

Clinical analysis and nonsurgical management of 11 dogs with aural cholesteatoma

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Background – Aural cholesteatomas, also called tympanokeratomas, are destructive and expansile growths of keratinizing epithelium that develop in the middle ear. They have been reported sporadically in dogs, and surgery is usually the recommended treatment.

Objectives – To describe the common clinical, radiological and histological findings of cholesteatoma; to report on the outcome of conservative management.

Animals – Eleven dogs (13 ears) with cholesteatomas.

Methods and materials – Medical records were reviewed for dogs diagnosed with cholesteatoma between 2012 and 2018. All dogs had computed tomography (CT) and/or magnetic resonance imaging (MRI) followed by trans-canal endoscopic procedure (TEP) for removal and biopsy of middle ear lesions. Dogs were then treated with in-clinic flushing initially weekly tapered to monthly, as well as at-home ear cleaning and application of topical otic steroid medication, initially daily then tapered to once or twice weekly.

Results – Nine dogs had a history of chronic otitis externa; head tilt or facial paralysis was present in seven and four cases, respectively. Otic examination identified a protruding nodule in seven ears. CT demonstrated soft tissue-like material in 12 bullae and expansion in seven bullae. MRI revealed minimally contrast-enhancing bulla contents in 12 ears. Post-TEP and with maintenance medical treatment, nine ears had no further signs of middle ear disease during a mean follow-up of 27.9 months.

Conclusions and clinical importance – The results suggest that otitis externa may not necessarily precede cholesteatoma in all dogs. MRI appears to be more sensitive than CT for identifying cholesteatomas. Conservative treatment of cholesteatomas could be useful before or as an alternative to surgery.

Introduction

Aural cholesteatoma is an epidermoid cyst that develops in the middle ear and is composed of keratin debris surrounded by keratinizing stratified squamous epithelium.^{1–3} It has been colloquially described as “skin growing in the wrong place”.^{4–6} The misplaced keratinizing epithelium constantly sheds keratin debris, resulting in gradual enlargement of the cyst and the eventual destruction of the adjacent tissue due to increasing pressure and osteoclastic bone resorption activated by inflammatory chemokines.⁷ In dogs, cholesteatoma is regarded as a severe complication of otitis media.⁴ The term tympanokeratoma has also been proposed for this condition.⁵

The clinical signs of cholesteatoma in dogs may be non-specific, including otic discharge, head shaking, rubbing and otic pain.^{1,6} Nasopharyngeal and/or neurological signs also may occur.^{1,3,7,8} In humans, early diagnosis of cholesteatoma depends on its identification with otoscopic examination.⁹ In veterinary medicine, otoscopy is used to diagnose the condition,^{2,10–12} although definitive diagnosis requires histopathological examination.^{1,4} Computed tomography (CT) and magnetic resonance imaging (MRI) are considered to be reliable methods for evaluating the middle ear and demonstrating middle ear-related lesions.^{13,14} CT is utilized to better define bony structures and can yield valuable information for the detection of cholesteatoma.¹⁵ MRI is used for more accurate assessment of soft tissue structures and can be a useful tool for the further characterization of soft tissue changes and recognition of potential complications;^{13,14} however, it is not routinely utilized in part because of the relatively high cost.

The only curative treatment for canine cholesteatoma reported to date is surgery with total ear canal ablation-lateral bulla osteotomy (TECA-LBO) and ventral bulla osteotomy.^{1,2,10,16} The prime objective of surgery for cholesteatoma is to remove all keratinous debris and

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stratified squamous epithelium;¹⁷ recurrence postsurgery is common in animals.^{1–3}

To the best of the authors' knowledge, 15 reports (covering a total of 70 cases) of canine cholesteatoma have been published.^{1–8,10,13,15,16,18–20} Reports in which the diagnosis of cholesteatoma was confirmed by histopathological evaluation in combination with CT and MR imaging are limited.^{1,8} No clinical studies of nonsurgical management for aural cholesteatoma have been reported. The purpose of the present study was to report the main clinical and imaging findings of aural cholesteatoma; and to report on the long-term outcome of a minimally invasive therapeutic approach in 11 dogs.

Methods and materials

Case selection and clinical analysis

Medical records of dogs diagnosed with cholesteatoma, presented between January 2012 and 2018 at the Synergy Animal General Hospital, Saitama, Japan, were examined to determine the following: (i) if histopathological reports stated the presence of keratinizing epithelium and/or thick lamellar keratin debris in the middle ear; (ii) if CT and/or MRI scanning were performed to identify middle ear disease; (iii) if trans-canal endoscopic procedures (TEPs) under anaesthesia were carried out to remove debris in the middle ear; and (iv) if a minimum follow-up of 12 month duration was possible. Signalment, history, physical examination, video-otoscopy findings, diagnostic imaging, cytological evaluation, aerobic microbial culture results, histopathological features and treatment were reviewed in each case. Dogs were followed up and the outcomes of dogs that did not remain in our direct care were determined by telephone interview between the referring veterinarian and client.

Video-otoscopic examination

Ear canal evaluations using a video-otoscope (Karl Storz GmbH & Co. KG; Tuttlingen, Germany, and/or Asuka Medical Inc.; Kyoto, Japan) were conducted both before and during TEPs. An initial examination was performed in conscious dogs to assess if the ear canal was adequately open to enable TEP. If stenosis of the ear canal – due to inflammation and proliferative tissue – blocked otoscope access, topical and/or oral steroids were administered to expand the canal before TEP.

Imaging with CT/MRI was performed with general anaesthesia. The middle ear and ear canal were evaluated using the video-otoscope and/or a 2.7-mm diameter, zero degree rigid endoscope (Asuka Medical Inc.). To facilitate visualization, the ear canal was lavaged using 3–5f feeding tubes with neutral electrolyzed water (NEW) (Asahi Pretec Corp.; Kobe, Japan).

Diagnostic imaging methods

Computed tomography scanning was performed under general anaesthesia with Somatom Emotion 16 (Siemens Healthineers Japan; Tokyo, Japan) to investigate the whole skull. Contiguous transverse 1 mm images were obtained before and after intravenous (i.v.) administration of 2.5 mL/kg (612.4 mg/mL) Iopamidol (Oypalomin 300 injection syringe, Fuji Pharma; Toyama, Japan) and were reconstructed using bone and soft tissue algorithms.

