Pathologic basis for rim enhancement observed in computed tomographic images of feline nasopharyngeal polyps

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Abstract

In post-contrast computed tomographic (CT) images, feline nasopharyngeal polyps typically demonstrate enhancement of the peripheral rim. CT images and histologic specimens of a case series of 22 cats with surgically-removed nasopharyngeal polyps were reviewed retrospectively in an attempt to elucidate the origin of rim enhancement. Polyps were present in the tympanic cavity in 15 (68%) cats (3 with extension into the nasopharynx), only in the nasopharynx in 4 (18%) cats, and only in the external ear canal in the remaining 3 (14%) cats. All polyps had variable degrees of epithelial injury. Hemorrhage and inflammatory infiltration were significantly more marked in the superficial stroma whereas edema was significantly more marked in the core stroma. In non-contrast CT images (n=22), the tympanic bulla was thickened in all 15 cats with a polyp in the tympanic cavity and enlarged in 8 (53%) of these cats. In post-contrast CT images (n=15), an outer zone of relatively increased attenuation compatible with a rim was observed in 11 (73%) polyps. The magnitude and extent of rim enhancement in CT images was positively correlated with the histologic grade of inflammation in the superficial stroma and negatively correlated with the grade of edema in the superficial stroma. It appears that inflammation is the major determinant of contrast medium accumulation in feline nasopharyngeal polyps, and the tendency for inflammation to affect predominantly the superficial layers explains the frequent observation of a rim in post-contrast CT images.

Introduction

Feline nasopharyngeal polyps are inflammatory masses that arise from the mucosa of the feline tympanic membrane, auditory tube or nasopharynx.[1-5] These polyps are liable to fill the tympanic cavity and can grow through the auditory canal into the nasopharynx or through the tympanic membrane into the external ear canal, and are associated with clinical signs of respiratory obstruction, stertor, otitis media and otitis externa.[1-6] Cats of all ages may be affected. The etiology of feline nasopharyngeal polyps is unknown. In young cats, a congenital origin has been suspected, in which the polyp is thought to develop from a branchial arch remnant.[7] Alternatively, feline nasopharyngeal polyps could arise secondary to a chronic inflammatory or infectious process, such as chronic otitis media or calicivirus.[8] Histopathologically, feline nasopharyngeal polyps have a core of fibrovascular tissue covered by ciliated pseudo-stratified columnar epithelium.[1,2] Chronic inflammation can induce a squamous metaplastic response in the originally ciliated epithelium. A zone of increased vascularity and inflammatory infiltration, including lymphoid aggregates, may be observed beneath the epithelium.[1,2] Treatment of nasopharyngeal polyps requires removal, which may be accomplished by traction to rupture the stalk or by bulla osteotomy and curettage.[6,9-11]

Radiographic signs in cats with nasopharyngeal polyps include soft tissue mass within the nasopharynx and/or tympanic cavity and/or external ear canal, and thickening of the tympanic bulla.[2,4,5] There have been few reports of computed tomographic (CT) imaging features of feline nasopharyngeal polyps.[12-15] In non-contrast CT images, a mass effect associated with the polyp and/or thickening of the osseous bulla may be observed. Alternatively, enlargement of the tympanic cavity as the result of a polyp may cause lysis of the bulla and adjacent petrous temporal bone.[15] In post-contrast CT images, enhancement of nasopharyngeal polyps is reported to be consistently most marked around the rim of the lesion, which enables the borders of the polyp and its stalk to be defined.[14] This regular pattern of contrast enhancement should help distinguish a nasopharyngeal polyp from a collection of exudate or a neoplastic mass; however, the features of polyp structure that contribute to rim enhancement in post-contrast CT images have not been elucidated. The aim

of the present study was to review CT and histological features in a series of feline nasopharyngeal polyps in order to determine the basis of the rim enhancement observed in post-contrast CT images.

Materials and Methods

For this retrospective case series, medical records of cats referred to the Queen Mother Hospital for Animals (QMHA) between 2008 and 2014 were reviewed. Inclusion criteria were CT imaging of the head that included the ears, and histologic diagnosis of a nasopharyngeal polyp within the same period of hospitalization. The signalment, history, clinical signs, CT signs, and details of surgical management were recorded.

