse; Boehringer, Paris, France). Bronchoalveolar lavage via bronchoscopy and vitreous paracentesis were declined by the owner. Cytological examination of the aqueous humor revealed a suppurative inflammation with no visible bacteria or fungal organisms.

Thoracic radiographs were repeated. Compared to first examination, the diffuse, hazy interstitial pattern and lung consolidation were mildly more extensive. Due to concerns about the progression of the disease and while awaiting culture results, marbofloxacin 4 mg/kg IV q24h was added (Marbocyl; Vetoquinol, Lure, France). A dose of 0.1 mg/kg meloxicam (Metacam; Boehringer) subcutaneously q24h was administered. Topical 0.1% dexamethasone/polymyxin B/neomycin q4h, 0.5% tropicamide q8h (Mydriaticum; Théa, Clermont-Ferrand, France), and 1% brinzolamide q8h (Azopt, Alcon, Rueil-Malmaison, France) were administered OS.

The cat started to demonstrate gradual improvement from 48 h after initiating treatment and the supplemental oxygen was discontinued. In the left eye, hyphema precluded examination of the rest of the intraocular structures but intraocular pressure had decreased to 20 mmHg.

The culture of the aqueous humor revealed the presence of *S. marcescens*. The strain was multidrug resistant but susceptible to marbofloxacin (Table 1).

As there were no signs of trauma and no history of previous surgery, EBE was suspected. Abdominal ultrasound and control echocardiography did not detect infection site, other than pulmonary. Based on these results, amoxicillin/clavulanate acid and intravenous fluids were discontinued.

Table 1. Antimicrobial susceptibility test results for the *Serratia marcescens* isolate.

Name of chemicals	Susceptibility
Amoxicillin	R
Amoxicillin-clavulanate	R
Cephalexin	R
Cefovecin	I
Ceftiofur	S
Cefoperazone	I
Cefquinome	S
Trimethoprim/Sulfonamide	S
Gentamicin	S/I
Kanamycin	S
Streptomycin	I
Marbofloxacin	S
Enrofloxacin	S
Doxycycline	I
Colistine	R

(S): susceptible; (I): intermediate; (R): resistant.

The cat was discharged on 4 mg/kg oral marbofloxacin q24h, 0.05 mg/kg oral meloxicam q24h, topical 1% brinzolamide q8h, and 0.1% dexamethasone/polymyxin B/neomycin q8h in the left eye.

Anterior uveitis OS decreased gradually during the first month of follow-up. *Iris bombe* OS was observed with a moderate fibrin clot. Thoracic radiographs performed at that time demonstrated resolution of the earlier observed pulmonary changes. Oral marbofloxacin was discontinued after 5 wk and topical medication was limited to 0.1% dexamethasone solution q12h OS and 1% brinzolamide q12h OS. Three months after initial presentation, the IOP was within reference limits but rubeosis iridis, secluded pupil, and mature cataract were noticed OS (Fig. 4). Topical treatment was gradually stopped. Six months after the initial presentation, the cat was free of respiratory signs and no change in ocular lesions was noted. Telephone follow-up with the owner revealed that the cat was still free of respiratory clinical signs 12 months after discharge from our hospital.

Discussion

EBE is a rare condition reported in veterinary medicine. Two cases of EBE were reported in cats and have been caused by *Actinomyces* spp., following multiple dental extraction, and by *Enterococcus faecalis*, with no primary infection site identified (Westermeyer *et al.*, 2013; Donzel *et al.*, 2014). In humans, EBE is a rare, but well-described, condition accounting for only 2% to 8% of all cases of endophthalmitis (Okada *et al.*, 1994).

In human EBE, an extraocular locus of infection was detected in 64% of patients (Jackson *et al.*, 2014). The most common sites of infection are liver, lung,



Fig. 4. Left eye at the 3-mo recheck. Note the rubeosis iridis with an extensive fibrovascular membrane (black arrow), *iris bombe* (white arrow), and mature cataract.

endocardium, and soft tissue. In particular, pneumonia was considered as the source of EBE in 8% of patients. In the present report, primary bacterial pneumonia was suspected and could have been the source of endophthalmitis but was not confirmed as owners declined bronchoalveolar lavage.

In human patients, cultures from intraocular samples were the most common means of confirming EBE. Positive cultures were obtained in 43% to 59% of the cases from the vitreous (Jackson *et al.*, 2014; Bjerrum and La Cour, 2017). Anterior chamber sample was not considered as the most reliable way of establishing the diagnosis, as a positive anterior chamber sample was obtained alongside vitrectomy in 21% of the cases of EBE and a positive vitreous culture was obtained in 41% during vitrectomy (Jackson *et al.*, 2014). Blood culture was also a common mean for diagnosis because positive cultures were obtained from the blood in 51% to 59% of the cases (Jackson *et al.*, 2014; Bjerrum and La Cour, 2017). In the two cases of EBE reported in cats, the bacteria were identified by bacterial culture from aqueous humor (Westermeyer *et al.*, 2013; Donzel *et al.*, 2014). Positive culture was also obtained from vitreous humor (Donzel *et al.*, 2014). In the present case, positive culture was obtained from aqueous humor sample but performance of cultures from vitreous humor and blood at the time of diagnosis of panuveitis would have been beneficial.