Magnetic resonance imaging was subsequently performed using Magnetom Essenza 1.5T (Siemens Healthineers Japan). Sagittal T2-weighted [T2W; slice thickness = 3.0 mm, repetition time (TR) = 4,000 ms, echo time (TE) = 91 ms], transverse T2W (slice thickness = 3.5 mm, TR = 4,000 ms, TE = 86 ms), dorsal T2W (slice thickness = 3.0 mm, TR = 4,000 ms, TE = 86 ms), transverse fluid-attenuated inversion recovery (FLAIR; slice thickness = 3.5 mm, TR = 8,500 ms, TE = 104 ms, Inversion time = 2,438.7 ms), transverse T1-weighted (T1W; slice

thickness = 3.5 mm, TR = 520 ms, TE = 11 ms) and dorsal T1W (slice thickness = 3.0 mm, TR = 500 ms, TE = 12 ms) were acquired. Additional transverse and dorsal T1W were obtained following i.v. administration of 0.2 mL/kg (0.5 mmol/mL) gadodiamide hydrate (Omniscan 32% i.v. injection syringe, Daiichi-Sankyo; Tokyo, Japan).

TEP for cholesteatoma

The TEP was performed in combination with CT and/or MRI examination. Preoperatively, the length, width and depth of the ear canal and middle ear cavity were measured, as well as the distance from the dorsal fold of the ear canal to the tympanic bulla on each CT/MR image of the cases. The dorsal fold (also called auricular projection) by the cartilaginous ridge represents a landmark that separates the vertical and horizontal ear canals.²¹ In addition, the type, number, structure, size and distribution of aural lesions were investigated to clarify the anatomical position of lesions within the ear canal.

Dogs were positioned in lateral recumbency with the affected side uppermost. Cleaning and flushing the ear canal were conducted with NEW, and any type of obstruction in the external ear canal was removed to access the middle ear. If a protruding nodule in the horizontal ear canal was present, it was grasped with curved mosquito forceps or aural forceps under endoscopic visualization and then removed by a traction–torsion manoeuvre. Residual portions of the nodule were completely removed under endoscopic visualization using 5f biopsy forceps with c.2.5 mm oval cups (Karl Storz GmbH & Co. KG), or vaporized by DLV-20 diode laser (Asuka Medical Inc.). Local irrigation with NEW was used to reduce and control the bleeding. In addition, for cases with stenosis due to proliferative lesions at the bony part of the ear canal, the top of the lesion was vaporized with a diode laser in the same manner as for ablation of residual mass fragments. For all cases, keratinaceous debris was directly removed from the middle ear using the 5f biopsy forceps and samples were placed in 10% formalin for histopathological evaluation separately from the tissues removed from the external ear canal. Impacted keratinaceous debris in the tympanic cavity was then removed by either aural forceps, suction and/or 3–5f feeding tubes under either video-otoscopic or rigid endoscopic guidance. The bulla was lavaged to remove remaining debris with NEW. Finally, 0.1 mL triamcinolone acetonide (Kenacort-A intradermal and intra-articular aqueous suspension infection, 1%, 50 mg/5 mL, Bristol-Myers Squibb; Tokyo, Japan) was administered to the middle ear cavity.

For prophylactic medical management post-TEP, repeated in-clinic tube flushing by a soft feeding tube with NEW was performed in awake dogs once weekly for two to four weeks, followed by tapering to once every two weeks for four weeks and eventually to once monthly. The indication for tapering was based on otic conditions, such as the presence of ear discharge and behaviours including scratching or head shaking. Additionally, routine home cleaning was performed with an ear cleaner (Zymox® ear cleanser, Pet King Brands, Inc.; Westmont, IL, USA), and/or Tromethamine-EDTA (Triz-EDTA Plus®, Dechra; Overland Park, KS, USA) and topical mometasone furoate (Fulmeta®, Shionogi & Co., Ltd.; Osaka, Japan) was applied to the dogs as prophylactic management to control canal inflammation. At-home ear cleaning and topical steroid administration was performed once daily for two to four weeks, tapering to once every two days for four weeks, then once to twice weekly. If otitis flared despite prophylactic flushes with NEW and topical steroid drops, dogs were treated with topical and/or systemic antimicrobials determined by clinician preference based on cytological evaluation and culture results.

Ear cytological evaluation and bacterial cultures

Under general anaesthesia, otic exudate was collected from either the middle ear or the deepest part of the ear canal with 3–5f feeding tubes under video-otoscopic guidance as cytological samples and sterile culture swabs. For cytological evaluation, samples were placed onto sterile slides. Then, slides were stained with Microscopic Hemacolor® Rapid staining of blood smear (Merck KGaA; Darmstadt,

Germany). Each slide was evaluated under a high-power field ($\times 40$ and/or 100) for the presence of cocci bacteria, rod-shaped bacteria, keratinized squamous epithelial cells and inflammatory cells. For aerobic bacterial culture and antimicrobial susceptibility testing, swabs were submitted to a diagnostic laboratory (LSI Medience Corporation; Tokyo, Japan). Swabs were inoculated onto sheep blood agar plates which were incubated at 35°C for 24 h. All isolates were identified phenotypically and biochemically. Antimicrobial susceptibility was performed using the broth microdilution method, which determined the minimum inhibitory concentrations of antimicrobial agents according to Clinical and Laboratory Standards Institute guidelines.²²

Histopathological diagnosis of aural cholesteatoma

Biopsy specimens were fixed in 10% neutral-buffered formalin. Representative trimmed tissues were routinely processed, embedded in paraffin, sectioned at 5 μm and stained with haematoxylin and eosin. The following criteria were used for diagnosis of cholesteatoma: (i) origin of tissue confirmed as the middle ear using the endoscopic procedure; (ii) presence of cornified epithelium and (iii) presence of amorphous thick lamellar keratin debris.^{1–3} A tentative diagnosis of cholesteatoma also was made for cases which satisfied (i) and (iii) but not (ii) (i.e. they lacked cornified epithelium).

Results

Signalment and clinical findings

Eleven dogs were included in this study; including French bulldog ($n = 5$); pug ($n = 2$), and one each of Chihuahua, Yorkshire terrier, shiba inu and Akita inu. There were two intact males, four castrated males and five spayed females. Ages ranged from 4 to 12 years, with a mean age of 8.2 years (median, 8 years). The durations of clinical signs varied from four to 104 weeks, with a mean duration of 28.1 weeks (median 12 weeks). Two dogs had bilateral disease, and nine dogs had unilateral disease, giving a total of 13 ears.

Nine of the 11 dogs had a history of chronic otitis externa in the affected ears. Five of the nine dogs had a history of recurrent otitis, and four of nine had a history of continuous otitis. Suspected primary causes of otitis externa were atopic dermatitis (two dogs), excessive cerumen (two dogs), foreign body (two dogs) and idiopathic (four dogs). The duration of chronic otitis externa ranged from six months to over five years. Onset of otitis media was suspected from one to 11 months before their presentation. Two of the 11 dogs had no history of chronic otitis externa and were presented for nasopharyngeal and/or neurological signs of possible middle ear disorders.