CT imaging was done using a 16-slice MDCT scanner (MX 8000 IDT, Philips Medical Systems, Cleveland, USA). CT series to examine bone were obtained using axial acquisition, 120kVp, 120-240mAs, 0.75-1.5 mm slice thickness, 80-256mm field of view, and 512x512 or 768x768 matrix (pixel size 0.12-0.17mm), and were reconstructed using a high frequency algorithm. CT series to examine soft tissues were obtained using axial acquisition, 120kVp, 120-240mAs, 1.5-3.0 mm slice thickness, 80-250mm field of view, and 512x512 or 768x768 matrix (pixel size 0.12-0.4mm) and were reconstructed using a medium frequency ('soft tissue') algorithm. Post-contrast CT images were obtained 60s after the start of rapid manual intravenous injection of 2ml/kg bolus of iohexol (Omnipaque 300, GE Healthcare, Oslo, Norway). Transverse CT images were reviewed with reference to extent of osseous bulla involvement (overall size and thickening), site of the polyp, and size of the retropharyngeal lymph nodes. The maximum diameter of the polyp and width of rim enhancement (if present) of the polyp were recorded. In post-contrast images, the extent of enhancement around the periphery of the polyp was estimated subjectively using a scale of 0-4 (0, absent; 1, <25%; 2, 25-50%; 3, 50-75%; 4, >75% rim enhanced). Pre- and post- contrast Hounsfield units (HU) were also recorded for each polyp by taking the median HU of a circular region of interest (ROI) placed in the center of the polyp in three consecutive images. Rim enhancement was quantified by taking the

median of HU values from a smaller circular ROI placed on the rim in the same three consecutive post-contrast images. In each instance, the ROI fitted to the post-contrast images was copied to the pre-contrast images.

CT image review was done by CRL without knowledge of the pathologic findings and pathologic examinations were done by SLP without knowledge of the imaging findings.

For histological examination, biopsy specimens were fixed in 10% neutral-buffered formalin, processed into paraffin wax, and 4μm sections were stained with hematoxylin and eosin (H&E). Archived histologic samples were reviewed by SLP with reference to the core stroma, the superficial stroma, and the epithelium. Differentiation between the core and superficial stroma was determined by viewing the whole polyp under low magnification (4X) and defining the outermost 10% of the stroma as the superficial stroma. A pre-determined set of variables were then assessed in each of these zones. The epithelium was assessed for cellular classification and the degree of epithelial injury, including both erosion and ulceration, was estimated subjectively using a scale of 0-3 (0, no signs of injury; 1, 1-10%; 2, 11-50%; 3, >50% epithelium injured). The core stroma and superficial stroma were each assessed for vascularization, edema, hemorrhage, and degree of inflammatory infiltrate. Vascularization, edema and degree of inflammatory infiltrate were all graded on a 0-3 scale (0, absent; 1, mild; 2, moderate; 3, marked). Hemorrhage was also graded on a 0-3 scale based on percent (0, no signs of hemorrhage; 1, 1-10%; 2, 11-50%; 3, >50% stroma affected by hemorrhage).

Statistical testing was done by CRL using SPSS Statistics version 19 (IBM Corporation, Chicago, IL). Differences in median grades of histologic features of core stroma and superficial stroma of polyps were tested using the Wilcoxon Signed-Rank test. Associations between attenuation values in CT images and median grades of histologic features of core stroma and superficial stroma of polyps were tested using Spearman's rank-order correlation coefficient. Results with $p<0.05$ were considered significant.

Results

Records were found of 22 cats that had CT and histologic diagnosis of nasopharyngeal polyp. The clinical and histologic features of polyps in all 22 cats are described, but 7 cats had only non-contrast CT images available for review, hence the CT features of polyps and correlations between histologic and CT imaging findings are based on the remaining 15 cats that had suitable post-contrast CT images.

Clinical Findings

Ten cats were male (9 neutered) and 12 were female (all neutered). Their median age at the time of diagnosis was 4 years (range 3 months – 16 years). There were 14 domestic shorthair cats, and one cat of each of eight other breeds. Median duration of clinical signs was 2 months (range 2 weeks – 4 years). All cats were referred for investigation of respiratory signs and/or signs of otitis. The prevalence of individual clinical signs was otorrhea in 12 (55%) cats, visible aural or oral mass in 11 (50%), head shaking and/or ear scratching in 11 (50%), stertor in 10 (45%), head tilt in 7 (32%), ataxia in 6 (27%), dyspnea in 6 (27%), nasal discharge in 5 (23%), Horner's syndrome in 5 (23%), sneezing in 4 (18%), dysphagia in 3 (14%), nystagmus in 3 (14%), and cough in 3 (14%).

