Vol 32, Issue 3, June 2018

VETERINARIA

MRI findings of middle ear cholesteatoma in the dog: 6 cases and literature review

Ilaria Pitzorno*, Med Vet

Marco Carrozza, Med Vet

Giulio Destrero, Med Vet

Canine middle ear cholesteatoma is a disease with an aggressive biological behaviour and with clinical signs that may vary according to the degree of involvement of structures adjacent to the affected tympanic bulla and which may cause possible damage to the nervous system. This article describes 6 cases of canine middle ear cholesteatoma presenting different lesions and clinical signs diagnosed by Magnetic Resonance Imaging and confirmed by histologic or cytologic examination, with a review of the literature.

Key words - Cholesteatoma, epidermoid cyst, middle ear, otitis, Magnetic Resonance, dog.

INTRODUCTION

Cholesteatoma, or more appropriately middle ear dermoid cyst, is a rare non-neoplastic lesion characterized by an aggressive biological behaviour.[1,2] In human medicine, both congenital and acquired forms are described; in the dog, forms secondary to chronic otitis media are mainly reported.[3,4] Clinical signs vary in relation to the involvement of the structures adjacent to the tympanic bulla, with temporomandibular pain being the most consistently described symptom, but neurological signs are also often reported.[3,4] Surgery is the only possible therapy, but in both human and veterinary medicine relapses are frequent.[4,5] Treatment consists in the surgical removal and control of the associated infection. This article describes the clinical, radiographic and MRI characteristics of 6 patients with middle ear cholesteatoma. In the cases treated surgically, the technique used and the results of the follow-up are reported.

CLINICAL CASES

Following the neurological examination the referred patients underwent general anaesthesia, exploration of the buccal cavity, chest X-rays and MRI examination (0.25 T, Vet Grande Esaote, Genoa) of the skull using the following protocol: T2-weighted scans, using the GE-STIR technique, and T1-weighted scans before and after the intravenous administration of a paramagnetic contrast medium (Gadopentetic acid dimegluminal salt, Magnevist®, Bayer Pharma AG, Berlin, Germany), at the dose of 0.1 mMol/kg, performed on three planes.

CASE 1

Nine-year-old male Shih-Tzu referred for localized pain to the head region and anorexia. The clinical history reported recurrent episodes of chronic otitis, treated with topical antibiotic therapy, and deafness.

Middle ear cholesteatoma is a non-neoplastic process characterized by continuous growth and clinical signs caused by compression of the structures adjacent to the tympanic bulla.

The physical examination revealed pain on palpation of the left temporomandibular region. The main differential diagnoses considered were myositis of the

Destrero Dr. Giulio e Carrozza Dr. Marco - Associazione Professionale Medici Veterinari, Roma

*Corresponding Author (ilaria.pitzorno@gmail.com)

Received: 28/10/2017 - Accepted: 07/05/2018

masticatory muscles and infection-inflammation of the outer/middle ear or of the oral cavity. Difficulty in opening of the mouth was evident at induction of the anaesthesia; exploration of the oral cavity revealed lateral swelling to the left, in correspondence with the proximal part of the mandibular branch, which extended to the hard palate. MRI showed ventral expansion of the left tympanic bulla, with the presence of material exhibiting a non-homogeneous signal: isointense to muscle tissue in T1-weighted scans and hyperintense in T2-weighted FLAIR and GE-STIR sequences (Figs 1A-C, 2). The bulla's profile extended laterally and ventrally to the ventral part of the left temporomandibular joint, extending medially well below the basisphenoid bone, crossing the midline and occluding the nasopharynx. In T1- and T2-weighted sequences the mastoid process of the ipsilateral temporal bone appeared increased in volume and with a hypointense signal, indicating the absence of bone marrow fat, probably related to sclerotic events (Figs 1A, B). In GE-STIR sequences the wall of the left tympanic bulla, of non-homogeneous thickness and irregular profile, appeared surrounded by a halo of hyperintense signal. Post-contrast sequences showed contrast medium uptake in the periphery of the bone wall of the middle ear cavity and of the cortical bone of the angular process of the mandible (Fig 1C). The right tympanic bulla was replete of hyperintense material in long TR sequences and hypo-isointense in T1-weighted sequences; post-contrast medium sequences showed peripheral enhancement at the wall of the bulla and mild uptake by the innermost layer of the lesion (Fig 1C). The examination was compatible with bilateral cholesteatoma, of greater severity in the left ear. Due to the extent of the lesion and the lateralization of symptoms, a ventral ostectomy of only the left tympanic bulla was planned. During the procedure a sample of the lesion was taken for histological examination as well as a swab for culture

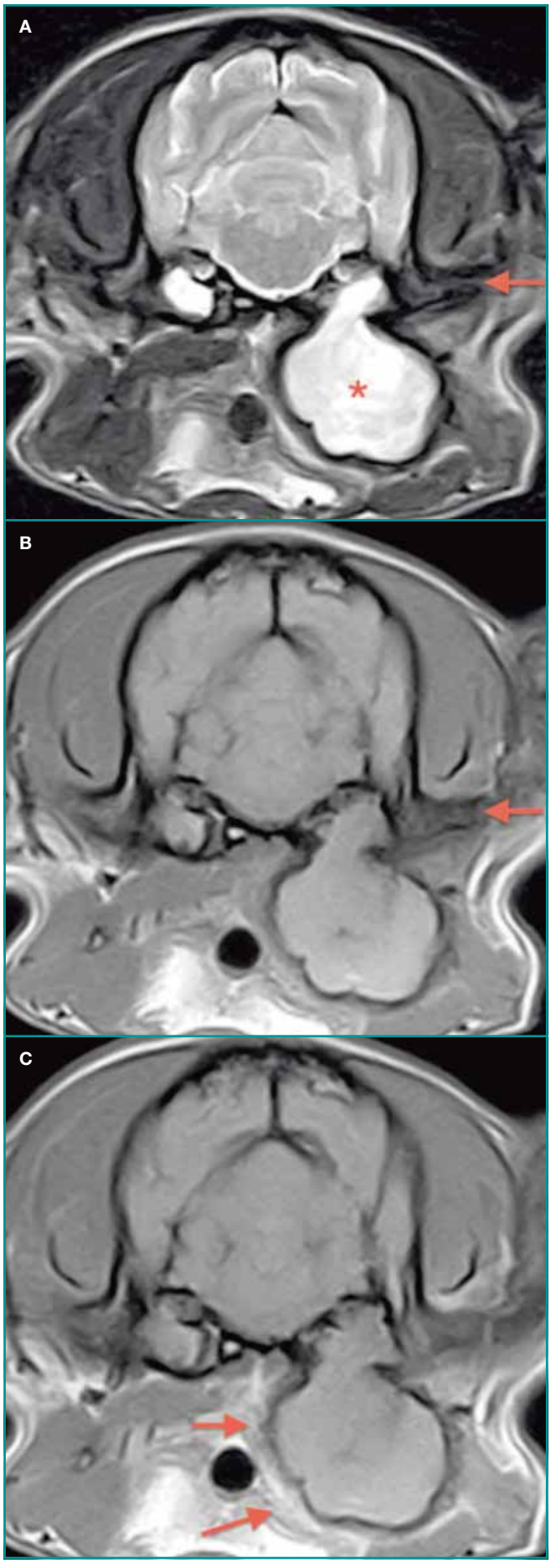

Figure 1 - Case 1. **A**) Transverse T2-weighted scan of the tympanic bullae. Both tympanic bullae are replete of material with inhomogeneously hyperintense signal compared to muscle tissue, the left bulla is significantly increased in volume (asterisk). The mastoid process of the temporal bone has a hypointense signal compared to the contralateral one, probably due to the presence of sclerosis (arrow). **B**) Pre-contrast transverse T1-weighted scan. The arrow highlights the mastoid process of the temporal bone. **C**) Post-contrast transverse T1-weighted scan. The arrows highlight the contrast medium uptake external to the wall of the tympanic bulla. There is no uptake of contrast medium by the content of the tympanic bulla.

examination and antibiogram. Histology confirmed the suspicion of middle ear cholesteatoma. Culture tests revealed the presence of beta-hemolytic Streptococcus and *Escherichia coli* sensitive to common antibiotics. Postoperative controls revealed a complete resolution of pain and the owner reported the resolution of dysphagia. A control MRI was performed at 4 months; VBO surgery of the right ear was performed a few days later. The histological examination confirmed the diagnostic suspicion and the cultural examination resulted superimposable to that of the left ear. The patient recovered from the second operation uneventfully and at the 30-month follow-up no signs of relapse were present.

