Nondomestic, Exotic, Wildlife and Zoo Animals–Original Article

Veterinary Pathology
2015, Vol. 52(2) 377-383

DOI: 10.1177/0300985814531499
vet.sagepub.com

Mucoperiosteal Exostoses in the Tympanic Bulla of African Lions (*Panthera leo*)

M. Novales[1], P. J. Ginel[1], A. Diz[2], B. Blanco[1], R. Zafra[3], R. Guerra[4], and E. Mozos[2]

Abstract

Mucoperiosteal exostoses (MpEs) of the tympanic bulla (TB), also referred as *middle-ear otoliths*, have been occasionally described in dogs and cats in association with clinical signs of otitis media or as an incidental finding, but they have not been recorded in other species. In this report, we describe the radiographic, gross, and histopathologic features of MpEs in 8 African lions (*Panthera leo*). All animals (5 males and 3 females) were adults that had been kept in captivity and had their skeletons conserved as part of an anatomic academic collection. A radiographic study revealed mineralized structures in the TB consistent with MpEs in 7 of the 16 examined TB; a computed tomography study identified MpEs in 12 of the 16 TB. Six TB from 4 lions were sectioned, and several MpEs were demineralized for histopathologic analysis. Grossly, MpEs appeared variable in number and shape. Some were globular structures that were loosely attached to the mucosal surface of the TB; others were isolated to coalescent bone spicules extending from the mucoperiosteum. Position was also variable, but MpEs frequently developed in the hypotympanum, especially on the ventromedial aspect of the TB wall. Microscopically, MpEs were composed of osteonal bone growing from the periosteum and not by dystrophic calcification of necrotic tissue debris, as is hypothesized in dogs.

Keywords

African lion, computed tomography, mucoperiosteal exostoses, middle ear, *Panthera leo*, pathology, tympanic bulla

The middle ear structure is well known in domestic animals, but it has only been occasionally studied in lions.[6] Three-dimensional anatomic reconstructions show that the middle ear of the lion and cat are similarly arranged but have large differences in absolute and relative size.[6,12] In mammals, the middle ear is lined by respiratory epithelium that is contiguous with the nasopharynx via the auditory tube; however, portions of the middle ear are lined by squamous to cuboidal epithelium, especially the petrous portion of the temporal and tympanic membrane.[1,12] In a recent exhaustive study on the histology and histopathology of the cat middle ear, Sula et al[12] introduced the term *auricular mucoperiosteum* to name this unique mucosal membrane lining the middle ear, which is characterized by the direct apposition of epithelia and submucosa with periosteal connective tissues.

Little is known about the pathology of the middle ear in the majority of animal species. Infectious (bacterial) otitis media has been more frequently described in dogs, cats, and cows.[7,12,13] Sula et al[12] recently described the histologic characteristics of diseased ears in a series of 50 cats and concluded that middle ear diseases in cats are far more common than gross lesions or clinical literature suggests.

Mucoperiosteal exostoses (MpEs) are new bone formations originating from the mucoperiosteum of the tympanic bulla (TB) in response to chronic injury. They have been occasionally identified in the TB of dogs[2,3,14] and cats[12] but have not been recorded, to the best of our knowledge, in any other species. The term *otolith* has been incorrectly used to describe these middle ear bony lesions, since otoliths are calcium-carbonate crystals that are part of the striola of the macula and saccule of the vestibular system. In the dog, MpEs are most easily visualized on computed tomography (CT) scans and are well-defined smooth, globular, singular, or multiple mineral concretions within the TB.[2] Although the widespread use of CT imaging in dogs has facilitated their recognition, MpEs can be considered fairly uncommon, since they have been reported in very few dogs[2,3,14] and cats.[12]

In the dog, MpEs can be associated with active signs of otitis externa or vestibular disease or can represent an incidental finding in dogs without signs of otitis media. The pathogenesis

[1]Department of Animal Medicine and Surgery, Faculty of Veterinary Medicine, University of Córdoba, Córdoba, Spain
[2]Department of Anatomy and Comparative Pathology, Faculty of Veterinary Medicine, University of Córdoba, Córdoba, Spain
[3]IUSA, University of Las Palmas de Gran Canaria, Las Palmas, Spain
[4]Zoological Garden of Córdoba, Córdoba, Spain

Corresponding Author:
Elena Mozos, Department of Anatomy and Comparative Pathology, Faculty of Veterinary Medicine, University of Córdoba, Campus de Rabanales 14014, Córdoba, Spain.
Email: an1momoe@uco.es

Table 1. Signalment, Radiographic, and Computerized Tomography Results for Mucoperiosteal Exostoses and Postmortem Findings of the 8 African Lions.

