Diagnosis and Management of Cholesteatomas in Dogs

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KEYWORDS

• Cholesteatoma • Middle ear • Diagnosis • Imaging • Surgical management

KEY POINTS

- Aural cholesteatomas are expansile lesions of the middle ear.
- Clinical symptoms are draining tracts, pain on opening the mouth, and neurologic impairment.
- Imaging findings include soft tissue density in the middle ear and destruction of the bone of the bulla with characteristics of an aggressive lesion.
- Patients with neurologic signs have a poorer prognosis.
- Long-term medical treatment of recurring or persisting signs is possible.

INTRODUCTION

Nature of the Problem

A middle ear cholesteatoma is an expansile lesion of the middle ear; it presents as a lesion that can be locally destructive, giving the appearance of an aggressive tumor, although it is a non-neoplastic condition.

This lesion consists of an epidermoid cyst that contains keratin debris and is lined by keratinizing squamous epithelium.[1–6] The keratotic material is accumulated because of secondary hyperkeratosis from misplaced keratinizing stratified squamous epithelium within the lesion. This accumulation leads to gradual enlargement of the cyst causing compression and potentially destruction of the surrounding tissues.[5] Expansion and rupture of the cyst cause an inflammatory condition and can become infected, as evidenced by positive cultures in most cases. This secondary infection of the cyst will then increase the inflammatory reaction exacerbating the response.[1]

In veterinary patients, this condition was initially thought to be secondary to a failed total ear canal ablation-lateral bulla osteotomy (TECA-LBO) procedure for otitis externa and media but has been proven to develop as a primary condition or

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component of otitis externa/media without prior surgery or iatrogenic trauma, as shown in a large case series.[1] The incidence of cholesteatoma in dogs with otitis media could be as high as 11%.[7]

Although the etiopathogenesis is not completely understood, by consensus, 2 broad categories are currently recognized: congenital and acquired (**Table 1**).[6] The congenital form is rare and has not been reported in dogs.[1–4] It is defined as a expanding cystic mass assumed to be present at birth but usually diagnosed in infancy or early childhood.[6]

The development of the congenital form can be further subclassified in the epithelial rest theory and the acquired inclusion theory.[5] In the epithelial rest theory, it is proposed that a nest of epithelial cells pathologically persist in the fetal temporal bones. If the cells are implanted into the middle ear because of a childhood event affecting the tympanic membrane (TM) or middle ear, it is termed *acquired inclusion*.[5]

Acquired cholesteatomas can be categorized according to their proposed pathogenesis into 4 different categories: a primary form and 3 secondary forms.[1–4] The primary form is thought to develop secondary to a dysfunction of the eustachian tube and chronic misventilation of the auditory tube, which in turn leads to invagination of the TM into the bulla (invagination or retraction theory).[2,4] Ligation of the eustachian tube in gerbils did induce cholesteatomas in 75% of animals in one study, but experimental ligation of the eustachian tube in other studies did not induce cholesteatomas.[8]

The secondary form is considered secondary to chronic otitis media, trauma to the middle ear, or secondary to surgery of the external ear canal and middle ear.[1–4] The metaplasia theory posits that the normally present modified ciliated respiratory epithelium in the bulla undergoes a metaplastic transformation into stratified squamous epithelium because of chronic inflammation. A second theory suggests that breaks in the TM (perforations, rupture, or after surgery) can lead to migration of the stratified squamous epithelium from the external ear canal into the tympanic bulla where it can lead to keratin formation and accumulation due to chronic inflammation (migration theory). The third theory (invasion theory) proposes that keratinizing epithelial cells of the TM migrate into the subepithelial space of the bulla through a basement membrane breach.

Regardless of the cause, the cholesteatoma expands and gradually erodes neighboring bone structures, after which it can expand further,[9] potentially explaining the lytic nature of the bone of the affected tympanic bulla. It has been hypothesized that osteoclasts might be activated during the formation of cholesteatomas and implicated in the bony lysis of the bulla. Osteoclasts have been found microscopically, leading to theorize about their possible involvement.[10–12] However, activated osteoclasts were not identified in bone collected from dogs with cholesteatomatous otitis media in a recent case series.[9]

Definition

It is an expansile cyst containing keratotic material in the middle ear.