CASE 2

Ten-year-old male Golden Retriever referred for the presence - for several months - of right head tilt and loss of balance. The neurological examination exhibited: right pleurothotonus, right head tilt, vestibular ataxia, decreased right menace response, decreased right palpebral and corneal reflexes, decreased swallowing reflex, right temporal and masseter muscle atrophy. The main differential diagnoses included a right brainstem mass or an infectious/granulomatous process. MRI exhibited a ventro-lateral expansion of the right tympanic bulla, with the same signal characteristics as in case 1. Furthermore a mass with hyperintense signal in T2-weighted sequences and isointense in T1-weighted sequences was detected at the level of the right brainstem, with peripheral contrast enhancement, in continuity with the lesion mentioned above (Fig 3A, B). Erosion of the inner ear, sclerosis of the temporal bone and marked atrophy of the ipsilateral temporal muscles were also evident. A needle biopsy of the lesion was performed via a myringotomy. Cytological examination of the material collected confirmed the suspicion of cholesteatoma. The owner did not give consent for surgery to remove the lesion as well as for any additional clinical follow-up.

Figure 2 - Case 1: Ventrodorsal X-ray of the skull. The arrows highlight the bony walls of the left tympanic bulla. Note the increased volume of the bulla and the inhomogeneous appearance of its walls, which appear irregular in profile with thickened and lithic areas.

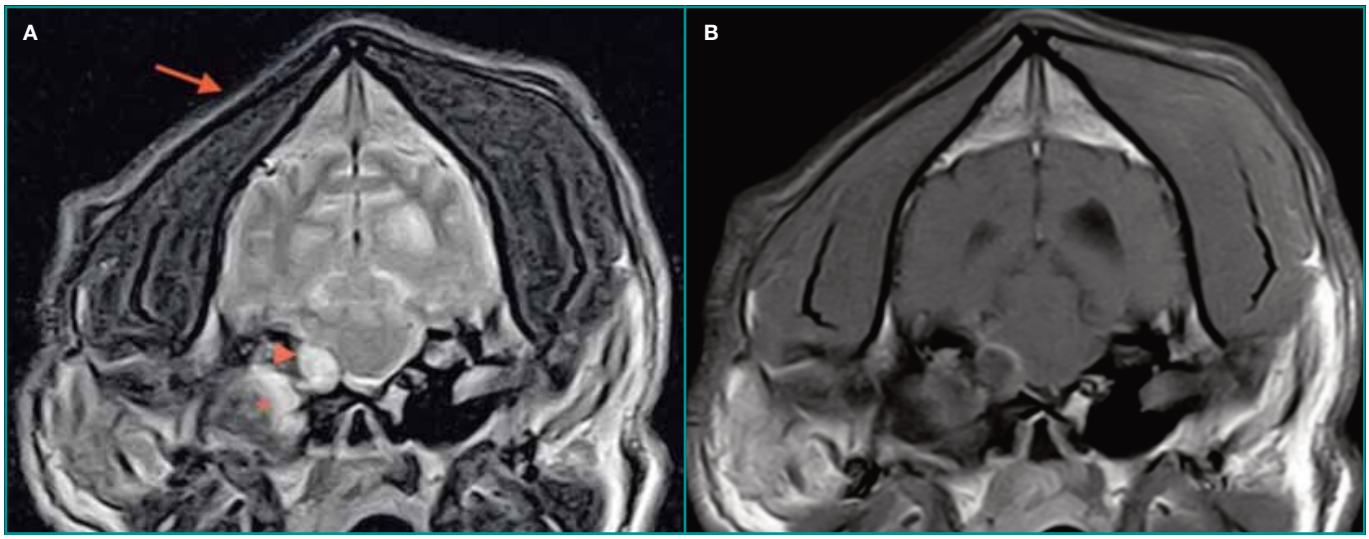

Figure 3 - Case 2. **A**) Transverse T2-weighted scan of the tympanic bullae. The right temporal muscle appears atrophic compared to the contralateral one (arrow). An oval mass of hyperintense signal with respect to the muscle tissue is observed in the T2-weighted sequences at the right brainstem (arrow head), in continuity with the ipsilateral tympanic bulla (asterisk); this appears increased in volume compared to the contralateral one, with inhomogeneously hyperintense signal content. **B**) Post-contrast transverse T1-weighted scan: uptake of contrast medium in the periphery of the described lesion.

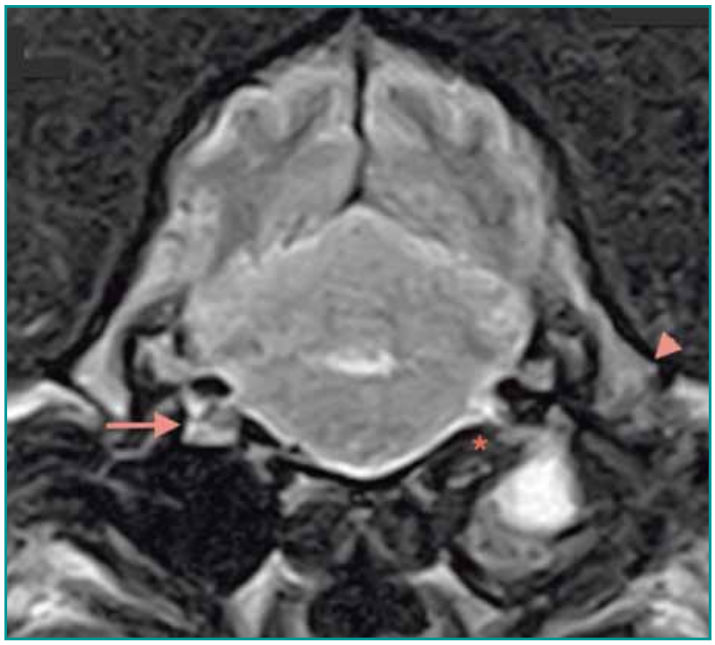

Figure 4 - Case 3: Transverse T2-weighted scan. A lesion of the inner ear is observed in correspondence with the cholesteatoma of the left tympanic bulla, identifiable by the absent signal (asterisk). The arrow indicates the right inner ear, with a normal signal. The mastoid process of the temporal bone appears increased in volume and with a hypointense signal compared to the contralateral one, probably due to the presence of sclerosis (arrowhead).

CASE 3

Five-year-old female Labrador Retriever referred for right head tilt and hearing loss present for one month. The neurological examination showed right head tilt and vestibular ataxia. MRI revealed the presence of material of unevenly hyperintense signal in T2-weighted sequences and isointense in T1-weighted sequences of the left tympanic bulla, signal loss at the level of the ipsilateral inner ear and sclerosis of the mastoid process of the temporal bone (Fig 4). Following the administration of gadolinium, peripheral contrast enhancement by the above lesion was observed. A ventral ostectomy of the tympanic bulla was performed with removal of the material and the collection of swabs for cultural examination and antibiogram. The histological examination confirmed the diagnosis of cholesteatoma while the culture examination was negative. The patient recovered from surgery without complications and no signs of relapse were present at the 12-month follow-up.