		X-Ray Findings		Computerized Tomography Findings[a]		
No.	Sex/Age	RB	LB	RB	LB	Postmortem Findings
1	Male, 3 y	None	Single	None	4 linear (6.2–16.5 mm); medial TB; single globular (2.6 mm); ventral TB	Multiple self-induced cutaneous wounds
2	Male, 1.5 y	None	None	Single linear (7.8 mm); ventral TB	None	Hypovitaminosis A, skull hyperostosis, and tracheal cartilage hypoplasia
3	Male, 12 y	Multiple	Multiple	Multiple globular (3.6–6.6 mm); medial, ventral, and lateral TB; attached or free	Multiple globular (2–5 mm); medial, ventral, and lateral TB; attached or free	Chronic hepatitis, hepatic carcinoma, and interstitial nephritis
4	Female, 12 y	Single	None	Single globular (4.5 mm); ventral TB; single small (2.4 mm); epitympanic cavity	None	Esophageal perforation by foreign body
5	Female, 13 y	None	Single	Single globular (2.8 mm); ventral TB	Single globular (2.5 mm); ventral TB	Polytrauma; fight between conspecifics
6	Female, 11 y	Multiple	Multiple	7 linear (2.1–2.9 mm); ventral TB	5 linear; ventral TB	Not available
7	Male, ND	None	None	Multiple linear (spiculated) (3.4–5.6 mm); ventral and medial TB	Multiple linear (spiculated) (3.4–5.6 mm); ventral and medial TB	Femur fracture
8	Male, ND	None	None	Single globular (2.3 mm); ventral TB	None	Not available

Abbreviations: LB, left bulla; ND, not determined; RB, right bulla; TB, tympanic bulla.
[a]Number, shape (size), and position of exostoses in the TB.

of MpEs remains undetermined; it has been suggested that they develop secondary to mineralization of necrotic debris from primary middle ear disease or otitis externa where the disease has resolved and the ear drum has healed.[13,14]

Surprisingly, during a CT study of African lion skeletons from the Academic Museum of Veterinary Anatomy at the University of Córdoba, we identified mineral opacities in the middle ears of several lions that were similar to MpEs described in dogs. After investigating all the available lion skulls, we found similar lesions in 8 animals. Here we describe the radiologic, gross, and histopathologic features of MpEs in the TB in the archived skeletons of 8 captive African lions.

Materials and Methods

Study material consisted of 8 skulls obtained from postmortem nonrelated adult African lions (5 males and 3 females) (Table 1). All animals were born and lived in captivity (5 in a zoo collection and 3 in a private house) and, after dying of different causes, were donated to the Museum of the Department of Comparative Anatomy and Pathology of the University of Córdoba.

A detailed clinical history and necropsy report were not available for 2 lions (Nos. 6 and 8), but neither clinical signs of middle ear disease nor otitis externa was recorded in the admission form for necropsy of the 6 remaining lions (examined from 2001 to 2011). The postmortem findings are summarized in Table 1. Lion Nos. 1, 4, 5, and 7 presented, respectively, with multiple self-induced cutaneous wounds, esophageal perforation by foreign body, multifocal trauma, and femur fracture. Lion No. 2 presented multiple moderate skull hyperostoses and tracheal cartilage hypoplasia associated with hypovitaminosis A and died of aspiration pneumonia. In lion No. 3, chronic interstitial nephritis and chronic hepatitis and hepatic carcinoma were diagnosed. Lion Nos. 1, 3, 5, and 7 were euthanized, whereas lion Nos. 2 and 4 died due to the severity of their lesions.

The skulls had been prepared anatomically, and in 2 of them, the calvarium (skull cap) had been removed. To describe their gross morphologic features, the ventral portion of 6 TB from 4 representative lions was removed with a bone saw. Samples of these MpEs and TB bones were collected for histopathologic evaluation.