Intracameral tPA is effective in the rapid dissolution of fibrin when large clots are present in the anterior chamber or the IOP is elevated secondary to fibrin blocking the iridocorneal angle as in the present case (Martin *et al.*, 1993). tPA should not be injected if recurrent bleeding is likely, however, the risk of rebleeding is low due to clot specificity (Crabbe and Cloninger, 1987). In the present case, intracameral injection of tPA and anti-inflammatory treatment leads to the resolution of intraocular hypertension. However, hyphema was observed several days after intracameral injection. This complication may be due to tPA activity or due to incomplete control of intraocular inflammation.

It is generally accepted that initial treatment of human endogenous endophthalmitis should include systemic antibiotic coupled with intravitreal antimicrobial injections (Vaziri *et al.*, 2015). Commonly, vancomycin and ceftazidime are associated for intravitreal injections (Jackson *et al.*, 2014). A posterior vitrectomy is also often performed to remove bacteria, inflammatory cells, membranes, and toxic debris, and to promote the distribution of antibiotics (Jackson *et al.*, 2003). There is a broad consensus that intravenous antibiotics are mandatory in the treatment of endogenous endophthalmitis but the role of intravitreal antibiotics, intravitreal steroids, and vitrectomy is unclear (Bjerrum and La Cour, 2017). In veterinary literature, there is no report regarding the use of intravitreal injections or vitrectomy in the treatment

of endogenous endophthalmitis. For the present case, systemic marbofloxacin was used. The penetration of marbofloxacin into the aqueous and vitreous humor has shown to be good in rabbit's normal eyes and was even enhanced in case of inflammation (Regnier *et al.*, 2008). Posterior vitrectomy was not available but intravitreal injection of marbofloxacin would have been useful.

Serratia marcescens is a Gram-negative, medium-sized, saprophytic rod-shaped bacterium belonging to *Enterobacteriaceae* and is considered an opportunistic pathogen (Hejazi and Falkiner, 1997). In humans, it has been implicated as a cause of nosocomial infections such as hospital-acquired pneumonia, urinary tract infection, and wound infection (Hejazi and Falkiner, 1997). There are only a few descriptions of *S. marcescens* infection in cats, and no ocular or lung involvement has been reported in any (Hohenhaus *et al.*, 1997; Kelly *et al.*, 2015). In humans, *S. marcescens* is a rare cause of endogenous endophthalmitis, mainly observed in patients with systemic illness, recent non-ocular surgery, indwelling catheters, and immunocompromised status, or patients with intravenous drug use (Wyler *et al.*, 1975; Alvarez *et al.*, 1990; Al Hazzaa *et al.*, 1992; Equi and Green, 2001; Williams *et al.*, 2006; Latorre, 2008; Jackson *et al.*, 2014; Shah *et al.* 2014). Moreover, a report described endophthalmitis due to *S. marcescens* in a woman with concurrent hospital-acquired *S. marcescens* pneumonia (Williams *et al.*, 2006). In the present case, risks factors such as FIV or diabetes were excluded. Nevertheless, the hypothesis of hospital-acquired infection cannot be ruled out but seems unlikely as ocular signs were observed soon after admission. Indeed, length of hospital stay more than 30 days has been shown to be a significant factor of *S. marcescens* acquisition in a newborn service unit (Friedman *et al.*, 2008).

In the case of EBE described in this report, the results of medical therapy were unsatisfactory for preservation of vision but the globe was preserved over a 12-months follow-up. Bacterial endophthalmitis in humans is known to have a poor visual outcome (Jackson *et al.*, 2014). More specifically, 44% of eyes achieved a visual acuity worse than 20/200 and 24% required enucleation or evisceration (Jackson *et al.*, 2014). The visual outcome associated to endogenous endophthalmitis secondary to *S. marcescens* is reported to be a particularly poor, as all case reports ultimately resulted in evisceration, enucleation, or phthisis despite early and appropriate treatment (Shah *et al.*, 2014).

This case report represents a unique presentation of a supposedly endogenous endophthalmitis secondary to *S. marcescens* in a cat with vision loss but preservation of globe over a 1-year period. Concurrent bacterial pneumonia was suspected but the relationship between these two lesions was not confirmed.

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Conflict of Interest

The authors declare that there is no conflict of interest.