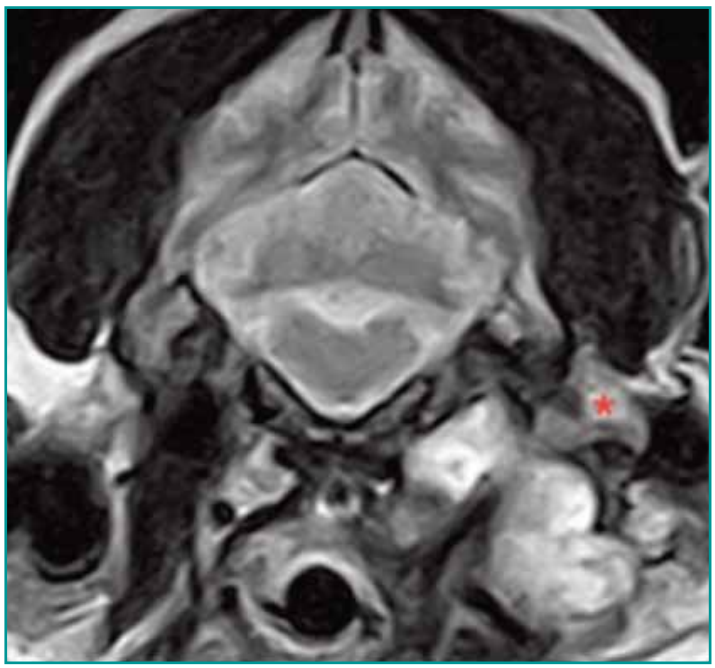

Figure 5 - Case 4: Transverse T2-weighted scan. The left tympanic bulla appears to be significantly increased in volume, with an irregular profile and inhomogeneously hyperintense content; the cholesteatoma extends to the outer ear canal (asterisk).

CASE 4

Fifteen-year-old female Cocker Spaniel referred for loss of balance and left head tilt. The neurological examination exhibited left head tilt and left vestibular ataxia. MRI exhibited ventro-lateral expansion of the left bulla, with the same signal characteristics as in the cases described above; the lesion extended to the medial section of the outer ear canal (Fig 5). TECA-LBO was performed. The biopsies confirmed the diagnostic suspicion, the culture examination revealed the presence of *Staphilococcus aureus* and Pseudomonas spp., multiresistant but sensitive to imipenem. The patient recovered from surgery with no signs of recurrence 15 months after surgery.

CASE 5

Six-year-old male Kurzahaar referred for right head tilt and loss of balance. The neurological examination exhibited right head tilt and vestibular ataxia. MRI exhibited the presence of material with unevenly hyperintense signal in T2-weighted sequences and isointense in T1-weighted sequences in both tympanic bullae, with involvement of the outer ear canal and signal loss at the level of the inner ear, more evident on the right; the wall of the right bulla appeared thicker medially. The lesion showed a remarkable contrast enhancement in the portion adjacent to the wall of the tympanic bulla and externally to the surrounding soft tissues (Fig 6). TECA-LBO was performed first on the right side and about a month later on the left. Histology confirmed the diagnostic suspicion and culture tests showed the presence of antibiotic resistant Pseudomonas spp and *Staphylococcus aureus* in both tympanic bullae. As a consequence of surgery there was paresis of the facial nerve and a slight left head tilt; about three months after the second operation a draining tract

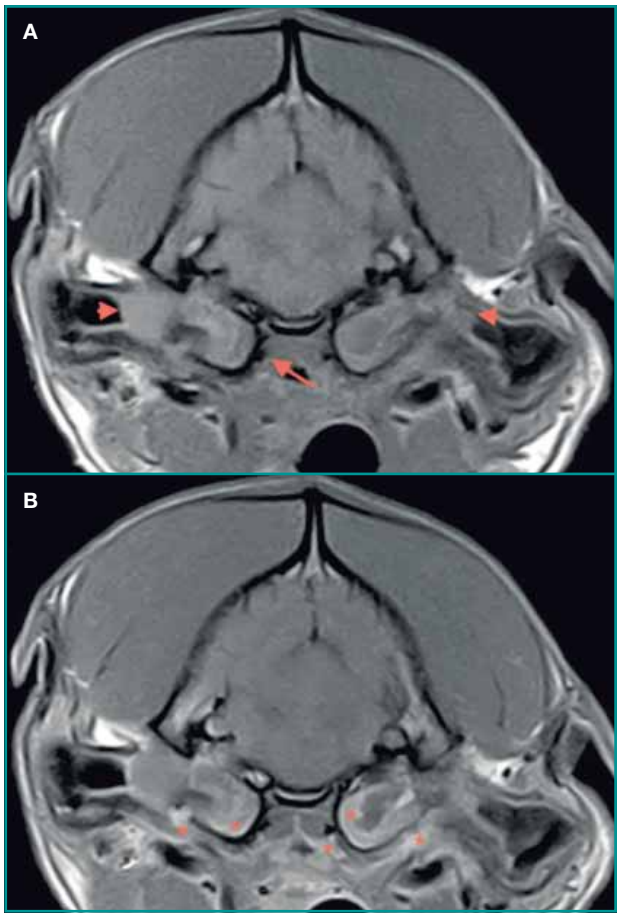

Figure 6 - Case 5. **A)** Pre-contrast transverse T1-weighted scan. The wall of the right tympanic bulla shows thickening and an irregular surface (arrow). The cholesteatoma affect also the horizontal tract of the external ear (arrowheads). **B)** Post-contrast transverse T1-weighted scan: the contrast enhancement is only in the portion of the lesion adjacent to the wall of the tympanic bulla and at the level of the soft tissues surrounding the bulla (asterisks).

The aggressive biological behaviour of the lesion is due to its continuous increase in volume consequent to deposition of keratin lamellae and bone erosion; different etiopathogenetic theories have been considered.

was detected at the level of the right tragus and a control MRI showed the presence of material compatible with inflammatory exudate at the level of the tympanic bullae, with a draining tract to the right (Fig 7). A culture of the purulent material detected the presence of *Escherichia coli* spp and Staphilococcus spp sensitive to ceftriaxone. Treatment with this antibiotic allowed an improvement of the clinical condition.

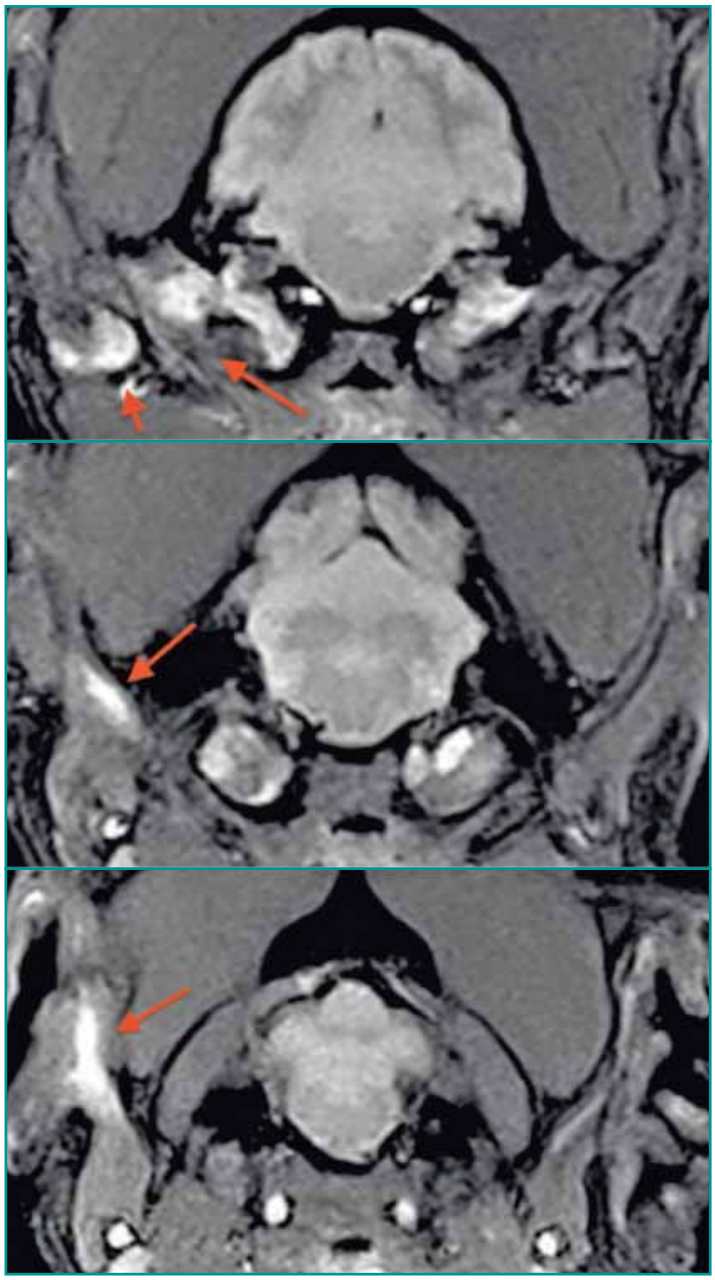

Figure 7 - Case 5. Transverse GE-STIR, consecutive images in oro-aboral direction; the arrows highlight the hyperintense signal lesion that identifies the draining tract.