Radiologic Study

The radiologic study was performed with a stationary X-ray machine (Odelmodel C306-20, Monza, Italy). Radiographs were processed by computerized radiology (Fuji Computed Radiography, Capsule XL, CR-IR 356, Tokyo, Japan). The obtained images were stored in DICOM format for further study.

The 8 skulls were radiographed in the lateral, dorsoventral, ventrodorsal, and left and right lateral 30° ventrolateral-dorsal views (lateral oblique). These are the radiologic views recommended for the diagnosis of middle ear diseases in dogs and cats[4] but with a higher head angle (30°) than that normally used in small animals (20°). Technical factors were 2 to 3 mA and 50 to 60 kVp; grid was not needed.

CT Study

CT scans of the 8 heads were performed with a helical CT scanner (CT Hi Speed CT/e Dual; General Electric Yokogawa Medical Systems LTD, Hino, Japan). Technical factors were 50 mA and 120 kVp. Contiguous 0.6-mm transverse slices were made from the level of incisive bone to the occipital condyles. To enhance bone structures, a wide window was used (window width: 2877 Hounsfield units; window level: 168 Hounsfield units). The original CT data were transferred as DICOM images to an image analysis with DICOM viewer (OsiriX v.3.3.1. 32-bit (Open source)) to perform image study. The original transverse slices were reformatted into the sagittal and dorsal planes. The window was also adjusted as required to better define bone margins.

Gross and Microscopic Studies

To analyze the gross and microscopic features of the MpEs, the ventral aspect of 6 TB was removed in 4 lions. Several MpEs, either extending from the inner surface of the TB or found free in the cavity, as well as bone samples from the walls of the bullae were collected for histopathologic study. Tissue samples were fixed in 10% neutral buffered formalin for 24 hours, decalcified for 2 hours (TBD-1TM from Thermo-Shandon Limited, Runcorn, Cheshire, UK), then routinely processed to paraffin embedding. Four-micrometer-thick sections were stained with hematoxylin and eosin, Alcian blue (pH 2.5), and periodic acid–Schiff.

Results

Radiologic and CT findings

MpEs were found in one or both TB from each of the 8 lion skulls. Four lions (Nos. 1, 2, 4, 8) had unilateral exostoses, and 4 lions (Nos. 3, 5, 6, 7) had bilateral exostoses. Therefore, overall, exostoses were present in 12 of 16 TB from the 8 lions. All 12 TB with exostoses were identified with CT; 7 of 12 were detected radiographically (Table 1). The lateral oblique views were the most sensitive for radiologic diagnosis of MpEs (Fig. 1). The lateral views were positive only in the animal with the highest number of exostoses (lion No. 3).

The CT studies allowed the appreciation of further details of the MpEs: their number, shape, size, as well as the exact location within the TB (Figs. 2, 3), even in the case where 1 MpE was located in the epitympanic cavity (Table 1). The smallest MpEs that could be identified by CT scan were about 2 mm in size. The dorsal slices visualized almost all MpEs; however, in certain occasions, the smallest lesions were not detected. The transversal slices showed that in some cases the MpEs were spiculated or needle-like and arose from the medial tympanic walls (Fig. 3). None of the animals studied showed radiographic or CT signs of reactive bone in the TB or in other middle and inner ear bone structures. In all animals, the density of the mineral concretions varied between 1400 and 2300 Hounsfield units,values even higher than the usual TB wall values and indicative of an osseous nature.

Gross Findings

Gross inspection of the TB in 4 lions (Nos. 1, 3, 7, 8, as representative of the different MpEs presentations) confirmed the radiographic and CT studies. Lion No. 1 had 5 MpEs in the intralumenal aspect of the left bulla, all but one with a spiculated form with a long axis ranging from 6.2 to 16.5 mm and extending from the ventral TB wall. Lion No. 3 had numerous globular lesions ($n = 10$–13), ranging from 2 to 6.6 mm in size, within each TB. Several of these exostoses arose from the TB wall, but a similar number were free in the lumen and mixed with a brown to yellowish exudate (Fig. 4). Lion No. 7 had multiple, bilateral, isolated to coalescent, delicate linear, spiculated MpEs resembling stalagmites or stalactites in a cave (Fig. 5). The position of the MpEs in the TB wall, when bilateral, was very symmetrical and preferentially on the ventromedial aspect of the wall. In all animals, the MpEs had a hard and smooth whitish surface very similar to the bone of the TB wall. Lion No. 8 had 1 small globular MpE in the right TB, whereas the left was normal. In all cases, the TB wall was normal or slightly thickened in the area of contact with the MpE. The remaining 4 skulls were not cut and were preserved intact.