References

- Al Hazzaa, S.A.F., Tabbara, K.F. and Gammon, J.A. 1992. Pink hypopyon : a sign of *Serratia marcescens* endophthalmitis. *Br. J. Ophthalmol.* 76, 764–765.
- Alvarez, R., Adan, A., Martinez, J.A., Casale, A. and Miro, J.M. 1990. Haematogenous *Serratia marcescens* endophthalmitis in an HIV-infected intravenous drug addict. *Infection.* 18, 29–30.
- Bjerrum, S.S. and La Cour, M. 2017. 59 eyes with endogenous endophthalmitis—causes, outcomes and mortality in a Danish population between 2000 and 2016. *Graefes. Arch. Clin. Exp. Ophthalmol.* 255, 2023–2027.
- Crabbe, S.J. and Cloninger, C.C. 1987. Tissue plasminogen activator: a new thrombolytic agent. *Clin. Pharm.* 6, 373–386.
- Donzel, E., Reyes-Gomez, E. and Chahory, S. 2014. Endogenous endophthalmitis caused by *Enterococcus faecalis* in a cat. *J. Small Anim. Pract.* 55, 112–115.
- Equi, R.A. and Green, W.R. 2001. Endogenous *Serratia* endophthalmitis with dark hypopyon case report and review. *Surv. Ophthalmol.* 46, 259–268.
- Friedman, N.D., Kotsanas, D., Brett, J., Billah, B. and Korman, T.M. 2008. Investigation of an outbreak of *Serratia marcescens* in a neonatal unit via a case-control study and molecular typing. *Am. J. Infect. Control* 36, 22–28.
- Hejazi, A. and Falkiner, F.R. 1997. *Serratia marcescens*. *J. Med. Microbiol.* 46, 903–912.
- Hohenhaus, A.E., Drusin, L.M. and Garvey, M.S. 1997. *Serratia marcescens* contamination of feline whole blood in a hospital blood bank. *J. Am. Vet. Med. Assoc.* 210, 794–798.
- Jackson, T.L., Eykyn, S.J., Graham, E.M. and Stanford, M.R. 2003. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. *Surv. Ophthalmol.* 48, 403–423.
- Jackson, T.L., Paraskevopoulos, T. and Georgalas, I. 2014. Systematic review of 342 cases of endogenous bacterial endophthalmitis. *Surv. Ophthalmol.* 59, 627–635.
- Kelly, E.J., Baldwin, T.J. and Chamberlain, A.P. 2015. Pathology in practice. Dermatitis, cellulitis, and myositis caused by *S. marcescens* infection in a cat. *J. Am. Vet. Med. Assoc.* 247, 897–899.
- Latorre, G. 2008. Endogenous *Serratia marcescens* endophthalmitis in a preterm infant. *Indian J. Pediatr.* 75, 410.
- Martin, C.L., Kaswan, R., Gratzek, A.T., Champagne, E., Salisbury, M.A. and Ward, D. 1993. Ocular use of tissue plasminogen activator in companion animals. *Vet. Comp. Ophthalmol.* 3, 29–36.
- Okada, A.A., Johnson, R.P., Liles, W.C., D'Amico, D.J. and Baker, A.S. 1994. Endogenous bacterial endophthalmitis. Report of a ten-year retrospective study. *Ophthalmology* 101, 832–838.
- Regnier, A., Schneifer, M., Concordet, D. and Toutain, D.L. 2008. Intraocular pharmacokinetics of intravenously administered marbofloxacin in rabbits with experimentally induced acute endophthalmitis. *Am. J. Vet. Res.* 69, 410–415.
- Shah, S.B., Bansal, A.S., Rabinowitz, M.P., Park, C., Bedrossian, E.H. Jr. and Eagle, R.C. 2014. Endogenous *Serratia marcescens* endophthalmitis. *Retin. Cases Brief Rep.* 8, 7–9.
- Vaziri, K., Pershing, S., Albini, T.A., Moshfeghi, D.M. and Moshfeghi, A.A. 2015. Risk factors predictive of endogenous endophthalmitis among hospitalized patients with hematogenous infections in the United States. *Am. J. Ophthalmol.* 159, 498–504.
- Westermeyer, H.A., Ward, D.A., Whittermore, J.C. and Lyons, J.A. 2013. *Actinomyces* endogenous endophthalmitis in a cat following multiple dental extractions. *Vet. Ophthalmol.* 16, 459–463.
- Williams, G., Morris, B., Hope, D. and Austin, M. 2006. *Serratia marcescens* endophthalmitis secondary to pneumonia. *Eye* 20, 1325–1326.
- Wyler, D.J., Glickman, M.G. and Brewin, A. 1975. Persistent *Serratia* bacteremia associated with drug abuse. *West. J. Med.* 122, 70–73.