Polyps were present within the tympanic cavity in 15 (68%) cats; 9 of these also had extension of the polyp into the external ear canal; 3 had extension of the polyp into the nasopharynx, and one had polyp extension into both nasopharynx and external ear canal. In 4 (18%) cats, the polyp was observed only in the nasopharynx. In the remaining 3 (14%) cats, the polyp was observed only in the external ear canal. Surgical treatment of nasopharyngeal polyps involved removal via ventral bulla osteotomy in 10 cats, removal by simple traction in 8 cats, removal by resection in 3 cats, and total ear canal ablation/lateral bulla osteotomy in 1 cat.

CT Imaging findings

In non-contrast CT images acquired to examine osseous structures, thickening of the tympanic bulla was observed in all 15 cats with a polyp in the tympanic cavity; in 12 of these cats osseous thickening was regular; in 3 it was irregular. The tympanic cavity was enlarged compared to the contralateral in 8 (53%) of these cats.

In CT images acquired to examine soft tissues, a focal, contrast-enhancing mass lesion compatible with polyp was observed in all 15 (100%) cats. Median pre-contrast attenuation of polyps was 28HU (range 11 – 56HU). An outer zone of relatively increased post-contrast attenuation compatible with a rim was observed in 11 (73%) polyps. The median extent of rim enhancement around the periphery of polyp was 75% (range 0-100%). In post-contrast CT images, the median diameter of nasopharyngeal polyps was 10.5 mm (range 6-22 mm), and the median width of the rim was 1.1mm (i.e. equal to approximately 10% polyp diameter). The median increase in attenuation of polyps in post-contrast CT images was 25HU (range 2 – 120HU) in the core and 71HU (range 5-151HU) in the rim. The median difference between attenuation of the core and rim of polyps in post-contrast CT images was 46HU (range 0 – 81HU). The medial retropharyngeal lymph node ipsilateral to the polyp was larger than the contralateral node in 10 (67%) cats. The median difference in maximum dimensions of ipsilateral and contralateral nodes was 3.0mm (range 0-9mm).

Histologic findings

Of 22 polyps examined histologically, 17 (77%) had a pseudostratified columnar ciliated epithelium (4 with regions of stratified squamous epithelium), 2 (9%) had entirely stratified squamous epithelium, 2 (9%) had pseudostratified columnar (non-ciliated) epithelium, and 1 (5%) had a pseudostratified cuboidal ciliated epithelium. All polyps showed variable degrees of epithelial injury. Median grade for epithelial injury was 2 (range 1-3). All but one polyp contained lymphoid follicles.

The core stroma of polyps could be distinguished from the superficial stroma on low-power microscopic examination of whole polyps. For core stroma, median grades were 1 (range 1-2) for vascularization, 0 (range 0-1) for hemorrhage, 2 (range 1-3) for edema, and 1 (range 1-2) for

inflammatory infiltration. For superficial stroma, median grades were 1 (range 1-2) for vascularization, 0.5 (range 0-1) for hemorrhage, 1 (range 0-1) for edema, and 2 (range 2-3) for inflammatory infiltration. Hemorrhage (p=0.02) and inflammatory infiltration (p=0.0005) within the superficial stroma were significantly more marked than in the core stroma. Conversely, edema within the core stroma was significantly more marked than in the superficial stroma (p=0.003).

CT-Histologic correlation

Significant positive correlations were found between pre-contrast HU and grade of inflammatory infiltration in core stroma of polyps (p=0.01), between the post-contrast HU of the rim and grade of inflammatory infiltration in superficial stroma (p=0.04), and between the increase in HU post-contrast HU of the rim and grade of inflammatory infiltration in superficial stroma (p=0.02) (Table 1). Also, the subjective extent of the rim observed in post-contrast CT images was positively correlated with the grade of inflammatory infiltration in the superficial stroma (p=0.04) and negatively correlated with the grade of edema in superficial stroma (p=0.04). Comparisons between whole polyp histologic sections and their corresponding CT images are illustrated in Figures 1 and 2.