Microscopic Findings

Histologically, both the MpEs extending from the bulla walls and those free in the cavity were composed of mature compact bone (Figs. 6–9). Despite the previous treatment of the skulls for anatomic preservation, microscopically the osseous structures were well preserved and allowed us to recognize a hyaline fibrillar matrix forming multiple concentric layers of lamellae arranged around a central channel (corresponding to the vascular spaces of the compact bone Haversian system). A lacunar system was recognized within the matrix, similar to those found in the osteon units in the compact bone, but in these cases, osteocytes were not observed (Figs. 6–9). The TB bone was composed of regular compact bone matrix that was locally modified at the base of the MpEs. In these areas, slightly distorted, juxtaposed, small osteons were present at areas of transition between the TB and MpE; these areas are thought to represent remodeling and new bone growth at initiation sites of MpE formation. The MpEs with spicular shape showed, in the outer areas, a predominant parallel arrangement of the organic matrix to the longitudinal axis. No evidence of inflammatory reaction, necrosis, or dystrophic calcifications was observed in any of the samples analyzed.

Discussion

A series of 8 skulls from captive African lions were found to contain MpEs in one or both TB. MpEs were bilateral in 4 lions

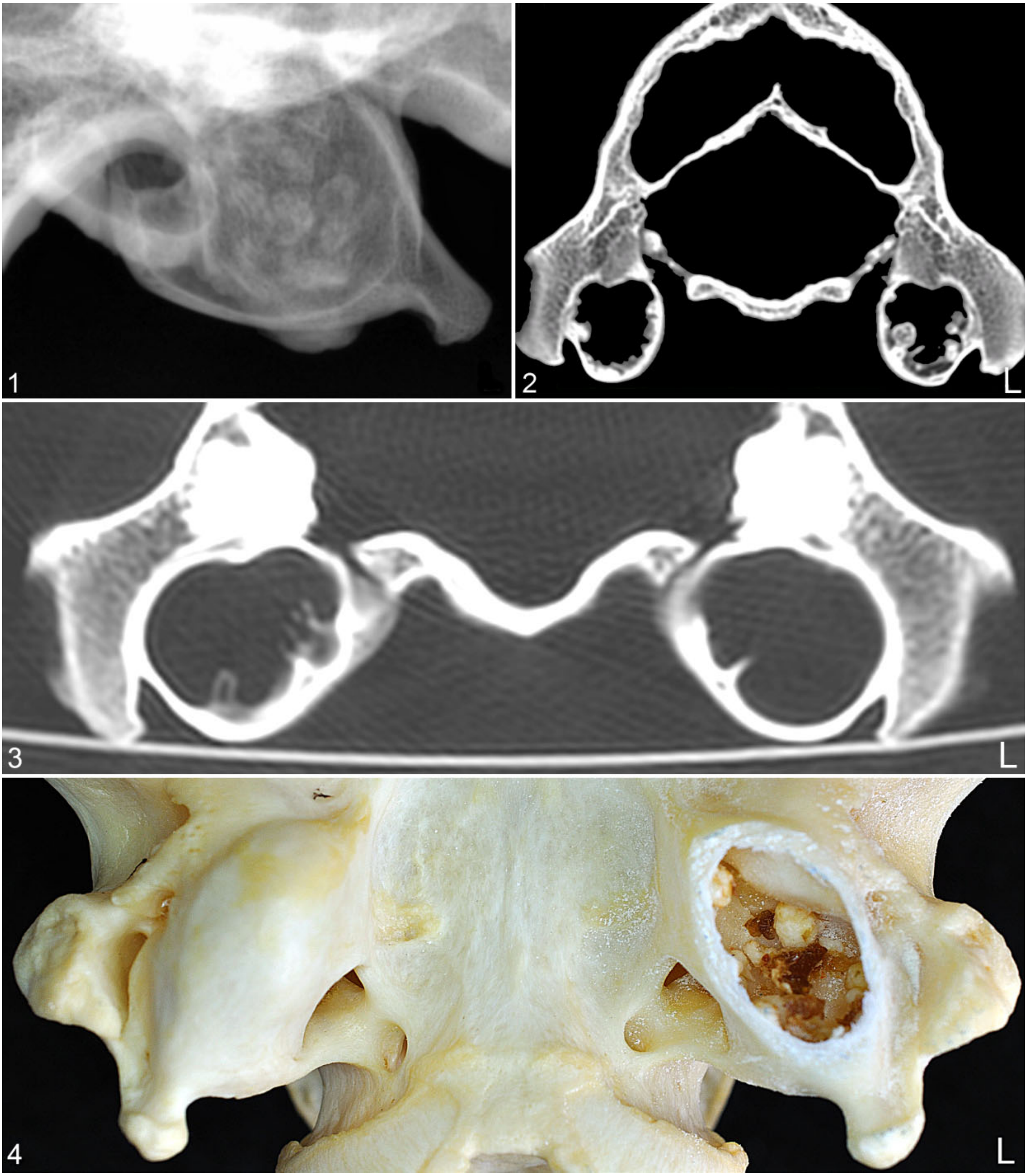
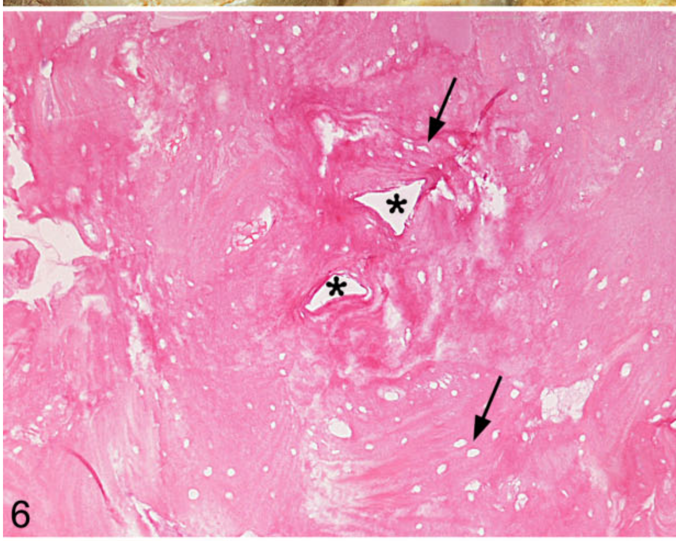
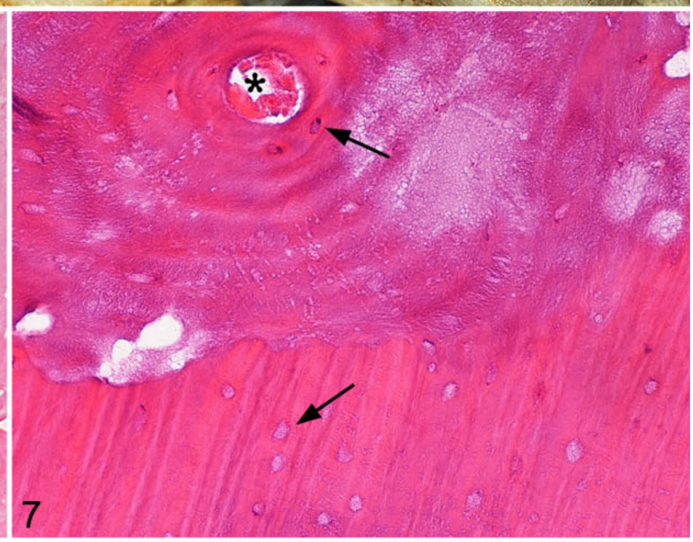
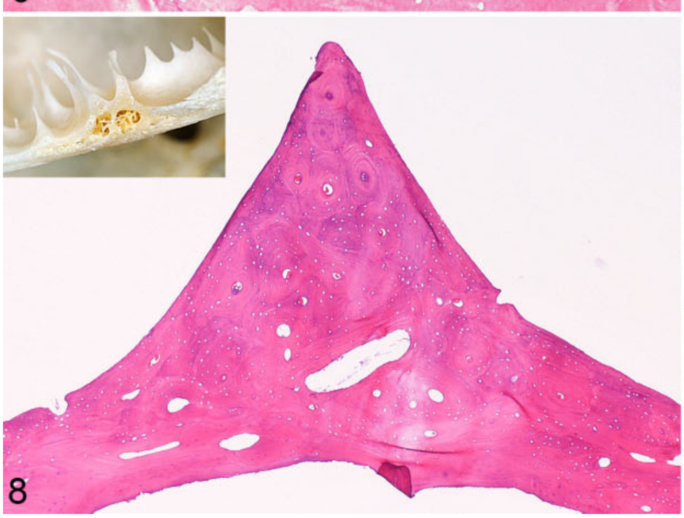