CASE 6

Twelve-year-old male Dogue de Bordeaux referred for the acute onset of ataxia and left head tilt and a clinical history of bilateral otitis. MRI revealed normal sized tympanic bullae, but replete with material with signal characteristics superimposable to those of the previous cases. Gadodiamide administration resulted in an intense soft tissue uptake adjacent to the walls of the tympanic bullae, especially to the left (Fig. 8). TECA-LBO was performed on the left; the bioptic examination confirmed the hypothesis of cholesteatoma and the culture examination showed

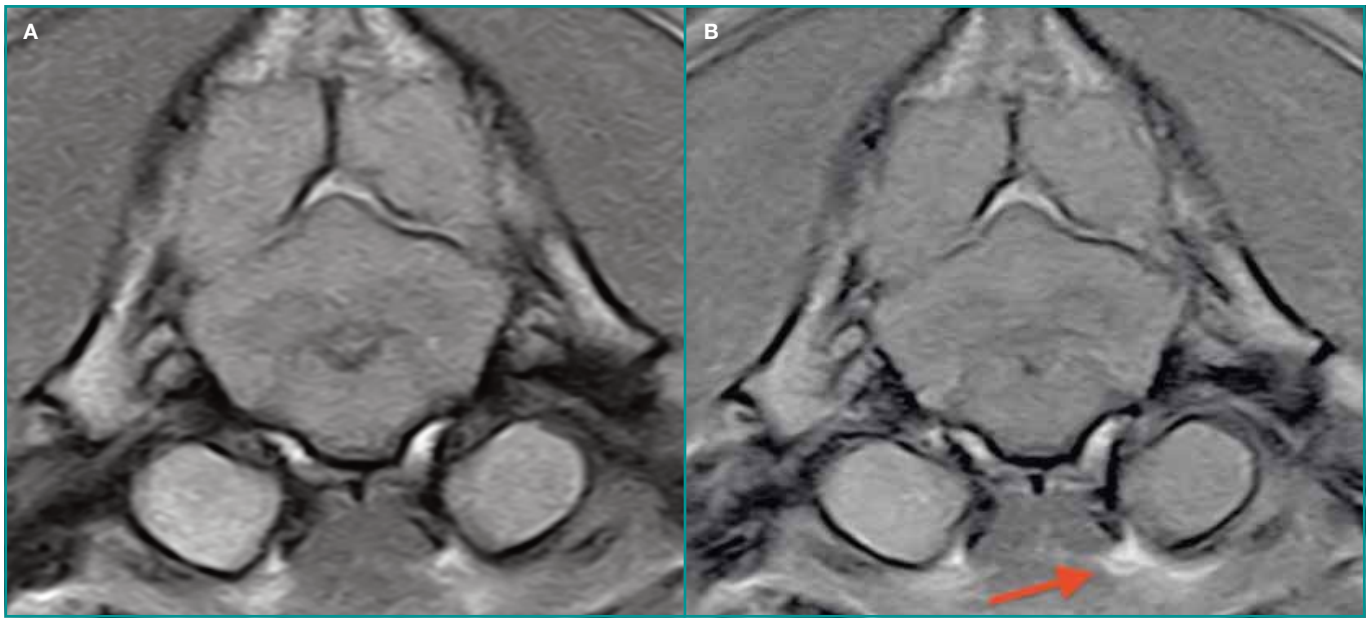

Figure 8 - Case 6. **A**) Pre-contrast transverse T1 scan. **B**) Post-contrast transverse T1 scan. The tympanic bullae appear of normal shape and size, but replete with isointense signal material in T1-weighted sequences. There is no contrast enhancement by the tympanic bullae content; contrast enhancement is evident at the level of the tissues surrounding the walls of the bulla, especially on the left side (arrow).

the presence of multiresistant *Staphylococcus aureus*, sensitive to ciprofloxacin. Despite the proposed bilateral intervention, 5 months after the first surgery the owners rejected the second operation as the patient no longer presented any clinical signs.

DISCUSSION

Middle ear cholesteatoma is a well delimited, non-neoplastic lesion that affects the temporal region; the correct name is middle ear dermoid cyst.[1] Although commonly used, the term cholesteatoma is in fact inappropriate, as only occasionally does the lesion contain lipids (cholesterol) and it is not of neoplastic nature.[6] Macroscopically, it consists of a circumscribed, friable, ovoid or roundish mass, with a poltaceous or macerated grey or yellow content; histologically, the mass consists of a multilayered keratinized squamous epithelium associated with the abundant production of mature lamellar keratin, supported by granulation tissue infiltrated by a mixed leukocyte population (Fig 9);[7] this results in different clinical signs, depending on the tissues involved in the compression,[2] caused by the continuous volume increase of the lesion and the eventual resorption of bone tissue.[8,9,10] Bone erosion is a fundamental characteristic of cholesteatoma and determines its invasiveness and the possibility of affecting nerve structures,[11,15-18] but the mechanism by which it occurs remains unknown and still the object of research; recent studies have shown that in human cholesteatoma, osteoclasts - previously identified as the possible cause -[13] are in fact not present in their activated form.[14]

In human medicine cholesteatomas are distinguished in congenital and acquired; the former originate from

In the dog, middle ear cholesteatoma is often associated with bacterial infections and male patients are more commonly affected. Cases secondary to ear surgery have been described.

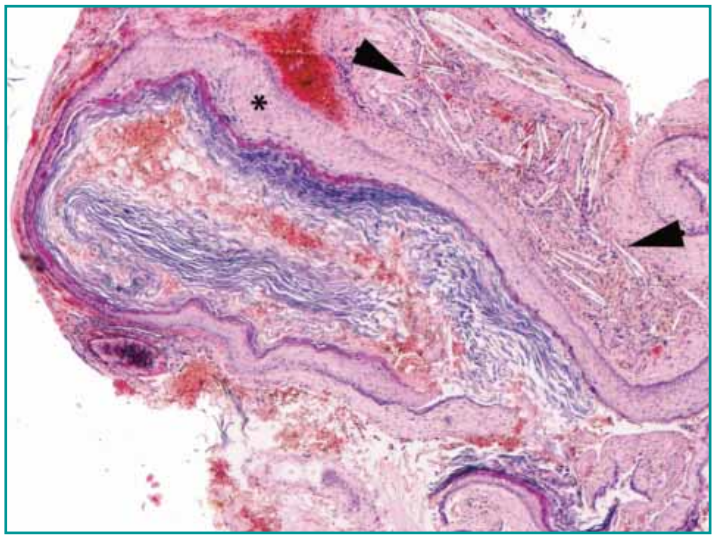

Figure 9 - Nine-year-old male Shih-tzu (Case 1). Middle ear cholesteatoma. The lesion consists of multilayered floor epithelium associated with the production of abundant lamellar keratin material (asterisk). It extends over a richly vascularized fibrous stroma in which cholesterol crystals and a slight leukocyte infiltration (arrowheads) are detected (H&E, x4) (courtesy of M.T. Mandara).