Aural signs included otorrhoea (eight dogs), ear scratching (two dogs) and head shaking (two dogs). During physical examination, neurological signs were identified in nine dogs. Head tilt was present in seven dogs, facial nerve paralysis in four dogs and ataxia in three dogs. Two dogs were reported to have had nystagmus, and one dog was said to have had a seizure, but these signs were not detectable at admission. Two dogs showed an algesic response on palpation of the bulla and temporomandibular joint. Two dogs had increased respiratory noise and/or inappropriate respiratory effort. Concurrent diseases were hypothyroidism (two dogs), spondylopathy (two dogs), pyoderma, urolithiasis, cardiological disease (AV-block), entropion, osteoarthritis and patella luxation (one dog each). Details are reported in Table 1.

Video-otoscopic findings

In 13 ears, video-otoscopy revealed otic discharge and the TM was not observed. In seven ears (cases 1, 2, 3, 4, 5, 10 and 11) a smooth-surfaced, whitish to pale-pinkish and rounded protruding nodule was detected, occluding the horizontal ear canal (Figure S1 in Supporting Information; Table 1). In four ears (cases 3, 4, 8 and 9), a narrowed horizontal ear canal was observed (Table 1).

Diagnostic imaging findings

Computed tomography

Computed tomography imaging was performed in 10 dogs (12 ears). All dogs had soft tissue-like material within the affected tympanic bullae. Absence of air contrast within the middle ear cavity was observed in all affected ears. Enlargement of the middle ear cavity was identified in seven ears, osteoproliferation in seven, lysis of the bulla in six, lysis of the cochlea in six (Figure 1a), sclerosis of the temporal bone in two and mineralization of the inner lining of the bulla in one.

Four ears, in two pugs and two French bulldogs, were affected by lysis of the petrous temporal bone and bulla expansion was present in three of four ears. Conversely, all dogs (five ears) without expansion of the bulla also were French bulldogs and only one of five had bulla lysis. Only one (Akita inu) of three nonbrachycephalic dogs had both expansion and lysis of the tympanic bulla wall.

Soft tissue-like material occupying the horizontal ear canal was observed in seven ears. In five of the seven ears, linear mineralization within the soft tissue-like material in the external ear canal was observed (Figure 1b) and four of seven ears had bulla osteoproliferation. Enlargement of associated lymph nodes was observed in seven dogs (seven ears), specifically the submandibular lymph nodes, retropharyngeal lymph nodes and parotid lymph node in five, six and one dogs, respectively.

Postcontrast CT images were available for two ears. In the images after administration of contrast medium, there was no appreciable contrast enhancement of the tympanic bulla content in either ear. One of the two had an enhancing soft tissue mass occluding the horizontal canal.

Magnetic resonance imaging

Magnetic resonance imaging was performed in all dogs (13 ears). It revealed the presence of material within the bulla which was isointense to slightly hyperintense relative to brain tissue in 12 ears (Figure 2a) and heterogeneous hyperintense in one ear on T1W images. The mass was heterogeneous hyperintense in nine ears, homogeneous hyperintense in three ears and heterogeneous hypointense in one ear on T2W (Figure 2b) and FLAIR images (Figure 2c). Following contrast administration, contents of the bulla did not enhance in all but one ear. However, the inner lining of the bulla showed some partial enhancement in 11 ears. In addition, contrast enhancement of cochleae was observed in nine ears. Heterogeneous contrast enhancement of the meninges also was observed with severe lysis of the petrous temporal bone in two dogs.

In eight ears, soft tissue-like material in the external ear canal was enhanced (Figure 2d). Before the injection of

Table 1. Signalment, clinical signs, duration of clinical signs, location of lesions, histopathological evaluation and outcome of the eleven dogs with aural cholesteatoma

Case	Breed	Sex	Age (years)	Duration of clinical signs (weeks)	Clinical signs (Otic)	Clinical signs (Non-otic)	Concurrent diseases	Location of cholesteatoma	Histopathological evaluation of cholesteatoma	Location of protruding nodule	Procedure for stenosis	Follow-up (months)	Outcome
1	Pug	SF	8	12	Otorrhoea	Left head tilt	Seborrhoeic dermatitis	Right	KE, KD	Right		32	No recurrence
2	Pug	CM	7	43	Otorrhoea	Right facial palsy	Urolithiasis	Right	KE, KD	Right		31	No recurrence
3	French bulldog	CM	4	4	Otorrhoea (left), ceruminous discharge (right), Ear scratching	Left head tilt, respiratory noise, inappropriate respiratory effort		Bilateral	KE, KD	Left	VOLA	28	Right: No recurrence/Left: First recurrence (recurrent cholesteatoma with a nodule confirmed) at two months, Second recurrence at one month
4	Akita inu	CM	8	4	Ceruminous discharge, head shaking	Right head tilt, ataxia	Pyoderma, hypothyroidism, spondylopathy, osteoarthritis, cardiac disease (A-V-block)	Right	KE, KD	Right	VOLA	31	Recurrence at one month
5	Chihuahua	SF	12	4	Otorrhoea		Spondylopathy, seborrhoeic dermatitis	Right	KE, KD	Right		28	Recurrence (recurrent cholesteatoma confirmed) at 13 months
6	Shiba inu	M	8	104	Ceruminous discharge, Ear scratching		Atopic dermatitis, Malassezia dermatitis, Hypothyroidism	Left	KD			35	No recurrence
7	French bulldog	M	7	42	Otorrhoea, Ceruminous discharge	Left facial palsy, Left head tilt	Osteoarthritis	Left	KE, KD			57	No recurrence
8	French bulldog	SF	10	8	Ceruminous discharge	Right facial palsy, right head tilt		Right	KD		VOLA	18	No recurrence
9	French bulldog	SF	11	12	Otorrhoea, ceruminous discharge (right), discharge (left)	Right head tilt, ataxia	Osteoarthritis, patella luxation, atopic dermatitis	Bilateral	KE, KD		VOLA	12	No recurrence
10	French bulldog	CM	7	24	Otorrhoea, head shaking	Right facial palsy		Right	KE, KD	Right		13	No recurrence
11	Yorkshire terrier	SF	8	52	Otorrhoea	Left head tilt, ataxia, respiratory noise		Left	KD	Left		11	Recurrence at two months

CM castrated male, F female, M male, KE keratinizing epithelium, KD keratin debris, SF spayed female, VOLA video-otoscopic laser ablation.

contrast medium, the material was iso-intense to brain tissue in all ears on T1W images, whereas it was heterogeneous hyperintense in five ears, slightly hypointense in two ears and hyperintense in one ear on T2W and FLAIR images.