Symptom Criteria

- Expansile lesion in the bulla
- Chronic otitis externa/media
- Presence or absence of pain on opening of the jaw
- Presence or absence of neurologic signs, either due to destruction of the petrous bone or due to facial nerve palsy

Table 1
Classification and etiopathogenesis of middle ear cholesteatomas

	Acquired				
	Primary	**Secondary**			**Congenital (Rare)**
Cause	Chronic misventilation of the auditory tube	Complication of otitis media or trauma			Dispersed cells during embryogenesis
Pathogenesis	The TM retracts into the TC leading to adhesions and cholesteatoma formation	Metaplasia of the epithelium into stratified squamous epithelium due to chronic inflammation	Migration of squamous epithelium into the TC after a trigger (inflammatory process) and across a bridge (granulation tissue) through perforations in or rupture of the TM	Invasion of epithelial cells into subepithelial space through a BM breach	No inflammatory trigger or defects are needed
Synonyms	Invagination theory Retraction theory	Metaplasia theory	Migration theory	Invasion theory	—
Species	Humans	Humans, dogs			Humans, Mongolian gerbil

Abbreviations: BM, basement membrane; TC, tympanic chamber; TM, tympanic membrane.
Data from Refs.[1–4]

CLINICAL FINDINGS

Signalment and History

No significant breed predilection has been reported in the literature, although spaniels and retrievers seem to be overrepresented (pugs [3], spaniels [10], and retrievers [6]),[1,3,4,13] and a higher incidence in male dogs was found; but this finding was not significant, most likely because of small patient numbers. In people, a similar, as of yet unexplained, sex bias has been reported.[14]

Although cholesteatomas are most commonly found in middle-aged to older dogs, the reported ages on presentation in the literature range from 2 to 12 years old.[1,3] Similarly, most dogs present with a protracted history of aural disease, although the reported duration of signs is variable, ranging from 3 weeks to more than 6 years.[1,3]

Presenting complaints include otitis externa, head shaking, pain on opening of the mouth or inability to fully open the mouth, and neurologic signs.[1,3,4,13]

Most cases reported in the veterinary literature have unilateral disease. In the earlier large case series by Hardie and colleagues,[1] 15 out of 19 patients had unilateral disease. In subsequent more recent articles, all but one case were unilateral (**Table 2**).[1,3,4,13]

The incidence of prior surgery varied extensively between the different studies: Hardie and colleagues[1] reported that 3 of the 20 included patients had had prior surgery (TECA-LBO 1, lateral wall resection 1, external ear canal mass resection 1), whereas all included cases in 2 other studies underwent surgery before presentation: The 2 patients reported by Schuenemann and Oechtering[4] had an LBO performed previously; and of the 11 patients reported by Greci and colleagues,[3] 10 underwent a TECA-LBO previously and one a VBO.

Physical Examination

Presenting complaints include signs related to chronic otitis externa/media (head shaking, pain on palpation, discharge, swelling, redness, ±draining tracts), pain on opening of the mouth or inability to fully open the mouth, and neurologic signs, including head tilt, facial nerve palsy, ataxia, and nystagmus.

Inability to open the mouth or discomfort on opening of the mouth is a common presenting complaint, reported in 6 out of 10 dogs[3] and 4 out of 20 dogs.[1] Respiratory signs can be present due to a space-occupying mass compromising the lumen of the nasopharynx/larynx, as reported by Schuenemann and Oechtering.[4]

Otoscopic Examination

Most dogs showed pain on palpation of the area of the bulla (9 out of 10 dogs) and/or otorrhea (8 out of 10 dogs).[3] Findings during an otoscopic or video otoscopic examination can resemble end-stage otitis externa. Greci and colleagues[3] described a total occlusion of the horizontal canal in 4 out of 11 ears with end-stage otitis. In other cases the external ear canal can be patent, allowing visualization of the cholesteatoma itself. These cholesteatomas appear as a pearly white to yellow growth protruding from the middle ear cavity into the external ear canal (Newman and colleagues,[5] 2015, one case) (Greci and colleagues,[3] 2011, 3 cases).