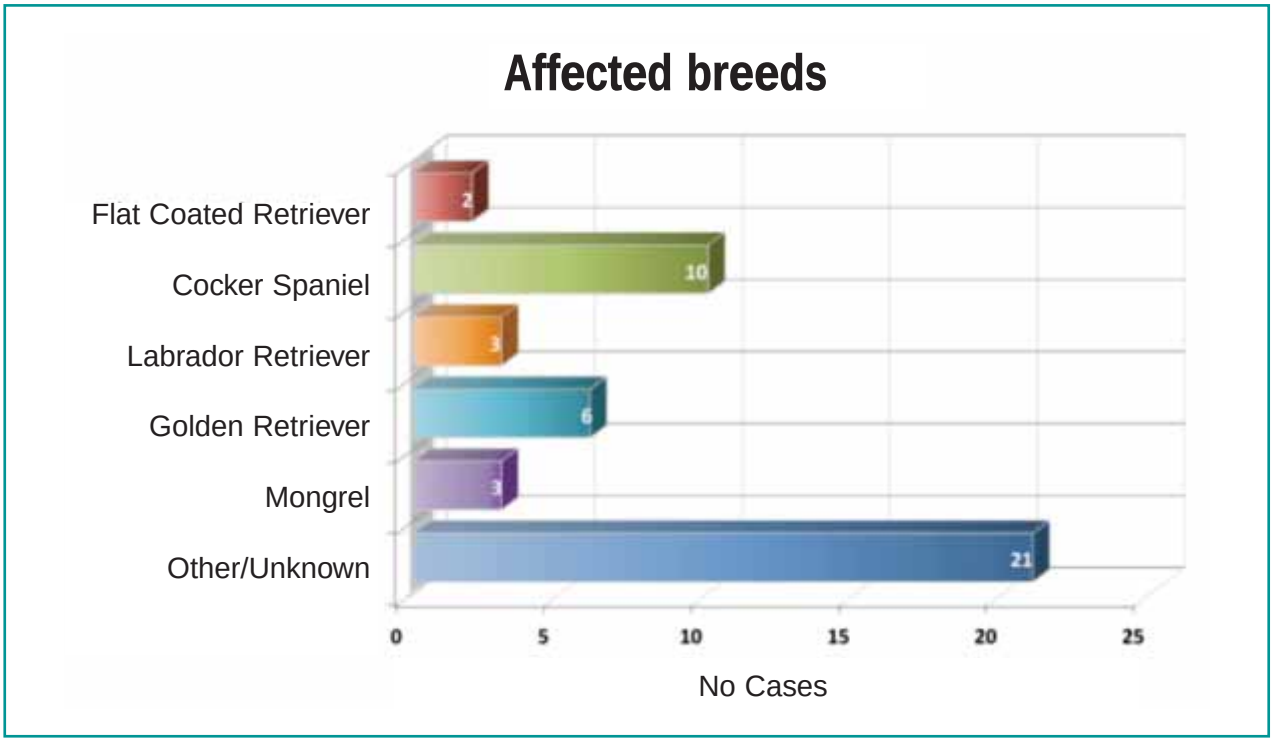

Figure 10 - Dog breeds of subjects affected by cholesteatoma. Although the total number of cases present in the literature reviewed is insufficient to claim the existence of a breed predisposition, Cocker Spaniels are overrepresented. Some studies hypothesize the predisposition of the disease in brachycephalic breeds; based on a review of the literature and on the cases of the present study this cannot be confirmed, as brachycephalic subjects are 7/38 (examining only the cases in which the breeds were specified).

the remains of the embryonic epithelium,[19] while the latter may develop by various etiopathogenetic mechanisms: by relocation of the squamous epithelium from the retracted or perforated tympanic membrane of the middle ear (Migration Theory);[20] by the proliferation of cells that break through the basal membrane (Basal Hyperplasia Theory);[21] by iatrogenic implantation of epidermal elements (Post-surgical/Post-traumatic Theory);[22] as a consequence of hypoventilation of the mastoid antrum and of the middle ear, because of dysfunction of the Eustachian tubes which causes, due to negative pressure, retraction and invagination of the eardrum and growth of hyperplastic epidermal tissue within the middle ear (Retraction Pocket Theory);[23] because of metaplasia of mucosal epithelium cells (Metaplasia Theory).[24]

Some authors believe that the mechanisms underlying the pathogenesis of cholesteatomas consist of complex processes involving hyperproliferation, invasion, migration, altered differentiation, aggression and frequency of relapses, each of which clarifies a specific aspect of the disease.[1,25,26]

In the dog, middle ear cholesteatoma is frequently associated with chronic otitis media and is therefore considered an acquired disease, as in Case 1; however, the existence of congenital cholesteatoma cannot be excluded, as the disease may be identified late in affected subjects.[3,4,27] Only one case of middle ear cholesteatoma which developed in the absence of infection has been published, in a 13-month-old German shepherd.[27]

Clinical signs may vary from pain in the temporomandibular region to neurological signs due to intra- or extracranial nerve-structure involvement caused by a mass effect or extension of the bacterial infection.

It has been proposed that cholesteatomas in the dog may develop through mechanisms based on the theory of migration or invagination.[3,4] In addition, two papers report the development of cholesteatoma following ear surgery,[4,28] endorsing the post-surgical/post-traumatic theory; in human medicine a higher incidence of the disease is reported in patients undergoing ear surgery.[29] Some authors believe that brachychephalic dogs, such as patients in Cases 1 and 6, may be more susceptible to the disease as a result of dysfunction of the auditory tubes and a restricted nasopharynx, both of which are considered predisposing factors in human medicine;[1,28,30,31] however, even if based on published data the Cocker Spaniel

Table 1A - Characteristics of the diagnosed cases reported in the literature

Authors	Nr. Cases	Breed	Sex	Age	Clinical Signs	Diagnostic Technique	Various	Surgery	Relapses	Culture	Follow up
Sturges et al., 2006	2	Golden retriever	ND	10	Intracranial signs	MRI	Intracranial extension, left	VBO 2 times	1 + 1 doubtful	Enterococcus spp, Streptococcus spp	24
		ND	ND		Intracranial signs	MRI	Intracranial extension,	VBO		Staphylococcus spp	ND
Hardie et al., 2008	20	8 Cocker spaniel, 2 Golden retriever, 1 Dobermann, 1 Shetland sheepdog, 1 English springer spaniel, 1 Labrador retriever, 1 English Setter, 1 Pug, 1 Rat terrier, 1 Chesapeake bay retriever, 1 Lhasa apso, 1 Crossbreed	11 MS, 9 FS	2-12 yrs median 8 yrs	Head tilt 6, unilateral facial n. paralysis 4, ataxia 3, nistagmus 1, circling 1, unilateral atrophy of masseter and temporal m.	CT	13 unilateral surgeries, 6 bilateral. 3 cases of previous ear surgery	1 NT, 1 VBO and subsequent TECALBO, 11 TECALBO, 6 VBO, 1 LBO	1 euthanasia after diagnosis, 10 cases of relapse of which 3 reoparated, 47% no relapases	6 Staphylococcus intemedius, 4 Pseudomonas aeruginosa, 3 Escherichia coli, 2 Enterococcus faecalis, 1 Staphylococcus aureus, 1 Group G Streptococcus spp	3-95 mm, mean 27
Greci et al., 2011	11	Pug	M	8	Bilateral otorrhea, ear pain, head tilt and left facial paralysis	CT	Bilateral	TECALBO		3 Staphylococcus intemedius, 2 Proteus mirabilis, 1 Pseudomonas aeruginosa, 1 Escherichia coli, 1 Klebsiella pneumoniae, 3 negative cultures	48
		Crossbreed	M	5	Otorrhea, ear pain, dysphagia, difficulty to open the mouth	CT	Left	TECALBO, VBO	4 months		28
		Flat coated retriever	M	10	Otorrhea, ear pain, left head tilt and facial paralysis, ataxia	CT	Left	TECALBO	Not confirmed		13
		Poodle	MS	5	Ear pain, pain when opening the mouth, dysphagia	CT	Right	TECALBO, VBO	13 mm		39
		Afghan hound	M	8	Ear pain, pain when opening the mouth, dysphagia	CT	Right	TECALBO, LBO, VBOx2	2, 26, 34 mm		36
		Weimaraner	F	9	Otorrhea, ear pain	CT	Right, CG	TECALBO			2
		Cocker spaniel	M	6	Otorrhea, ear pain, pain when opening the mouth, left head tilt and facial paralysis, ataxia	CT	Left	TECALBO			28
		Schnauzer	M	5	Otorrhea, ear pain	CT	Left	TECALBO			27
		Crossbreed	FS	9	Otorrhea, ear pain, pain when opening the mouth, left head tilt and facial paralys, ataxia	CT	Left, CG	TECALBO			12
		Golden retriever	F	4	Otorrhea, head tilt, facial paralysis, ataxia	CT	Left, CG	VBO			12
		Labrador retriever	M	9	Ear pain, pain when opening the mouth	CT	Left, CG	TECALBO			13
Harran et al., 2012	1	Flat coated retriever	MS	8	Ear pain, pain when opening the mouth	RM	Left	TECALBO		Staphylococcus pseudointermedius	ND
Schuenemann et al., 2012	2	Bouledogue francese	M	7	Head tilt, circling, ataxia, ventral strabism, right facial and trigeminal paralysis, absence of right menace response, left fore limb proprioceptive deficit, seizure in clinical history	CT, RM	TECALBO in cl. history, right, intracranial extension	NT	Euthanasia 4 months post diagnosis		4
		Pug	M	6	Head tilt, circling, ataxia, otodynia, pain to open the mouth	CT, RM	TECALBO in clinical history	VBO		Staphylococcus pseudointermedius	5
Witsil et al., 2013	1	Golden retriever	FS	6	Left head tilt, ataxia	CT		TECALBO		Malassetia pachydermatis	6
Furcas et al., 2014	1	Beagle	F	5	Head tilt dx	CT	Right, GC	VBO	8 mm, no additional surgeries		48
Newman et al., 2015	1	German Shepherd	FS	10	Neurogenic conjuntivitis sicca, left central vestibular syndrome, disorientation, pain when opening the mouth and when palpating the left temporomandibular joint, paralysis of left facial nerve, hypermetria, ventral positional strabism, absense of right menace reflex, right proprioceptive deficit	RM	Left	VBO		Stahylococcus pseudointermedio, Streptococcus group B beta-hemolytic streptococcus	3