Cytological evaluation and microbial culture

Cytological examination of otic discharge was performed in seven ears. Bacterial cocci, rods or a combination of both, were present in four, one and two of seven ears, respectively. Keratinized squamous epithelial cells and neutrophils were identified in four and six of seven ears, respectively. Aerobic bacterial culture of the middle ear was performed in five ears, and all cultures were positive. More than one species of organism was isolated in three ears. Bacteria isolated were *Pseudomonas aeruginosa* (four of seven ears), group G *Streptococcus* spp. (two of seven ears), *Staphylococcus pseudintermedius* group (one of seven ears) and *Staphylococcus schleiferi* (one of seven ears).

Histopathological findings

Tissue samples taken from 10 middle ears demonstrated keratinizing epithelium and keratin debris consistent with

cholesteatoma (Figure 3). In the other three middle ears (cases 6, 8 and 11), a tentative diagnosis of cholesteatoma was made because cornified epithelium was not identified.

In seven dogs, histopathological evaluation of protruding nodules within the external ear canal (Figure 4) revealed dense fibrous connective tissue surrounded by squamous epithelium. In addition, five of seven had variable degrees of central cores of osseous metaplasia (OM). In Case 1, a markedly abnormal bony architecture was found.

In one of seven ears, histopathological results for a tissue sample taken from the deeper part of the external acoustic meatus exhibited hyperplasia and hyperkeratosis of the epidermis, dermal oedema, fibrosis and lymphocytic infiltration with dilation of ceruminous glands with stasis of secretum.

Outcome of TEP

All dogs, except for Case 6, were discharged with pain medication as a postprocedure in TEP. The duration of pain medication varied from one to five weeks. One dog (Case 5) was given Robenacoxib (Onsior®, Elanco Japan K.K.; Tokyo, Japan) 2.0 mg/kg orally (p.o.) once daily.

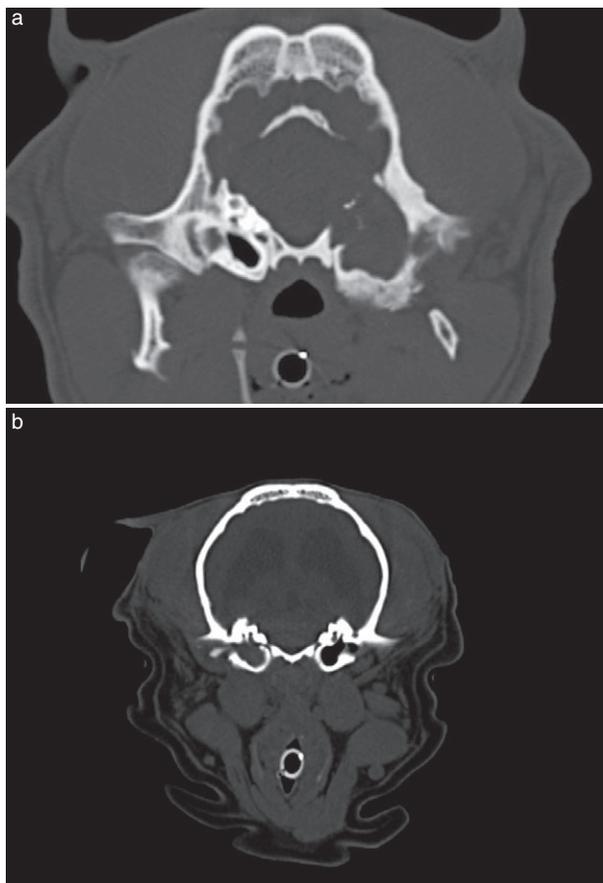


Figure 1. Computed tomography lesions of aural cholesteatoma of dogs.

(a) At the level of the tympanic cavity, soft tissue-like material fills the left tympanic bulla, creating enlargement, lysis and osteoproliferation of the tympanic bulla wall, with lysis of the cochlea (Case 7). (b) At the level of the tympanic cavity, a soft tissue mass appeared in the right external ear canal with mineralization in the centre (Case 1). Soft tissue-like material also fills the right tympanic bulla, causing mild enlargement of the tympanic bulla wall.

Eight dogs were administered prednisolone (Predonine[®], Shionogi & Co., Ltd.; Osaka, Japan) 0.5–1.0 mg/kg p.o. once daily and one dog (Case 4) was given prednisolone 0.5–1.0 mg/kg p.o. once every other day; then the corticosteroid treatment was tapered down. No serious post-procedural complications were observed in any dogs, except for Case 3 which developed temporary facial nerve paralysis that spontaneously resolved within eight weeks.

Follow-up ranged from 12 to 58 months, with a median follow-up of 29 months (mean, 27.9 months). Post-TEP, in-clinic tube flushing and at-home ear cleaning were performed for all the cases once weekly and once daily, respectively. The frequency of treatment was gradually tapered based on assessment of clinical signs; maintenance treatment of once monthly or twice monthly tube flushing in clinic was performed for six and five dogs, respectively. Routine regular home cleaning was recommended once weekly in five dogs, every other day in one dog and every day in two dogs. The owner of Case 4 declined to continue home cleaning due to difficulties in performing the procedure alone, but monthly in-clinic flushes continued. For all but one dog (Case 4), at-home

and in-clinic management continued until the end of the study. In seven ears, glucocorticoid eardrops were applied as a proactive therapy. Initially, three to five drops were applied to each ear once daily. The frequency of administration of topical glucocorticoids was tapered by one half each week to a maintenance frequency of once or twice weekly. For management of chronic aural inflammation, in addition to topical steroid drops, oral oclacitinib was administered to Case 11 after the second TEP and to Case 10 beginning four weeks after the first TEP. For control of concurrent atopic dermatitis, oclacitinib (Apoquel, Zoetis; Parsippany, NJ, USA) was prescribed to Case 9 and oral prednisolone was intermittently administered to Case 6.

Nine ears (seven dogs) had no recurrence of middle ear disease in this study. Four ears (four dogs: cases 3, 4, 5 and 11) had recurrent clinical signs after the first endoscopic procedure. The mean time to recurrence was 4.3 months (range: one to 12 months; median: two months). In Case 3, a protruding nodule recurred two months after the initial procedure, despite the dog receiving prophylactic care. As the owners declined otic surgery, a second TEP was immediately performed, and the dog received systemic and topical antimicrobial medication. Recurrence of cholesteatoma was confirmed with histopathological evaluation. No significant aggravation was observed on either CT or MRI findings, except for osteoproliferation in the bony part of both external ear canals. Clinical signs waxed and waned, and then the dog underwent a third TEP for removal of remnants of keratin debris after which clinical signs resolved. In Case 4, ear discharge recurred at one month after the initial procedure. The owners declined an endoscopic or surgical approach, and the dog was managed with only monthly tube flushing. Unfortunately, clinical signs persisted. In Case 5, ear discharge recurred at 12 months after the initial procedure. Clinical signs waxed and waned, and eventually second TEP was performed due to deterioration of signs 25 months after the first procedure. Recurrence of cholesteatoma was confirmed with histopathological evaluation. No significant changes in CT and MRI findings compared to the first procedure were observed. Clinical signs resolved after the second procedure. In Case 11, otitis recurred two months after the initial procedure. The dog received appropriate home cleaning with administration of oclacitinib. Subsequently, otitis resolved.