Focused Neurologic Examination

More than 50% of dogs present with concurrent neurologic signs, or neurologic abnormalities were found on physical examination (head tilt, facial nerve paralysis, ataxia) in 5 out of 10 dogs[3] and 7 out of 20 dogs.[1] The presence or absence of neurologic signs can serve as a prognostic indicator for recurrence of symptoms or disease after surgical treatment.[1]

Table 2
Imaging findings described in the veterinary literature

	Radiographs (1 out of 1)[3]	CT	MR (1 out of 1)[13]
Unilateral vs bilateral	Unilateral	Unilateral (15 out of 19)[1] (11 out of 11)[2] (10 out of 11)[3]	—
Middle ear contents	Loss of air contrast	Soft tissue density or soft tissue–like material	Isointense to brain tissue (T1W) Mixed intensity (T2W & FLAIR)
Bulla	Sclerosis of the tympanic wall Expansion of the bulla	Osteoproliferation (13 out of 19)[1] (9 out of 11)[2] (9 out of 11)[3] Lysis of the bulla (12 out of 19)[1] (8 out of 11)[2] (5 out of 113) Expansion of the bulla (11 out of 19)[1] (10 out of 11)[2] (11 out of 11)[3]	Expanded bulla Thickened and irregularly shaped wall: hypointense (T1W), mixed intensity (T2W)
Calvarium	Sclerosis of petrosal bone	Bone lysis within the squamous or petrosal portions of the temporal bone (4 out of 19)[1] (5 out of 11)[2]	Petrous temporal bone hypointense on T1W and T2W images
Soft tissue	—	Lymph node enlargement (7 out of 19)[1]	—
TMJ	—	Sclerosis of ipsilateral TMJ (10 out of 11)[2,3]	—
Contrast	—	Contrast enhancement of the tissue in the middle ear (7 out of 10)[1] No contrast enhancement of the tissue in the middle ear (11 out of 11)[2,3] Peripheral ring enhancement (4 out of 11)[2]	Partial enhancement of inner lining (T1W)

Abbreviations: CT, computed tomography; FLAIR, fluid-attenuated inversion recovery; MR, magnetic resonance; T1W, T1 weighted; T2W, T2 weighted; TMJ, temporomandibular joint.
Data from Refs.[1–3,13]

IMAGING

Although different modalities are discussed, computed tomography (CT) or alternatively magnetic resonance (MR) are the methods of choice for assessing the middle ear and middle-ear associated lesions, as they provide improved detail for lesions in areas of complex architecture (see **Table 2**).[15]

Radiographs

A radiographic evaluation might be chosen as a first-line assessment or in the absence of access to either CT or MR. It should ideally be performed under anesthesia and should include a lateral view, a 20° lateral oblique view, a dorsoventral view, and a rostrocaudal open mouth view to best visualize the individual bullae. Described radiographic features of chronic otitis media include lack of air in the bulla, thickening of the bulla wall, and with or without increased size of the bulla; however, the external ear canal can be air filled. Radiographic features of neoplasia include lysis of the bulla and bony proliferation with or without soft tissue lesion filling or extending into the bulla. These findings are nonspecific and can be found in otitis media as well as other lesions affecting the tympanic bulla.[15]

Ultrasonography

The use of ultrasonography has been described in assessing middle ear lesions but has been determined to be less accurate than radiographs and highly operator dependent.[16] It might, however, be of value for obtaining either fine-needle aspiration or true-cut biopsy samples.