The difference in maximum dimensions of ipsilateral and contralateral medial retropharyngeal nodes was not significantly associated with either the grade of inflammation of polyps (p=0.9) or the grade of edema (p=0.02).

Discussion

The range of clinical signs associated with nasopharyngeal polyps and the wide age range of affected cats in the present study correspond to previous reports.[1-6] Similarly, the appearance of polyps in CT images corresponded with previous descriptions with respect to size and location of polyps, nature of changes affecting the tympanic bullae, attenuation values of polyps, and enhancement of a thin rim following contrast medium administration.[12-15] A rim was observed in post-contrast images in a slightly smaller proportion of cats (73% versus 100%), and the degree of enhancement of the rim

was also slightly less marked (median 46HU versus average 105HU) than reported previously.[14] The CT techniques and contrast medium administration were comparable between these studies, hence the reason for these differences is unclear. The rate of change of contrast enhancement of parenchymal lesions is most rapid soon after contrast injection and slows subsequently.[16,17] As a result, slight variations in rate of manual injection of contrast medium, in circulation time, and in timing of post-contrast CT images are likely to have a relatively minor effect on the degree of contrast accumulation in lesions at 60s post-injection. Hence the differences observed in the degree of polyp enhancement between the previous[14] and present studies probably reflect variations in the pathologic features of polyps.

There was variable post-contrast enhancement of polyps in the present study (range 2 – 120HU), with the lower end of this range potentially indicating a lack of contrast accumulation. This observation is potentially important clinically because a polyp in the tympanic cavity lacking contrast accumulation could be interpreted erroneously as a sign that the content is non-vascularized material, such as exudate or hemorrhage. Other cats with polyps that were not detected by CT (and cats with polyps whose signs were controlled by non-surgical treatments) will have been omitted from the present study, which therefore overestimates the sensitivity of CT for nasopharyngeal polyps. It is likely that inability to detect contrast enhancement in some instances of polyps in the tympanic cavity represents a limitation of CT images obtained to examine soft tissues adjacent to bone. Use of relatively thick slices, low frequency reconstruction algorithm and relatively narrow window settings, which are necessary for examination of soft tissues, result in an apparent increase in thickness of the tympanic bulla that masks adjacent tissue.[18] An example of this problem affecting CT images of a cat in the present study is illustrated in figure 3. Similarly, errors could have occurred in placement of ROIs for HU measurements because of difficulty resolving the border of polyps adjacent to nasopharyngeal mucosa, which also enhances after contrast administration. Presence of air in the nasopharynx or external ear canal thought to outline the polyp surface was used as an aid

to ROI placement but the possibility exists that in some instances the ROI included adjacent non-polyp tissue and/or exudate.

Marked variations may be observed in the histologic appearance of feline nasopharyngeal polyps. For example, although a pseudostratified columnar ciliated epithelium (typical of respiratory mucosa) predominated in the present study, squamous metaplasia, erosions and ulceration were observed frequently. Some polyps were markedly edematous with minimal evidence of inflammation while others were highly cellular with numerous, mixed inflammatory cells, lymphoid follicles, and extensive fibroplasia. Hemorrhage and inflammation were significantly more marked in the superficial stroma than in the core stroma, whereas edema was significantly more marked in the core stroma than in the superficial stroma. Prevalence of hemorrhage in the superficial stroma likely reflects epithelial damage associated with stertor or pressure. In human nasal polyps, both epithelial and inflammatory cells can have increased expression of vascular and inflammatory mediators.[19-21] It is possible that similar variations in protein expression occur in feline nasopharyngeal polyps, which share histologic features with human nasal polyps. Recruitment of inflammatory cells by damaged epithelial cells could account for the increased cellularity observed within the superficial stroma. Increased vascularity directly beneath the epithelium of feline polyps has also been reported[1,2]; however, no significant difference in the degree of vascularization between the superficial and core stroma was found in polyps in the present study. Ipsilateral draining node enlargement observed in cats with nasopharyngeal polyps likely represents a secondary reactive inflammatory process, but that cannot be confirmed because nodes were not examined pathologically.