None of the owners reported any adverse effects with regard to the management regimen during this study.

Discussion

In the veterinary literature, no significant breed predilection for cholesteatoma has been reported. In this report, over half of the dogs were brachycephalic breeds. Previous reports documented that dysfunction of the auditory tube and the narrow nasopharynx could be predisposing factors for developing primary acquired cholesteatoma.^{6,8} In addition, hypertrophic bulla walls and stenotic bony parts of the horizontal ear canals also could predispose brachycephalic breeds to secondary acquired cholesteatoma.⁸

In our study, nine dogs had a history of chronic otitis externa, which can be considered as an important

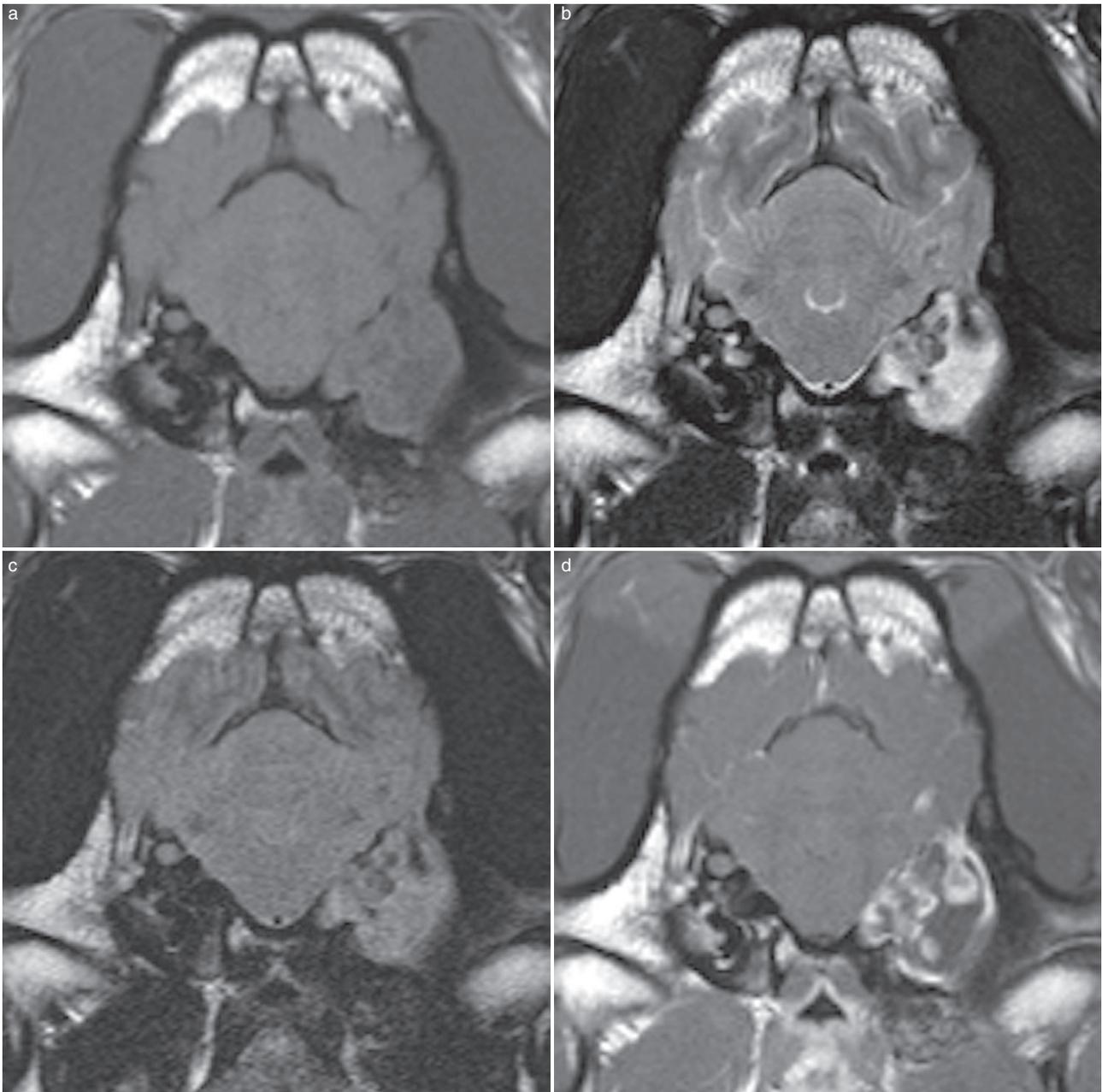


Figure 2. Magnetic resonance images (MRIs) of aural cholesteatoma of a dog at the level of the tympanic cavity (Case 7).

(a) T1-weighted, (b) T2-weighted, (c) fluid-attenuated inversion recovery and (d) postcontrast T1-weighted transverse MRIs. The expansile left bulla includes material isointense to brain tissue on T1-weighted images and heterogeneous hyperintense on T2-weighted and fluid-attenuated inversion recovery. On postcontrast T1-weighted images, partial enhancement is identifiable, particularly in the inner lining of the left bulla, whereas the contents of the left bulla are not significantly enhanced.

predisposing factor for secondary acquired forms in any breed.^{1,2,15} However, two of the cases were evaluated for a history of neurological issues, not the typical chronic history of otitis externa. The primary acquired form of cholesteatoma may occur in dogs, although the secondary acquired form appears to be more common.

Computed tomography scanning plays an important role in the assessment of dogs with middle ear diseases.^{15,23} It has been proposed that a nonenhancing but expansile lesion, which is hyper-attenuating to brain, is likely to be a cholesteatoma.¹⁵ However, expansion of the bulla is not regularly observed.^{1,16} Our study identified expansion of the bulla in 53.8% of the ears and 75% of

the brachycephalic breeds with expansile bulla also had lysis of the bulla. By contrast, 80% of the brachycephalic breeds without expansile bulla did not have bulla lysis. In humans, it is hypothesized that cholesteatoma slowly enlarges in the middle ear and gradually erodes adjacent bony structures with activated osteoclasts.²⁴ Thus, the early stages of cholesteatoma might remain unidentified by CT scanning. Bulla expansion in these breeds could be impeded due to their hypertrophic bulla wall.