Computed Tomography

Reported findings of the tympanic bulla include osteoproliferation, lysis, and sclerosis. The bulla is expanded (**Figs. 1–3**) and filled with soft tissue–like material. The external ear canal can be involved and filled with fluid or soft tissue, although in other cases the external ear canal can be air filled (see **Fig. 2**).

Bone lysis within the squamous or petrosal portions of the temporal bone have been described in 25% (Hardie and colleagues[1]) to 50% (Greci and colleagues[3]) of cases.

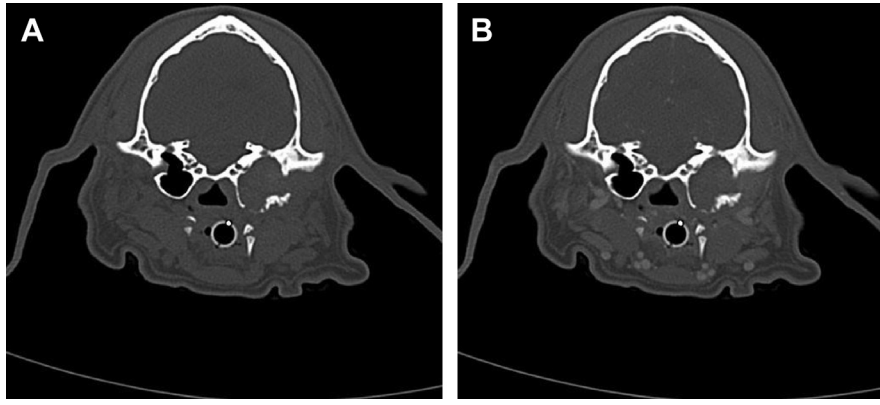

Fig. 1. A transverse image of a CT of a 7-year-old male castrated cocker spaniel with a left-sided cholesteatoma. (*A*) Before contrast and (*B*) after contrast administration. An expansile soft tissue mass of the left tympanic bulla is shown with sclerosis of the left temporal bone. The wall of the bulla shows lytic areas as well as thickening and remodeling. The mass itself is minimally contrast enhancing.

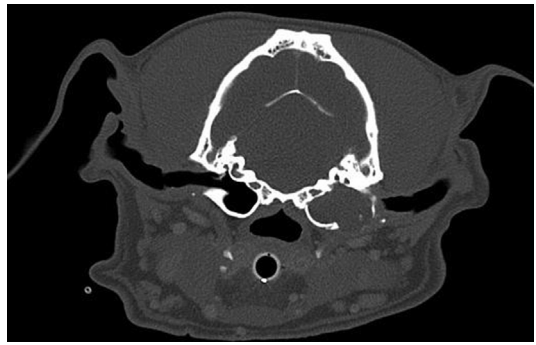

Fig. 2. A transverse image of a CT of a 6-year-old male castrated mixed breed dog with a left-sided cholesteatoma. Note the noninvolvement of the external ear canal and the expansion and destruction of the bulla. A soft tissue attenuating mass expands and fills the entire left tympanic bulla. The ventral margin of the bulla is thin and disrupted; the lesion is localized to the middle ear cavity.

Initial reports indicated that the tissue in the bulla enhances after contrast administration; however, later descriptions further define the contrast enhancement to be only localized around the lining of the bulla and not to involve the entire soft tissue structure filling the bulla.[3] Other reports indicate that contrast enhancement of the epithelial lining of the tympanic bulla in chronic otitis media cases is confined to an area directly adjacent to the bone (Garosi and colleagues[15]), similar to cholesteatomas. Neoplastic lesions are most commonly an extension of external ear canal tumors into the bulla, and contrast enhancement of the mass within the external ear canal might allow differentiation. Aggressive neoplastic lesions originating within the tympanic bulla are extremely rare but might exhibit some of the same features, such as filling of the bulla with soft tissue and lysis of the bulla wall, but do not typically exhibit the same general expansion of the entire tympanic bulla.