In the present study, positive correlations were found between the grade of inflammation in the core stroma and the pre-contrast HU of polyps, and between the grade of inflammation in the superficial stroma of polyps and the degree of rim enhancement observed in post-contrast CT images. Hence it appears that inflammation is the major determinant of contrast medium accumulation in feline nasopharyngeal polyps, and the tendency for inflammation to affect predominantly the superficial stroma explains the frequent observation of a rim in post-contrast CT

232 images. Conversely, more marked edema in the superficial stroma of polyps will tend to diminish the
233 appearance of a rim in post-contrast CT images.

234

235 Table 1. Results of rank-order correlation testing of histologic and CT features of nasopharyngeal polyps in 15 cats

	Histologic features (grade)								
	Core stroma				Superficial stroma				Epithelial injury
CT features	Vascularization	Hemorrhage	Edema	Inflammatory infiltrate	Vascularization	Hemorrhage	Edema	Inflammatory infiltrate	
Pre-contrast HU	NS	NS	NS	0.63, p=0.01	-	-	-	-	-
Post-contrast HU	NS	NS	NS	NS	NS	NS	NS	0.53, p=0.04	NS
Increase in HU post-contrast	NS	NS	NS	NS	NS	NS	NS	0.60, p=0.02	NS
Extent of rim (grade)	-	-	-	-	NS	NS	-0.53, p=0.04	0.52, p=0.04	NS

236

237 Values are Spearman's correlation coefficient

238 NS, non-significant, p>0.2

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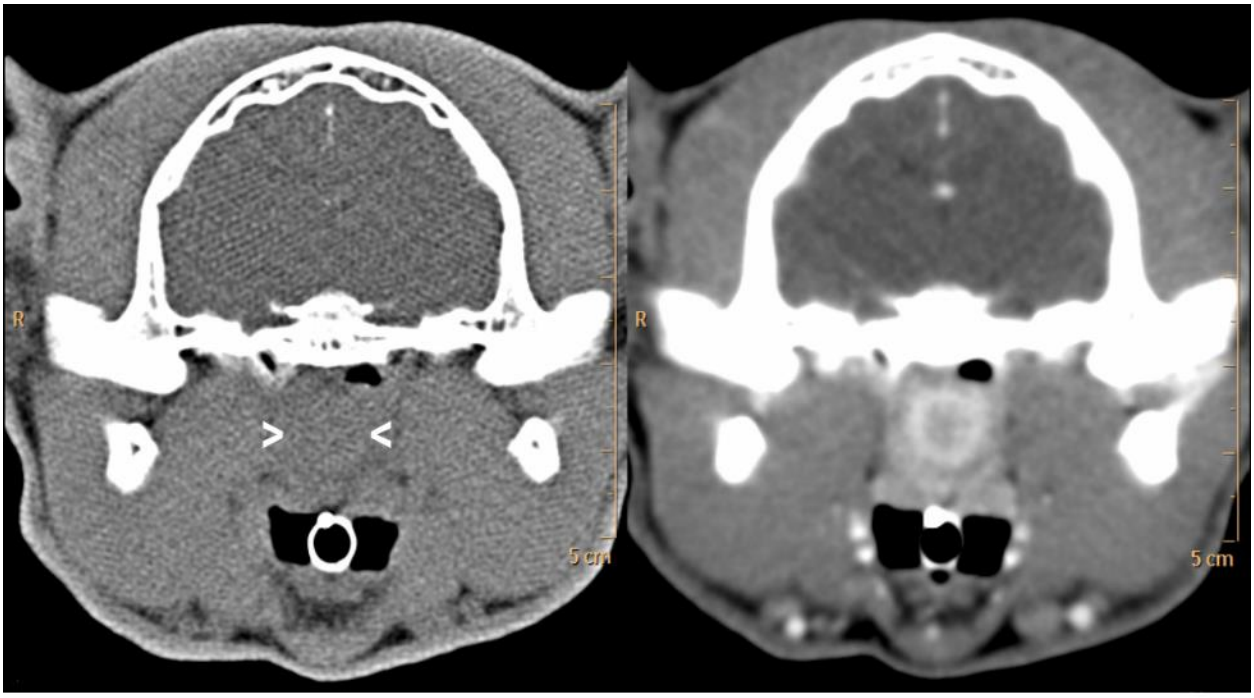
284 **Legends**