Legend: NA not available, NT not treated, CG cholesterol granuloma.

seems overrepresented, given the limited number of cases examined it is not possible to speak about breed predisposition (Fig. 9, Table 1A). In veterinary medicine the predominance in male subjects is known, as in human medicine, in which a male-female ratio of 1:4 is described (Fig. 10).[1,2] The clinical signs of the disease vary depending on the progression, compression of surrounding structures, presence of osteolysis and involvement of intra- or extracranial nerve structures;[3,4,32-35] compression of facial and trigeminal nerves, lysis of the temporal bone, intracranial extension through the internal acoustic meatus with meningitis or bacterial meningoencephalitis or mass effect involving the brainstem and rhinopharynx invasion may occur.[3,4,32-35] The clinical signs described in veterinary literature are scratching of the ears, head shaking, otorrhea, pain when opening the mouth or inability to open it completely, dysphagia, pain when palpating the bulla (otodynia) and the temporomandibular joint, head tilt, ataxia, nystagmus, circling, atrophy of the masseter and temporal muscles, facial nerve deficit, increased respiratory sounds with dyspnoea and hearing loss;[3,4,32-35] a case of neurogenic keratoconjunctivitis sicca has been described.[34] The most consistent clinical sign is pain, the only symptom found in Case 1, which may be caused by periosteal reaction,

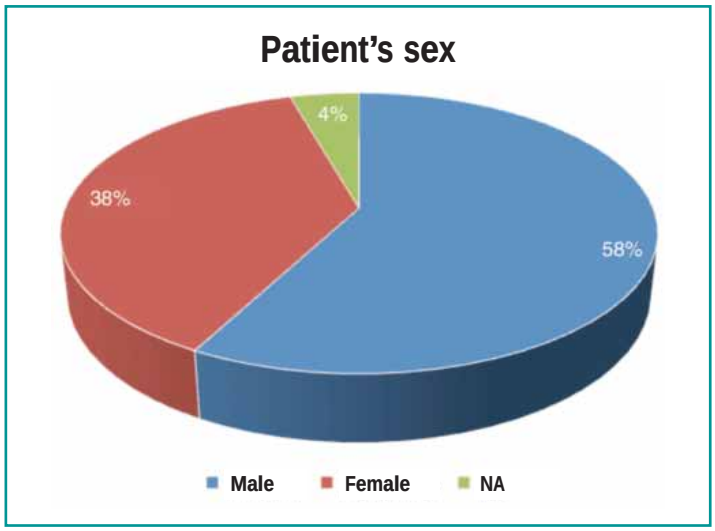

Figure 11 - Data in the literature show a prevalence of the disease in male subjects. The graph shows all the cases described in the literature and in the present study. NA: gender data not available.

by sclerosis of the temporomandibular joint or by the inflammatory involvement of muscle insertions in the paracondilar process.[3] If only pain is present, other possible differential diagnoses are: presence of retrobulbar masses or abscesses, extra-ocular myositis, myositis of the masticatory muscles, presence of foreign bodies.[36,37] Table 1B summarizes the clinical

Table 1B - Characteristics of the cases of cholesteatoma in the present study

No. cases	Breed	Sex	Age	Clinical Signs	Diagnostic Technique	Various	Surgery	Relapse	Culture	Follow up
6	Shih tzu	M	9	Ear pain, anorexia, pain when palpating the temporo-mandibular joint	RM		Bilateral VBO		Beta-hemolytic Streptococcus and Escherichia coli	30
	Golden retriever	M	10	Pleurothotous, right head tilt, ataxia, decreased right menace, palpebral, corneal and swallowing reflex, atrophy of right temporal muscles	RM	Right, intracranial extension	NT		ND	ND
	Labrador retriever	F	5	Head tilt, hypacusis, ataxia	RM	Right	VBO		Negative	12
	Cocker spaniel	F	15	Left head tilt, ataxia, ear pain	RM	Left	TECALBO		Staphylococcus aureus and Pseudomonas spp	15
	Kurzhaar	M	6	Right head tilt, ataxia, ear pain	RM	Bilateral, post-surgery left facial n. paralisis	Bilateral TECALBO	Purulent infection 3 months post surgery	Staphylococcus aureus and Pseudomonas spp	5
	Dogue de bordeaux	M	12	Left head tilt, ataxia, otodynia	RM	Suspected bilateral, cofirmed hystolotigically left	TECALBO sn		Staphylococcus aureus	4

Legend: NA not available, NT not treated.

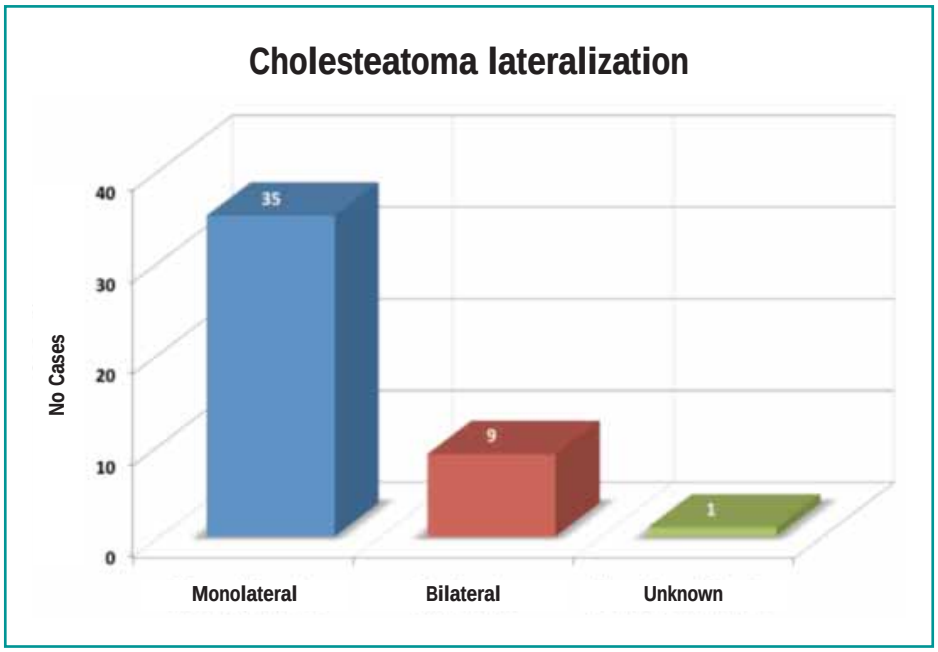

Figure 12 - The graph shows the prevalence in the literature of subjects with unilateral disease. In our study, 2/6 subjects had bilateral cholesteatoma; in 1 subject a bilateral cholesteatoma was suspected but the owners gave their consent for only one surgery.

signs found in the 6 cases described. Most of the cases reported in the literature presented a unilateral condition;[4,3,35] in our study, 3 patients presented the lesion bilaterally (Cases 1, 5 and 6), 2 patients on the right (Cases 2 and 3) and one on the left (Case 4) (Fig. 11).