Figure 1. Tympanic bulla; lion No. 3. Radiographic detail of the left tympanic bulla (TB) filled by multiple globular mucoperiosteal exostoses. **Figure 2.** Skeletonized skull; lion No. 3. Computed tomography (CT): 0.6-mm-thick slice of both TB shows multiple, bilateral, well-delineated, variably sized and shaped, bony concretions arising from TB walls. Note how large bony concretions are occupying most of the left TB. L, left side. **Figure 3.** Skeletonized skull; lion No. 7. CT: 0.6-mm-thick slice showing both TB with multiple, bilateral, well-delineated, spicular, bony concretions arising from the ventromedial aspect of the cavity. L, left side. **Figure 4.** Skeletonized skull, ventral aspect; lion No. 3. Left TB after being opened; multiple, large, globular, mucoperiosteal exostoses are extending from the TB wall, whereas others are free in the lumen mixed with a brown to yellowish exudate.







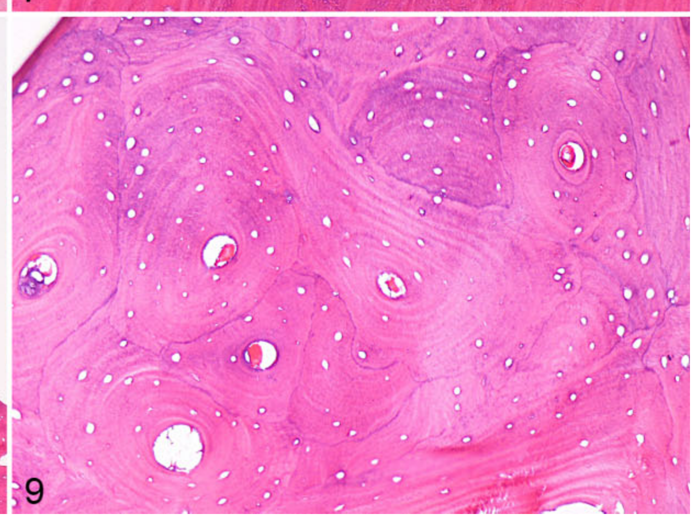


Figure 5. Skeletonized skull, ventral aspect; lion No. 7. Gross view of both TB after being opened; mucoperiosteal exostoses appeared as multiple elongated projections resembling stalagmites with a wide base of implantation (see Fig. 8, inset) in the wall and sometimes displaying bulbous ends. **Figure 6.** Tympanic bulla; lion No. 3. Low-magnification view of 1 decalcified globular mucoperiosteal exostosis, characterized by the arrangement of a hyaline matrix forming multiple concentric layers of lamellae (partially disorganized by the decalcification process) disposed around a central channel (asterisks). Note the distribution of empty spaces corresponding to osteocyte lacunae (arrows). Hematoxylin and eosin (HE). **Figure 7.** Tympanic bulla; lion No. 3. Microscopic structure of a decalcified globular mucoperiosteal exostosis; the proliferative bony lesion is characterized by a hyaline matrix forming concentric layers of lamellae around a central channel (asterisk) corresponding with a vascular space. Note the regular distribution of empty spaces (arrows) corresponding to osteocyte lacunae (pattern of the osteon units in

and unilateral in the other 4 lions. The number, location, morphology, and radiographic signs varied markedly from one lion to another but always appeared as mineral opacities at different positions in the middle ear and most frequently located on the ventromedial aspect of the TB. Diagnosis was unequivocal with radiography and CT imaging, since small concretions could not be identified by radiographic examination alone. The mineral nature of MpEs allowed a detailed description of their radiographic and CT features as well as gross and histologic descriptions. This study demonstrates the value of archived museum specimens in retrospective identification and characterization of bone lesions.