285 Figure 1. Example of an inflamed nasopharyngeal polyp in a 14 year old domestic short haired cat. A)
286 The polyp (arrowheads) has moderate attenuation (40HU) in pre-contrast CT image (at left) and is
287 difficult to distinguish from the surrounding tissues. In post-contrast CT image (at right), the polyp has a
288 relatively marked increase in attenuation of the core (120HU) and rim (191HU). The rim appears
289 complete in this image. A slight amount of non-contrast enhancing material, probably exudate,
290 separates the polyp from adjacent nasopharyngeal mucosa. B) Corresponding histologic section of the
291 polyp (maximal diameter 10mm), which was graded as having moderate edema and inflammatory
292 infiltrate in the core stroma and marked inflammatory infiltrate in the peripheral stroma (note deep
293 staining). (H&E stain)



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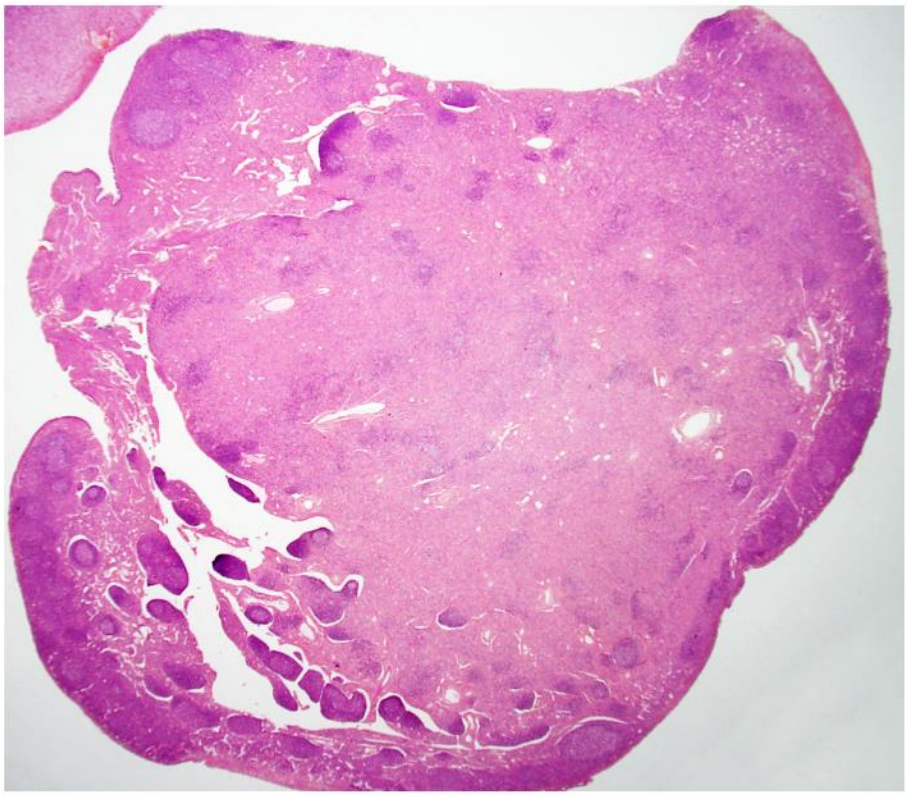