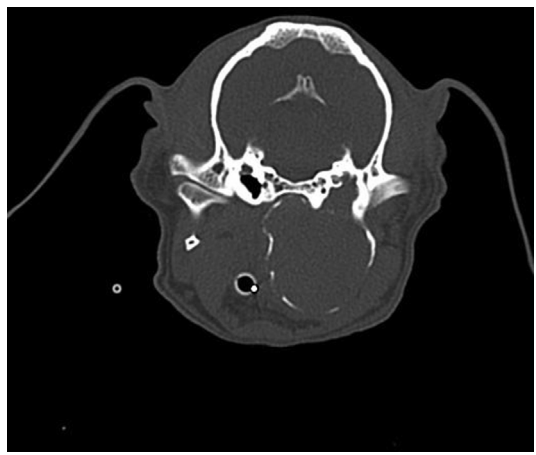

Fig. 3. A noncontrast transverse image of a CT of a 10-year-old male castrated shih tzu is shown with a left-sided cholesteatoma. The left tympanic bulla is severely expanded and is filled with a soft tissue mass. The expanded bulla attenuates the nasopharynx and is markedly attenuating and displacing the oropharynx and larynx to the right. The temporal and masseter muscles on the left are atrophied compared with the contralateral side.

Other findings include enlargement of the local lymph nodes (7 out 19 cases)[1] or sclerosis of the ipsilateral temporomandibular joint in 10 of 11 patients.[3]

MRI

MR has been used to further define the intracranial extent of the disease or in the absence of CT imaging capabilities on site.[1,5,13,17] MR is better suited to define the soft tissue structures, such as nerves, vessels, and inner ear structures, whereas CT is better suited to assess the bony structures.[15]

MR findings include a severely expanded bulla containing material isointense to brain tissue on T1-weighted and of mixed intensity on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images.[13] Similar to the CT findings, the tissue in the tympanic bulla was found to be minimally contrast enhancing, with contrast enhancement localized to the area immediately adjacent to the bone, in the location of the inner (epithelial) lining of the bulla.[5] Other findings include lysis of the petrous temporal bone.[5] MR features of neoplasia of the tympanic bulla have been described, but the number of cases in the literature might be too low to define distinct characteristics between cholesteatomas of the middle ear and malignant neoplasia of the middle ear.

Differential Diagnoses

Differential diagnoses to be considered are chronic otitis externa/media and aural neoplasia, either extending from the external canal into the tympanic bulla or neoplasia arising from the bulla.

In chronic otitis media, CT would also show a bulla filled with tissue or fluid, with or without lysis of the bone of the bulla, but lacks the expansile nature of growth and expansion of the bulla.

Neoplasia of the tympanic bulla in dogs is very rare. The most commonly described neoplasias extend from the external ear canal into the bulla (such as ceruminous gland adenoma, ceruminous gland adenocarcinoma, squamous cell carcinoma).[18] Contrast enhancement of the external portion of the mass could help differentiate between these and middle ear cholesteatomas and middle ear neoplasia.

Imaging findings that are described for middle ear neoplasia are similar to imaging findings for middle ear cholesteatomas but seem to have more contrast enhancement than cholesteatomas. Histologic sampling would be the only definitive differentiation between cholesteatomas and neoplastic lesions; but the otoscopic, cytologic, and imaging findings, in addition to the very rare incidence of primary middle ear neoplasia, should make middle ear cholesteatoma the primary differential.

PATHOLOGY

Cytology

Impression smears taken of a biopsy in one report revealed anucleate squamous epithelial cells, low numbers of inflammatory cells, small groups of spindle cells (presumed fibroblasts), and extracellular bacteria (cocci).[5]

Histopathology

Biopsy results are consistent with finding keratinizing epithelium and keratin debris (6 ears).[3]

A core of fibrous connective tissue can be present, covered by a hyperplastic keratinizing stratified squamous epithelium. A cystic lesion lined by a multilayered intensely hyperplastic keratinizing epithelium has also been described.[3]