It was reported, albeit in only one case, that findings on MR imaging included an expansile bulla containing material isointense to brain tissue on T1W and of mixed intensity on T2W images.¹³ In addition, material in the bulla

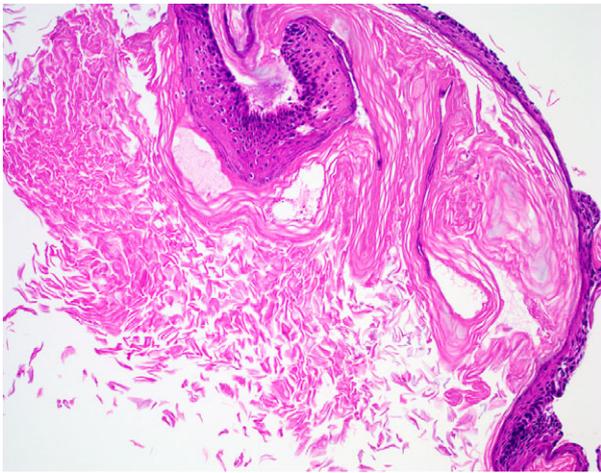


Figure 3. Photomicrograph of the histopathological findings of canine aural cholesteatoma (Case 7).

Section of the cholesteatoma wall constituted a multilayered squamous epithelium lining a cystic lumen filled with abundant lamellar eosinophilic keratin debris. Haematoxylin and eosin stain, $\times 20$.



Figure 4. Gross appearance of a protruding nodule in the ear canal of a dog (Case 1).

A whitish to pinkish, oval and pedunculated nodule was removed by the traction-torsion manoeuvre.

was found to show minimal postcontrast enhancement, with enhancement localized to the region immediately adjacent to the bone.¹³ In our cases, the bulla contents commonly appeared isointense on T1W images, heterogeneous hyperintense on T2W images and minimally enhanced after contrast injection, with partial enhancement in the location of the inner epithelial lining of the bulla. In humans, the inner component of a cholesteatoma consists of keratin debris that is avascular,²⁵ so the absence of contrast enhancement of the contents on MR imaging was not unexpected.¹ Furthermore, in humans, vascularity associated with the abnormal epithelium may be increased due to angiogenic growth factors produced by inflammatory cell populations in the matrix and perimatrix of cholesteatoma.^{17,26} Findings of heterogeneous intensity and enhancement on MRI could reflect the histopathological features of cholesteatoma, such as increased vascularity on hyperproliferative epithelium and absent vascularity within keratin debris. Moreover, in

humans, it was reported that pre- and postcontrast conventional MRI allows the differentiation of inflammatory mucosa, granulation tissue and cholesteatoma, whereas CT was not able to differentiate between the diseases.²⁷ Thus, MRI might be a helpful diagnostic tool to ensure accurate and early diagnosis of canine cholesteatoma.

For seven of the 11 dogs in this study, a protruding nodule consisting of fibrous connective tissue surrounded by squamous epithelium was found in the external ear canal. Histopathologically, the lesions in dogs appeared to be different in character from typical aural polyps in cats. Presence of ciliated columnar epithelial cells is a prerequisite for the histopathological definition of a polyp,²⁸ and as a consequence, in terms of terminology, polyp is not an appropriate description for the canal nodules seen in this study.¹⁹ In dogs, the association between the protruding nodules and cholesteatoma remains to be fully elucidated.^{1-8,10,13,15,16,18-20} It has been reported that a pug with cholesteatoma had an external ear canal mass with a thick, keratinizing epithelium.⁸ The authors noted that the lesion might be related to the cholesteatoma.⁸ In the present study, histopathological evaluation of external ear canal nodules in five cases revealed a core of OM. Likewise, it has been reported in a German shepherd dog with a cholesteatoma in the middle ear, accompanied by a cholesterol granuloma with a core of OM in the horizontal ear canal.¹⁰ OM is a type of ectopic ossification of fibrous connective tissue.²⁹

Postoperative short-term complications after TEP occurred in only one dog (9.1%) which developed facial palsy. Procedures involving the middle ear potentially can cause facial nerve palsy and cholesteatoma may be attached to vulnerable underlying structures including the facial nerve. In the veterinary literature, facial nerve palsy and dryness of the nostrils was reported postoperatively in two (18.2%) of 11 dogs that underwent surgery for cholesteatoma.² In previous retrospective studies of canine TECA and LBO, 13–46% had facial nerve paresis,³⁰⁻³² and 4–23% had residual deficits in facial nerve function after TECA-LBO.^{30,32,33}

It has been reported that surgical treatment is curative in only 50% of cases of canine cholesteatoma.^{1,12} Recurrence was seen in one of four dogs (25.0%) at 12 months postsurgery in one study and in 10 of 19 dogs (52.6%) at a mean time of 11.3 months in another study.^{1,3} In addition, one study reported that recurrence was suspected in five of 11 dogs (45.5%) at a mean time of 7.5 months.² Postsurgical recurrence is likely due to the difficulty of complete surgical removal of abnormal keratinizing epithelium and keratin debris.⁶ In the present study, clinical signs recurred in four of 11 dogs (four of 13 ears: 30.8%) at a mean time of 4.3 months post-TEP. For these cases, the involved tissues could not be adequately removed from the middle ear with an initial TEP because of their advanced stage. The remnants of cholesteatoma might lead to recurrence sooner. Moreover, even in cases without recurrence after TEP, the possibility remains that residues of cholesteatoma may persist in small cavities of the bulla and keratin accumulation can slowly create clinical signs. Thus, the need to manage ongoing diseases suggests that owners should be prepared for monitoring

after TEP, lifelong maintenance therapy and repeated TEP, if necessary.

As part of maintenance therapy, oclacitinib was used in three cases in this study. In Case 9, oclacitinib was prescribed for concurrent atopic dermatitis. The other two dogs (cases 10 and 11) had unilateral chronic otitis without any cutaneous lesions or identifiable primary disease. Oclacitinib is presumed to inhibit both proallergic and proinflammatory cytokines (IL-2, 4, 6, 13 and 31) as a specific JAK1 and -3 inhibitor. Although it is an extra-label indication, we prescribed oclacitinib to the latter two dogs in an attempt to treat the chronic aural inflammation, which seems to play a fundamental role in multiple aetiopathogenic mechanisms of acquired cholesteatoma.³⁴ Additionally, it is suggested in humans that the IL-6/STAT3 signalling pathway is active and may play an important role in the epithelial hyperproliferation of acquired cholesteatoma.³⁵ During this study, the clinical signs were managed with no relapse in the dogs treated with oclacitinib. More study is necessary to elucidate the efficacy and risk of oclacitinib as a component of postprocedural management in canine cholesteatomas.