In human medicine, the diagnostic approach consists in carrying out an otoscopic examination, eventually with video-otoscopy, and a CT or MRI examination. To diagnose the disease the new MRI algorithms are superior in terms of specificity and sensitivity, thanks to the use of post-contrast sequences (DP-MRI Delayed Post-Contrast MRI) or diffusion studies (DW Diffusion-Weighted); in addition, MRI allows to avoid exposure to ionizing radiation.[10,38] Similarly, in veterinary medicine, otoscopic examination, video-otoscopy, CT or MRI are performed.[39]

MRI characteristics of cholesteatoma are an inhomogeneous hyperintense signal in T2-weighted sequences of the tympanic bulla content and contrast enhancement of the surrounding soft tissues.

In veterinary medicine a study has correlated video-otoscopy findings with those obtained by CT examination;[35] the suspicion of cholesteatoma is based on the detection of nodules or pearl-grey or yellowish scales protruding from the tympanic surface. Although some information on the increased volume of the tympanic bulla, the absence of internal air and wall lysis can be obtained by radiographic examination,[40,44] as in Case 1, several studies have shown the importance of advanced diagnostic imaging in the assessment of the middle ear.[3,4,32-35,40-44] The use of ultrasonography for the diagnosis of middle ear diseases has been described, but data shows that ultrasonography has a low sensitivity, especially in the presence of non-severe conditions, and it is extremely operator-dependent.[43,44] CT has a high spatial resolution and is of great help in the evaluation of bone alterations, but has a limited specificity in the study of soft tissues; the elements of cholesteatoma detectable by CT examination are osteoproliferation, lysis, sclerosis and expansion of the tympanic bulla, which appears replete with a material compatible with soft tissue.[3,4,35] Bone lysis of the squamous or petrosal portion of the temporal bone is described in 25% and 50% of cases, respectively.[4,3] Other common findings are lymphadenomegaly of local lymph nodes and sclerosis of the temporomandibular joint.[3,4,35] Following the administration of intravenous iodized contrast medium the uptake is in the deepest layers of the lesion, adjacent to the wall of the tympanic bulla,[3,4,35] although in some patients an uptake present throughtout the lesion has been described.[4] In this study the diagnostic protocol used was based on MRI, in view of its higher resolution for soft tissues and as it allows to collect detailed information in the presensce of neuritis or intracranial extension of the lesion,[45] as in Case 2.[32,39-44] In human medicine the diagnostic protocol used envisages DW or post-contrast sequences. In Italy, most of the MRI machines used in veterinary medicine are low-field units and the execution of DW sequences is not possible; as a valid alternative, post-contrast sequences are used,[38] as done in the present study. In the literature, only 4 studies have described the use of MRI for the diagnosis of canine cholesteatoma (Table 2).[29,32-34] The MRI diagnosis of cholesteatoma is made in the presence of a tympanic bulla with isointense content in

Table 2 - Main characteristics of cholesteatoma cases diagnosed by means of RMI in the literature

Authors	N. cases	Breed	Brachycephalic	Age	Sex	Clinical Signs	Otoscopy	RMI	Other	Surgery	Infection	Prognosis
Schuenemann RM, Oechtering G	1	French Bulldog	Yes	7	M	Right vestibular syndrome (head tilt, circling, ataxia), right facial nerve paralysis, right trigeminus n. sensory neuropathy	No	Increased-size tympanic bulla, iso T1, hyper T2, no contrast medium uptake, pars petrosa erosion of the temporal bone with continuity of the lesion with the meninges	Post TECA-LBO. Previously diagnosed hydrocephalus with previous RMI	Retrograde endoscopic nasopharingeal biopsy	Not examined	Euthanasia after 4 weeks
Schuenemann RM, Oechtering G	1	Pug	Yes	6	M	Right vestibular syndrome (head tilt, circling, ataxia), pain when opening the mouth and anorexia, ear pain	No	Bulla cavity full of isointense tissue for muscle at T1, hyperintense at T2, no contrast medium uptake (no inner ear involvement)	Post TECA-LBO	VBO	Staphylococcus pseudointemedius	Control CT 5 months post-surgery negative
Harran NX, Bradley KJ, Hetzel N et al.	1	Flat coated retriever	No	8	M	Pain when opening the mouth, head tilt, circling, enophthalmos, head shaking	Bilateral tympanum rupture; mass on the left	Severely expanded left bulla, thickened and irregular wall, petrous part of the temporal bone with signs of sclerosis, slight uptake of contrast medium by the layer of the lesion adjacent to the wall of the bulla. Isointense content in T1, mixed in T2 and FLAIR. Involvement of the inner ear, hypertrophy of the left retropharyngeal lymph node.		TECA-LBO	Malassetia, Staphylococcus intermedius	Not specified
Newman AW, Estey CM, McDonough S et al.	1	German Shepherd	No	10	FS	Neurogenic conjutivitis sicca, left central vestibular syndrome, loss of orientation, pain when opening the mouth and at left temporomandibular joint palpation, left facial nerve paralysis, hypermetria, ventral positional strabism, absence of right menace response, right proprioceptive deficit	Mass within the horizontal canal, debris to the left	Increased left tympanic bulla with isointense signal content in T1, slight contrast medium uptake, lysis of the petrous portion of the temporal bone; intracranial extension of the lesion with contrast uptake in the intracranial portion, meningeal contrast uptake and by the soft tissues around the temporomandibular joint	Chronic external otitis, histological diagnosis of cholesteatoma (associated cholesterol granuloma?)	VBO	Staphylococcus pseudointermedius, Group B beta-hemolitic Streptococcus	Died due to gastric torsion 3½ months post-surgery
Sturges BK, Dickinson PJ, Kortz GD et al.	2	NA	NA	NA	NA	Central vestibular syndrome and dulled senses	Waxy-like debris and otitis externa	Globular masses which extend from the tympanic cavity to the brainstem and to the ponto-cerebellar angle; uptake of contrast medium by the adjacent meninges. Tympanic bulla signal hyperintense in T2, osteomyelitis of the bulla's wall; cerebral oedema	Only neurolocial cases with chronic evolution	VBO	One case Staphylococcus spp and one Enterococcus spp and Streptococcus	One patient: first relapse at 1 yr new surgery; control at 12 months, tissue compatible with relapse or granulation tissue

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Table 3 - MRI characteristics of the cases included in this study

Case	Side	Tympanic bulla volume	Tympanic bulla wall	Bone base	Tympanic bulla signal	Contrast enhancement	Various
1	Bilateral	Left increased, right normal	Inhomogeneous thickness, irreguar profile on the left, within the norm to the right	Mastoid part increased in volume, hypointense in T1 and T2 to the left	Inhomogeneous, isointense in T1, hyperintense in T2, GE-STIR, FLAIR	Soft tissues adjacent to left and right bulla, cortical of the angular process of the left mandible, part of the lesion adjacent to the wall of the right bulla	Rhinopharynx occlusion, soft tissues adjacent to the left bulla hyperintense in T2 and GE-STIR
2	Right	Increased	Inhomogeneous thickness, irregular profile	Mastoid part, jugular process and parts contiguous to the occipital bone increased in volume and hypointense in T1 and T2, widening of the inner ear canal	Inhomogeneous, isointense in T1, hyperintense in T2, GE-STIR, FLAIR	Soft tissues adjacent to the bulla, peripheral portion of the mass at brainstem level, adjacent meninges	Intracranial extension with mass at brainstem level, atrophy of right temporal and masseter m., erosion of the inner ear. Hyperintensity in GE-STIR of soft tissues adjacent to the bulla
3	Left	Preserved	Slightly increased thickness on the medial side which appears slightly irregular	Mastoid part increased in volume hypointense in T1 and T2	Inhomogeneous, isointense in T1, hyperintense in T2, GE-STIR, FLAIR	Soft tissues adjacent to the bulla, part of the lesion adjacent to the tympanic bulla wall	Erosion of the inner ear
4	Left	Increased	Inhomogeneous thickness, irregular profile	Mastoid part increased in volume hypointense in T1 and T2	Inhomogeneous, isointense in T1, hyperintense in T2, GE-STIR, FLAIR	Soft tissues adjacent to the tympanic bulla	Partial rhinopharynx occlusion, extension to the outer ear canal. Hyperintensity in GE-STIR of soft tissues adjacent to the left bulla
5	Bilateral	Preserved	Inhomogeneous thickness, irregular profile to the right, within the norm to the left	Mastoid part increased in volume hypointense in T1 and T2 to the left	Inhomogeneous, isointense in T1, hyperintense in T2, GE-STIR, FLAIR	Adjacent soft tissues, part of the lesions adjacent to the walls of the tympanic bullae	Loss of signal right inner ear, extension to the outer ear canal bilaterally, hyperintensity in GE-STIR of soft tissues adjacent to the left bulla