Otoliths are calcium-carbonate crystals that are part of the striola of the macula and saccule of the vestibular system. In the veterinary literature, the terms *otolith* and *otholitiasis* have been incorrectly used in dogs,[2,3,14] to describe bony concretions that arise within the TB[3,13] and appear radiographically as mineral opacities most commonly identified on CT scans.[2] As these lesions are new bone proliferation from the mucoperiosteum,[7,12] the term *mucoperiosteal exostoses* is more appropriate. In the first described domestic dog case, the diagnosis was made radiographically and the ''otolith'' removed surgically, but no further details were given.[3] Another report specifically described the incidental diagnosis of MpEs in 3 dogs. In 2 of them, lesions were detected by CT and consisted of small, mineral-dense foci, usually adherent to the wall of a gas- or fluid-filled tympanic cavity and possibly associated with focal thickening of the TB.[14] To the best of our knowledge, MpEs have not been reported in lions, but the finding of 8 affected, unrelated, captive lions housed and managed under different conditions suggests that MpEs could be more common in African lions than in dogs. MpEs may be an underdiagnosed condition in lions because CT studies, a reliable diagnostic method for identifying MpE, are rarely performed in this species. In fact, references in the veterinary literature reporting the radiographic and CT features of the lion head are scarce. A study on head malformations in white lions (*Panthera leo krugeri*) included the CT scan and radiographic imaging of a deceased lion; MpEs were not reported.[9] In another study, MpEs were not present on the CT scans of 5 live captive African lions: 3 normal animals and 2 affected by calvarial hyperostosis.[5] Although MpEs can be easily identified macroscopically, their prevalence may also be underestimated if middle ear examination is not routinely performed during necropsy, unless clinical history includes signs of middle ear disease.

In contrast to the radiographic findings previously described in dogs,[3,14] we did not find significant thickening of the walls of the TB at the site of MpE attachment in the middle ears of any of the affected lions. In general, radiographic imaging of the lion skulls was less sensitive than CT imaging, especially when mineral opacities were very small and located in the ventral portion of the TB or dorsally, within the epitympanic cavity, where other bony structures appeared superimposed. It is generally recognized that many chronic changes of otitis media can be identified radiographically, but normal radiographic findings do not exclude middle ear disease.[10] As expected, CT provided superior detail in comparison to radiography and revealed MpEs in 5 ears that were radiographically normal—even very small MpEs located in the ventral TB or in the epitympanic cavity, a presentation not reported in the dog. Thus, it has to be considered that in living lions without the use of CT imaging, MpEs may remain undetected.

Gross and microscopic findings showed the mature lamellar bony nature of the MpEs and its formation from the inner lining of the TB. Moreover, their variable number, size, and shape could suggest different stages of bony proliferation of the TB in response to injury.[8,12] Sula et al[12] reported an active inflammatory infiltrate as well as extensive fibrosis of the auricular mucoperiosteum with or without bony proliferation, lysis, or remodeling in cats with chronic otitis media. Unfortunately, in the series of 8 lion skulls, the skeletonized condition of the samples restricted our histologic findings to the bone lesions but should encourage further investigations in postmortem studies of large felines.

The pathogenesis of MpE has not been clearly established. In dogs, Ziemer et al[14] hypothesized that ''otoliths'' could represent dystrophic mineralization of necrotic debris or inflammatory polyps or be heterotopic new bone formation. A previous study in dogs with otitis media reported the formation of dense granulation tissue within the lamina propria of the mucoperiosteum, occasionally containing spicules of bone. In as many as 24 of 62 ears, new bone deposition or bone remodeling was found on the intraluminal aspect of the TB.[7] Also, in the first case reported in dogs, the surgically removed ''otolith'' was embedded in inflammatory soft tissue within the TB.[3] In the studied lions, chronic otitis media also seems to be the most probable hypothesis to explain the formation of MpEs. In 4 lions, lesions were unilateral, and apart from lion No. 2, which presented with hyperostosis associated with hypovitaminosis A (Table 1), the rest of the animals did not have any other bone abnormalities in their skulls or recorded in their postmortem studies that could suggest an underlying primary metabolic disease. These findings suggest that chronic otitis media may be the cause of new bone formation within the TB. However, uniform otosclerosis (thickening) of the TB walls, as reported in chronic middle ear infections in dogs,[8] was not observed in lions. Unfortunately, we could not assess soft tissue changes associated with the MpE in the skeletonized lion skulls and could not determine if MpEs were associated with chronic inflammation.