In the present study, around 70% of ears were treated successfully by a single TEP, followed by maintenance treatment involving daily to weekly ear cleaning at home and weekly to monthly tube-flushing in the clinic. Likewise, it was reported that the condition in a dog was controlled by removal of keratin debris from the bulla under video-otoscopic guidance, although the dog died from unrelated causes 29 months later.¹ We suggest that conservative treatment of cholesteatoma by TEP with regular removal of the inflammatory stimulus in the middle ear could be useful before or in place of surgery.

Limitations in the evaluation of TEP in this study include its retrospective nature, the small sample size, the referral nature of the population and the lack of objective criteria to define treatment outcome. In the future, a large-scale prospective controlled cohort study should be conducted to conclusively evaluate therapeutic outcomes.

In conclusion, chronic otitis externa may not necessarily precede acquired cholesteatoma in dogs but the presence of a protruding nodule in the external canal may be a significant predictor of cholesteatoma and the use of MRI can facilitate the early diagnosis of this disease. Nonsurgical therapy is not curative as surgery may be; however, early conservative treatment of cholesteatoma could be an effective option before or as an alternative to surgery, even though it requires long-term at-home and in-clinic maintenance care.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Figure S1. Video-otoscopic appearance of a protruding nodule in the external ear canal of a dog (Case 2).

Résumé

Contexte – Les cholestéatomes auriculaires, aussi appelés tympanokératomes, sont une croissance expansive et destructrice de l'épithélium kératinisé qui se développe dans l'oreille moyenne. Ils ont été décrits sporadiquement chez le chien et une chirurgie est le traitement recommandé.

Objectifs – Décrire les données cliniques, radiologiques et histologiques des cholestéatomes ; décrire l'évolution d'une gestion conservatrice.

Sujets – Onze chiens (13 oreilles) avec cholestéatomes.

Matériel et méthode – Les données médicales ont été revues pour les chiens diagnostiqués avec un cholestéatome entre 2012 et 2018. Tous les chiens ont eu un examen tomographique (CT) et/ou une imagerie par résonance magnétique (MRT) suivi d'une endoscopie trans-canal (TEP) pour le retrait et la biopsie des lésions de l'oreille moyenne. Les chiens ont ensuite été traités par un nettoyage en clinique une fois par semaine puis une fois par mois, associé à des nettoyages auriculaires par les propriétaires ainsi que l'application d'un traitement auriculaire stéroïdien initialement une fois par jour puis une ou deux fois par semaine.

Résultats – Neuf chiens présentaient des commémoratifs d'otite externe. Une tête penchée ou une paralysie faciale était présente dans sept et quatre cas respectivement. L'examen auriculaire identifiait un nodule protruif dans sept oreilles. Le CT mettait en évidence un matériel tissulaire dans 12 bulles avec expansion dans sept bulles. Le MRI révélait un contenu de la bulle augmentant le contraste de façon minimale pour 12 oreilles. A la suite des TEP et avec le traitement de maintenance, neuf oreilles ne présentaient pas de signe d'otite moyenne au cours d'une période de suivi moyenne de 27,9 mois.

Conclusions et importance clinique – Les résultats suggèrent que l'otite externe peut ne pas nécessairement précéder un cholestéatome chez tous les chiens. La MRI semble être plus sensible que le CT pour leur identification. Le traitement conservateur des cholestéatomes pourrait être utile en alternative à la chirurgie.

Resumen

Introducción – los colesteatomas auditivos, también denominados queratomas timpánicos, son crecimientos destructivos y expansivos del epitelio queratinizante que se desarrollan en el oído medio. Se han descrito esporádicamente en perros, y la cirugía suele ser el tratamiento recomendado.

Objetivos – describir los hallazgos clínicos, radiológicos e histológicos comunes del colesteatoma; describir los resultados de un tratamiento conservador.

Animales – Once perros (13 orejas) con colesteatomas.

Métodos y materiales – se revisaron los historiales clínicos de perros diagnosticados con colesteatoma entre 2012 y 2018. Todos los perros se sometieron a tomografía computarizada (CT) y/o resonancia magnética (MRI), seguidos de un procedimiento endoscópico transcanal (TEP) para la extracción y biopsia de lesiones del oído medio. Los perros se trataron con lavado semanal en el hospital, inicialmente de forma semanal y después mensual, así como limpieza del oído en su hogar y la aplicación de medicamentos tópicos esteroides óticos, inicialmente a diario y luego se redujeron a una o dos veces por semana.

Resultados – nueve perros tenían antecedentes de otitis externa crónica; inclinación de la cabeza o parálisis facial se observaron en siete y cuatro casos, respectivamente. El examen ótico identificó un nódulo que sobresalía en siete orejas. La CT demostró material similar a tejidos blandos en 12 casos y expansión en siete de las bullas. La MRI reveló contenidos de bulla que se realizaban mínimamente con contraste en 12 oídos. Después de la TEP y con tratamiento médico de mantenimiento, nueve oídos no mostraron más

signos de enfermedad del oído medio durante un seguimiento medio de 27,9 meses.

Conclusiones e importancia clínica – los resultados sugieren que la otitis externa no necesariamente precede al colesteatoma en todos los perros. La MRI parece ser más sensible que la CT para identificar colesteatomas. El tratamiento conservador de los colesteatomas podría ser útil antes o como una alternativa a la cirugía.

Zusammenfassung

Hintergrund – Cholesteatome im Ohr, die auch Tympanokeratome genannt werden, sind destruktive und ausgedehnte Gewächse, die aus keratinisierendem Epithel bestehen und im Mittelohr entstehen. Sie sind sporadisch bei Hunden beschrieben worden und eine chirurgische Entfernung ist in der Regel die empfohlene Behandlung.

Ziele – Eine Beschreibung der üblichen klinischen, radiologischen und histologischen Befunde von Cholesteatomen; sowie ein Bericht über das Ergebnis konservativer Behandlung.

Tiere – Elf Hunde (13 Ohren) mit Cholesteatomen.

Methoden und Materialien – Es wurden die Krankenakten von Hunden durchgesehen, die zwischen 2012 und 2018 mit Cholesteatomen diagnostiziert worden waren. Bei allen Hunden war eine Computertomografie (CT) und/oder eine Magnetresonanztomografie (MRI) durchgeführt worden. In der Folge wurde eine Trans-Kanal Endoskopie (TEP) durchgeführt, um die Veränderungen im Mittelohr zu biopsieren und zu entfernen. Die Hunde wurden danach zunächst wöchentlich mit einer Ohrspülung in der Klinik behandelt, was danach zu wöchentlich und monatlich reduziert wurde sowie einer Ohrreinigung zu Hause und topische Applikation von Kortisonmedikation im Ohr, anfangs täglich, dann reduziert auf ein- bis zweimal wöchentlich.