In the submucosal layer, a large accumulation of cholesterol clefts was present, whereas the center of the lesion contained areas of mineralization and fragments of

woven bone, leading to the histopathologic diagnosis of a cholesterol granuloma with osseous metaplasia (incisional biopsy).[5]

Microbiology

The culture results reflect a similar outcome as would be expected in chronic otitis externa cases. Hardie and colleagues[1] found positive aerobic cultures in 14 out of 16 cultured ears, with 3 dogs having more than 1 bacterial species cultured. Greci and colleagues[3] reported positive aerobic cultures from 8 out of 12 ears, and more than one species was recovered from one ear. *Staphylococcus* species were the most prevalent, with *Enterococcus* spp, *Pseudomonas aeruginosa*, *Staphylococcus* spp (3), *Proteus* (2), *Pseudomonas*, and *Escherichia coli* (1) making up the remainder of reported bacteria.[1,3]

A recent retrospective study on patients with chronic otitis externa/media reported positive cultures in 89% of cultured ears (n = 127), with *Staphylococcus* spp in 43% of ears, and found *Enterococcus* spp, *Pseudomonas*, *E coli*, and *Proteus mirabilis*.[18]

TREATMENT

Surgery

Surgical treatment can be curative in 50% of cases. Early surgical intervention is preferred; but even in later stage disease, surgery is recommended to remove the diseased tissue and remove as much of the space-occupying soft tissue and lesion, both from a diagnostic and from a palliative approach. Palliation might be obtained by removing the painful stimulus by removing the material from the bulla.

A caudal auricular approach has been described, but a ventral or lateral approach to the bulla is favored for the initial surgical treatment. The caudal approach was described in an attempt to preserve hearing and cosmetic outcome by preserving the external ear canal and reconstructing the ossicles.[19] A ventral approach has been preferentially used for cases with recurrent disease, especially if a lateral approach has been used previously, as it will provide better exposure to the bulla.[1,3,19]

Cases with chronic otitis externa are treated by TECA-LBO, as the disease involves both the external ear canal and the bulla (see **Fig. 1**). In these cases, the middle ear cholesteatoma could be an extension of the chronic disease in the external ear, with destruction of the tympanic membrane, allowing ingrowth of metaplastic ear canal epithelium into the middle ear. Care is taken to create good access to the tympanic cavity allowing for aggressive removal of the diseased tissue. If the expansive lesion of the bulla cannot be adequately accessed through a lateral approach, a combination of a lateral and ventral approach can be used to maximize exposure.[3] Complete removal is the goal of curative-intent surgery, and inspection of the bulla to check for remaining diseased tissue can be performed with an endoscope to facilitate this. Additionally, care must be taken not to transplant stratified squamous epithelium from the external ear canal into the middle ear during surgery, as this is one of proposed etiopathogeneses of canine middle ear cholesteatomas.[1]

In some cases the cholesteatoma of the middle ear can be contained within the middle ear, without overt external ear canal involvement (see **Fig. 2**). In such cases, a ventral approach (ventral bulla osteotomy [VBO]) can be used. Care must be taken to ensure that there is no diseased tissue in the external meatus. Magnification, such as surgical loupes, could help guide surgical dissection and removal of the tissue.

Regardless of the approach used, care is taken to remove as much of the diseased tissue as possible. Microscopic or endoscopic visualization, or a combination of both,

is used in the surgical management of people with middle ear cholesteatomas.[20] This visualization might also help identify neurovascular structures more readily.

No difference in outcome was found between cases managed by a lateral approach or ventral approach. Cases managed with a TECA-LBO, or LBO only if a TECA had been performed previously, were evenly distributed over the 2 groups in the article by Hardie and colleagues.[1] They found that the cured cases had a lateral approach in 5 and a ventral approach in 4 cases, whereas the cases with recurrence had a lateral approach in 8 and a ventral in 2 patients. Three cases that had a second surgery all had a lateral approach in the revision surgery.[1]

It is key to remove all diseased/affected tissue to prevent recurrence. However, even in cases whereby removal was incomplete because of proximity of vital structures, a long-term survival was achieved despite needing chronic intermittent broad-spectrum antibiotics.[1,3]

Postoperative complications include facial nerve palsy/paresis/paralysis, recurrence of signs, development of draining tracts, and failure to resolve the preexisting neurologic signs.[1] These numbers are similar to the reported postoperative complication rates for TECA-LBO in dogs for otitis externa/interna[18] or VBO in dogs.