Figure 7. (continued) the mature compact bone). HE. **Figure 8.** Tympanic bulla; lion No. 7. Microscopic structure of the mucoperiosteal exostosis shown in the inset; at low magnification, it is characterized by multiple, juxtaposed, concentric lamellae disposed around a central channel (bony proliferating tissue). Note the wide base of implantation in the moderately thick TB wall. HE. **Figure 9.** Tympanic bulla; lion No. 7. High magnification of the mucoperiosteal exostosis showed in Figure 8; concentric lamellae are regularly disposed around central channels forming new bony proliferating tissue. The osteon pattern of mature compact bone is well preserved in this sample. HE.

In the 6 lions where clinical medical information was available, signs of middle ear disease were not recorded, but otitis media, if not associated with vestibular signs, may be clinically overlooked. In dogs, some cases of MpEs were considered incidental findings in animals with no previous history of otitis media. However, TB filled with fluid or soft tissue material are commonly seen on CT in dogs with no clinical history of ear disease,[4] and chronic external or middle ear otitis cannot be excluded solely by the clinical history. The same situation occurs in cats where, compared with otitis externa, otitis media is relatively more common than in dogs. In contrast to otitis externa, where diagnosis is relatively easy based on physical examination, clinical signs of true otitis media may be difficult to detect. Otitis media can result from descending disease as an extension of otitis externa, from ascending nasal or respiratory infections through the auditory (Eustachian) tube, and from hematogenous spread. In dogs, only extension from otitis externa is considered a common cause of otitis media, but in cats, upper respiratory infections are known causes of otitis media.[10] Recently, it has been estimated that 31.8% of cats presenting with signs of respiratory disease had severe disease in the ears, whereas in cats without clinical respiratory signs, this proportion was significantly lower (5.2%). Respiratory infections appear to be one major cause of otitis media in cats.[12]

In the absence of otitis externa and its usually evident clinical signs, a large proportion of middle ear disease cases in cats are subclinical. Two studies have provided ample information to support this conclusion. In a retrospective study to determine the prevalence of subclinical middle ear disease in cats undergoing CT scans, owners did not notice any clinical sign of middle ear disease in 75% of domestic cats.[11] Even gross inspection of middle ear lesions has shown a low diagnostic sensitivity. A recent study in 50 cats found histologic lesions in 34 of 100 ears (34%) lacking gross evidence of disease.[12] Three-dimensional anatomic reconstructions show that the middle ear structures of the lion and cat are similarly arranged but have large differences in absolute and relative size.[6] If in African lions there is a similar proportion of subclinical middle ear disease as occurs in domestic cats, it is not surprising that clinical signs of middle ear disease were not recorded in the lions.

In conclusion, we describe, for the first time, the correlation among radiographic, CT imaging, gross postmortem findings, and histopathologic features of MpEs in 8 captive adult lions. As with otitis media, CT imaging was more sensitive than radiography, especially when MpEs were small and located in the ventral aspect of the TB or in the dorsal epitympanic cavity. In contrast to what have been described in dogs, MpEs in lions were not always globular but most often adopted a linear or spiculated shape arising from the mucoperiosteal TB wall. Finally, our histopathologic results suggest that MpEs are formed as new bone and not by calcification of necrotic tissue debris. The significant number of lions with MpEs in this small cohort of unrelated captive lions should encourage thorough evaluations of the TB during clinical examinations and at necropsy in this and other large feline species.

Acknowledgements

We thank J. Miguel Navas and Joao M. Negrini for their generous technical assistance and Katy Gómez for her collaboration preparing the figures.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The research was funded, in part, by the Plan Propio de Apoyo a la Investigación of the University of Córdoba to the Research Groups PAIDI AGR-262 and BIO-307.

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