Ergebnisse – Neun Hunde hatten eine Anamnese einer chronischen Otitis externa; Kopfschiefhaltung bzw. Gesichtsparalyse bestanden bei sieben bzw vier Fällen. In sieben Ohren wurde bei der Ohruntersuchung vorragende Knoten gefunden. Die CT zeigte Weichteil-ähnliches Gewebe in 12 Bullae und eine Erweiterung bei sieben Bullae. Die MRI Untersuchung zeigte minimale Kontrast-reiche Bulla-Inhalte in 12 Ohren. Post TEP und nach Erhaltungstherapie mit Medikamenten, zeigten neun Ohren keine weiteren Anzeichen einer Mittelohrerkrankung während der Follow-Up Periode von 27.9 Monaten.

Schlussfolgerungen und klinische Bedeutung – Die Ergebnisse bedeuten, dass eine Otitis externa den Cholesteatomen bei Hunden nicht unbedingt vorausgehen muss. Zur Identifizierung scheint die MRT Untersuchung sensibler zu sein als die CT Untersuchung. Die konservative Behandlung von Cholesteatomen könnte als Alternative zur chirurgischen Behandlung sinnvoll sein.

要約

背景 – 鼓膜角化腫とも呼ばれる耳性真珠腫は、中耳に発生する角化上皮の破壊性かつ膨張性腫瘍である。犬で散発的に報告されており、通常は、外科手術が推奨される治療法である。

目的 – 本研究の目的は、真珠腫の一般的な臨床的、放射線学および組織学的所見を記述することである。また、保守的管理による成果を報告することである。

被験動物 – 真珠腫を伴う11頭の犬(13個の耳)。

方法と材料 – 2012年から2018年にかけて真珠腫と診断された犬について、病歴をレビューした。犬全頭において、CT検査および/または磁気共鳴画像検査(MRI)を実施し、中耳病変の除去および生検のため経管内視鏡検査(TEP)を実施した。その後、院内における耳洗浄を、最初は週1回実施し、次第に月1回に減少させた。同様に自宅での耳洗浄および点耳ステロイド薬の塗布を、最初は1日1回実施し、次第に週1回または2回に減少させた。

結果 – 犬9頭に慢性外耳炎の病歴を認めた。頭部斜頸または顔面麻痺をそれぞれ7頭および4頭に認めた。耳道検査では、7つの耳道に突出した結節を認めた。CT検査では、水泡および7つの水泡の拡大を12の軟部組織様物と認識した。MRI検査では、12個の耳にコントラストが強調された水泡内容を最小限に示した。TEP後および維持療法を実施した9個の耳において、平均27.9ヵ月の追跡期間中に中耳炎の兆候を認めなかった。

結論と臨床的重要性 – 本研究結果は、外耳炎が必ずしも全ての犬において真珠腫に先行するとは限らないことを示唆している。MRI検査は、真珠腫の同定に対しCT検査よりも感受性が高いようである。真珠腫の保守的治療は、手術前治療または手術の代替療法として有用であり得る。

摘要

背景 – 耳的胆脂瘤,也称鼓膜角质瘤,是角化上皮在中耳的破坏和扩张性增生。犬的病例仅有零星报道,通常建议外科治疗。

目的 – 描述胆脂瘤的常见临床、影像学和组织学表现;报告保守治疗的效果。

动物 – 十一只(13只耳朵)胆脂瘤患犬。

方法和材料 – 对2012年至2018年诊断为胆脂瘤犬的医疗记录进行回顾性分析。所有犬都进行了计算机断层扫描(CT)和/或磁共振成像(MRI),接着进行耳内镜手术(TEP),以便对中耳病变进行切除和活检。每周在医院冲洗耳道一次,逐渐减少为每月一次;并且在家清洁耳朵和外用耳类固醇药物,最初每天,然后逐渐减至周一到两次。

结果 — 9只犬有慢性外耳炎病史,7只出现头倾斜,4只出现面瘫。耳道检查发现七只耳道有突出结节;CT显示12例犬鼓室有软组织样物质蓄积,其中7例鼓室扩张;MRI显示12只耳道至少存在鼓室内内容物对比度增强。经TEP治疗和维持治疗后,9只耳道在平均27.9个月的随访期间没有进一步的中耳疾病症状。

结论和临床价值 — 结果提示,所有犬外耳炎不一定先于胆脂瘤发生。对于识别胆脂瘤,MRI似乎比CT更敏感。胆脂瘤的保守治疗可以作为手术前的备选方案。

Resumo

Contexto — Os colesteatomas aurais, também chamados de timpanoqueratomas, são formações de epitélio queratinizado destrutivas e expansíveis que se desenvolvem no ouvido médio. Eles são relatados esporadicamente em cães, e o tratamento cirúrgico é geralmente o mais recomendado.

Objetivos — Descrever os principais achados clínicos, radiográficos e histopatológicos de colesteatomas e relatar os resultados de tratamentos conservativos.

Animais — Onze cães (13 ouvidos) com colesteatomas.

Métodos e materiais — Os históricos clínicos dos cães diagnosticados com colesteatoma entre 2012 e 2018 foram revisados. Todos os cães foram submetidos à tomografia computadorizada (TC) e/ou ressonância magnética (RM) seguido por procedimento endoscópico trans-canal (TEP) para remoção e coleta de biópsia das lesões no ouvido médio. Posteriormente, os cães foram submetidos à limpeza otológica na clínica inicialmente uma vez por semana e depois mensalmente, bem como limpeza otológica em casa e aplicação de formulação ótica com esteroide tópico, inicialmente diariamente e depois reduzido para uma a duas vezes por semana.

Resultados — Nove cães possuíam histórico de otite externa crônica; inclinação de cabeça ou paralisia facial foram observadas em sete e quatro casos, respectivamente. O exame otológico revelou um nódulo proeminente em sete ouvidos. A TC demonstrou presença de material similar a tecido mole em 12 bulas e expansão em sete bulas. A RM revelou em 12 ouvidos a presença de conteúdo na bula timpânica que realçava minimamente após administração de contraste. Após TEP e com o tratamento de manutenção, nove ouvidos não apresentavam mais sinais de otopatia de ouvido médio por um tempo médio de acompanhamento de 27,9 meses.

Conclusões e importância clínica — Os resultados sugerem que a otite externa não necessariamente precede o colesteatoma em todos os cães. A RM parece ser mais sensível que a TC para a identificação de colesteatomas. O tratamento conservativo para colesteatomas pode ser útil antes ou como uma alternativa à cirurgia.