T1-weighted sequences, inhomogeneously hyperintense in T2-weighted sequences and with contrast medium uptake by the tissues surrounding the bone wall; as the matrix of the cholesteatoma is avascular there is no uptake of the contrast medium. The profile of the tympanic bulla can be maintained, as in the right bulla of Case 1 or as in Case 3, or severely altered (left tympanic bulla of Case 1, Case 2 and Case 4), with increased volume and thickened areas alternating with lithic ones. Other findings may include temporal bone sclerosis, detectable via a hypointense signal in T1- and T2-weighted sequences, lysis of surrounding bone structures, such as petrous bone lysis (Case 2) with intracranial extension of the lesion, loss of cochlear signal (Cases 2, 3 and 5), indicating involvement of the inner ear, and the uptake of contrast medium in the part of the cholesteatoma adjacent to the wall of the tympanic bulla (Case 5);[46,47] Table 3 summarises the MRI findings of the current study. In MRI studies the presence of peripheral enhancement on the outer wall of the tympanic bulla is characteristic of cholesteatoma and is therefore helpful in assessing the differential diagnoses of granulomatous lesions, otitis media and neoplasms; at times, due to the presence of granulation tissue, the uptake of contrast medium involves the deepest layer of the lesion. In some studies[3,35,48,49] the hystological examination identified both cholesteatoma and cholesterol granuloma, this latter not suspected with the CT; however, to the author's knowledge, in the dog, no studies exist in which the diagnosis of cholesterol granuloma has been made with MRI. In otitis media, sclerosis and osteoproliferation of the wall of the tympanic bulla may occur, but its expansion is a characteristic trait of cholesteatoma.[3,50] In neoplasms bone erosion is diffused and there is permeative lysis, unlike in middle ear cholesteatomas, in which lysis is associated with the expansion of the bulla.[3] Unlike CT, MRI allows to distinguish cholesteatoma from cholesterol granuloma, which, containing lipids, presents a hyperintense signal in T1- and T2-weighted MRI sequences.[51] In human medicine, MRI allows the detection of even very small cholesteatoma-related le-

The only possible therapy is surgery, followed by antibiotic therapy to control the infection; due to incomplete removal of the lesion a high number of relapses is reported.

sions; additional investigations are warranted in order to understand if this diagnostic approach may be helpful also in small-sized cholesteatomas in the dog; however, the rarity of the condition and the fact that the diagnosis is made when the clinical signs are already significant makes such an assessment difficult. In both human and veterinary medicine the only possible treatment is surgery, aiming to remove the keratin debris and the stratified squamous epithelium and control the eventual infection; in advanced-stage patients surgery also has a palliative effect, reducing pain.[52] The risk of recurrence after surgery is high and in human medicine relapses occur in 5-13% of cases,[4,5] especially in large-sized lesions with bone erosion.[51] In veterinary medicine, the presence of severe neurological lesions are considered an unfavourable prognostic sign.[4] In the literature, relapses vary between 36% (follow-up between 12 and 39 months) and 47% (follow-up between 3 and 95 months) and are attributed to incomplete removal of keratin debris and of tympanic bulla epithelium during surgery.[3,4,2] One study suggests monitoring patients for the appearance of relapses for a minimum of one year.[35] In veterinary medicine both a ventral (VBO) and a caudal approach to the tympanic bulla have been described;[3,4,35,27] should the cholesteatoma also affect the outer ear canal or if stenosis of the canal is present a lateral ostectomy of the bulla is performed, together with the complete ablation of the outer ear canal (TECA-LBO Total Ear Canal Ablation-Lateral Bulla Osteotomy).[3,4,35] In the literature, no differences in outcome are reported in relation to the surgical technique used.[4] Post-operative complications consist of facial nerve paralysis, development of draining tracts or abscesses and the development of relapses.[4] Given the invasiveness of the operation and the possibility of serious complications and relapses, in this study it was decided to treat cases of bilateral cholesteatoma with two successive interventions, choosing the side of the first surgery based on the severity of the clinical signs or the appearance of MRI lesions. Post-surgery antibiotic therapy was initially based on broad-spectrum antibiotics and was then changed, if necessary, based on the results of the cultural examination and the antibiogram; in one case, the cultural examination was negative (Case 3), in Case 1 both samples were positive for *Escherichia coli* and Beta-haemolytic Streptococcus, in Case 6 the culture detected *Staphylococcus aureus* while in the remaining cases multiresistant Pseudomonas spp and *Staphylococcus aureus* were detected.

Ideally, the histological diagnosis of middle ear cholesteatoma is based on the detection of ciliated epithelial tissue, subepithelial connective tissue and keratin debris (better if organized into overlapping lamellae);[5,7] in veterinary medicine, the presence of keratin debris alone is considered acceptable;[4,32,35] in human medicine, the presence of keratin debris arranged in an ovoid mass is highly suggestive of cholesteatoma and the diagnosis is based on diagnostic imaging findings and the intraoperative presentation of the lesion.[5,7] It for this reason that Case 3 was included in the study: no bioptic examination was performed but cytology of the material obtained by myringotomy was compatible with cheratotic material.

CONCLUSIONS

MRI allows to establish a strong diagnostic suspicion of middle ear cholesteatoma and provides important information on soft tissue involvement and on the surrounding nerve structures. To the authors' knowledge, this is the first study describing a detailed series of cases diagnosed using this imaging approach.

ACKNOWLEDGEMENTS

The authors thank Prof. Maria Teresa Mandara for the support received during the drafting of this article and for the histological image. We also thank for their collaboration Dr. Cinzia Boccanera and Dr. Francesca Gerosolimo. Furthermore we acknowledge Dr. Patrick Caruana for proofreading the manuscript.

KEY POINTS

- Aural cholesteatoma is an expansive, non-neoplastic lesion, characterized by an aggressive biological behaviour, rarely found in human and canine patients. In dogs, acquired forms due to chronic middle ear otitis are described while in human medicine congenital forms are well known.
- Given the rarity of the disease and the scarcity of cases, it is not possible to claim the existence of a breed predisposition, althought it is well known that there is predominance in male patients, as described in human medicine.
- Clinical signs are a consequence of the expansion of the tympanic bulla due to the accumulation of keratin debris and the bone erosion and the concurrent presence of infection; symptoms vary from otodynia to severe neurological signs in the case of intracranial involvement.
- Advanced imaging is required to produce the diagnostic suspicion; CT can show the typical bone involvement but MRI is more sensitive to detect soft tissue and neurological damage.
- The therapy of cholesteatoma consists in the removal of pathological tissue, and treatment of the infection but relapse is frequent; therefore at least a one-year follow-up is required.

MRI Findings of middle ear cholesteatoma in dogs: 6 cases and literature review

Summary

Canine middle ear cholesteatoma is a disease showing an aggressive biological behaviour, with clinical signs that may vary according to the degree of involvement of stuctures adjacent to the affected tympanic bulla and the possible damage to the nervous system. This article describes 6 cases of canine middle ear colesteatoma, diagnosed by Magnetic Resonance Imaging and confirmed by histologic or cytologic examination, with different lesions and clinical signs and a review of the literature.

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