Medical Management

Chronic antibiotic therapy has been described for management in cases with recurrence after surgery or in cases whereby surgery was declined. The disease unfortunately is progressive, and the continued expansion of the cholesteatoma will lead to worsening of neurologic and/or respiratory signs over time.

PROGNOSIS/RECURRENCE

The combined reported rate of ears without recurrence after surgical therapy is 50%. In the case series by Hardie and colleagues,[1] 9 dogs had no recurrence and 10 had persistent or recurrent signs, whereas in the case series by Greci and colleagues,[3] 7 ears had no recurrence.

Greci and colleagues[3] reported a mean time until recurrence of 7.5 months (range 2–13 months postoperatively, 5 ears, confirmed in 4). Of the noncured animals in the study by Hardie and colleagues,[1] 5 dogs were readmitted for neurologic signs 1 to 16 months postoperatively. Three dogs were readmitted for inability to open the mouth at 2, 16, and 31 months postoperatively and underwent a second surgery (lateral approach) and, although requiring chronic intermittent antibiotic therapy, did not die of their cholesteatoma (37, 40, >52 months after the first surgery).

Clinical signs on presentation or imaging that were found to have a significant effect on the development of recurrence (univariate analysis) were inability to open mouth, neurologic signs, lysis of the tympanic bulla wall, and lysis within the temporal bone. However, only neurologic signs were shown to be a statistically significant predictor for the development of recurrence when using stepwise multivariable analysis.[1]

Of the neurologic signs reported by Greci and colleagues,[3] facial palsy and ataxia resolved after surgery, whereas preoperative head tilt persisted postoperatively.

Risk factors that were identified for recurrence or nonresolution of clinical signs were inability to open mouth in 19 cases (1 cured, 7 not cured), lysis of the bone of the tympanic bulla was present in 11 out of 18 cases imaged (4 cured, 7 not cured), expansion of the bulla was present in 11 out of 18 cases imaged (4 cured, 7 not cured), and bone lysis of the temporal bone was present in 6 out of 18 cases imaged (0 cured,

6 not cured). *Pseudomonas* was only cultured in cases that were not cured. Factors not associated with recurrence were osteoproliferation (6 out of 9 cured, 6 out of 9 not cured), lymph node enlargement (4 out of 9 cured, 3 out of 9 not cured).[1]

Of the dogs with recurrence reported by Greci and colleagues,[3] 2 were successfully treated (no recurrence at 32 and 42 months after second surgery). Two other dogs that had recurrence had a combination of multiple surgeries and continued medical management: one dog was treated surgically 4 times (LBO once, VBO 3 times) and still had persistent signs after the fourth surgery and one dog had 2 surgeries and medical management (antiinflammatory dose of steroids in conjunction with broad-spectrum antibiotics) after its second recurrence.[3]

Of the cases with recurrence described by Hardie and colleagues,[1] 3 of the 5 dogs with neurologic signs were euthanized without a revision surgery and 2 were managed with chronic systemic antibiotic therapy (one alive at the time of writing, one died of unrelated causes 29 months after the initial surgery). All 3 dogs presenting for inability or reluctance to open the mouth had a second surgery, and all required chronic intermittent systemic antibiotic therapy. Two died of unrelated causes at 37 and 40 months after the initial surgery, whereas the third was alive at the time of writing (52 months after the first surgery).[1]

SUMMARY

Surgical intervention can be curative. Dogs with early stage disease have a better outcome than dogs with more chronic disease and with temporal bone involvement.[1] Dogs with recurrent disease can be reoperated or managed medically with long-term resolution or palliation of clinical signs.

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