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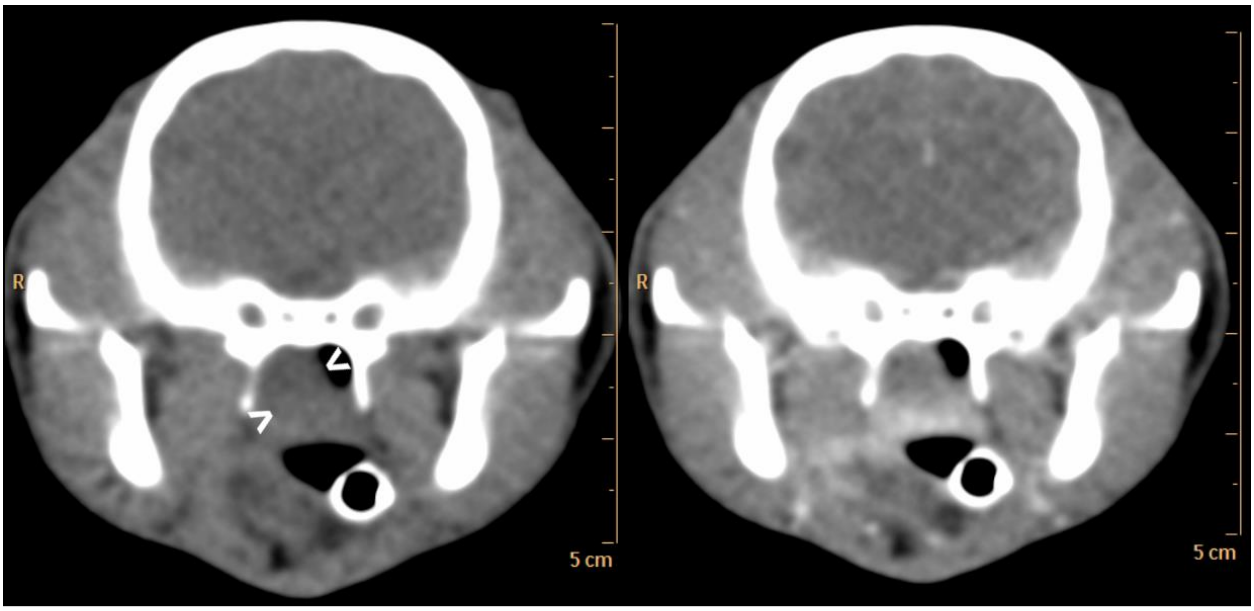
Figure 2. Example of an edematous nasopharyngeal polyp in a 4 month old domestic short haired cat. A) The polyp (white arrowheads) has moderate attenuation (47HU) in pre-contrast CT image (at left) and is difficult to distinguish from the surrounding tissues. In post-contrast CT image (at right), the polyp has a moderate increase in attenuation of the core (83HU) and rim (130HU). The rim appears relatively narrow and incomplete in this image. B) Corresponding histologic section of the polyp (maximal diameter 9mm), which was graded as having marked edema in the core stroma (note pale staining), and moderate edema and minimal inflammatory infiltrate in the peripheral stroma. Scattered small lymphoid follicles are visible (black arrowheads). (H&E stain)



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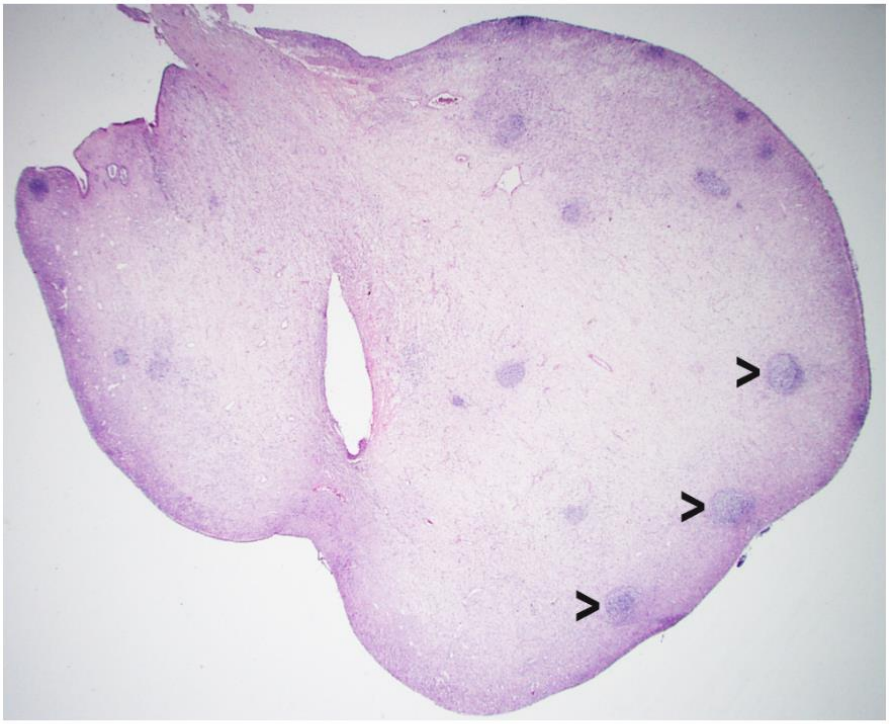

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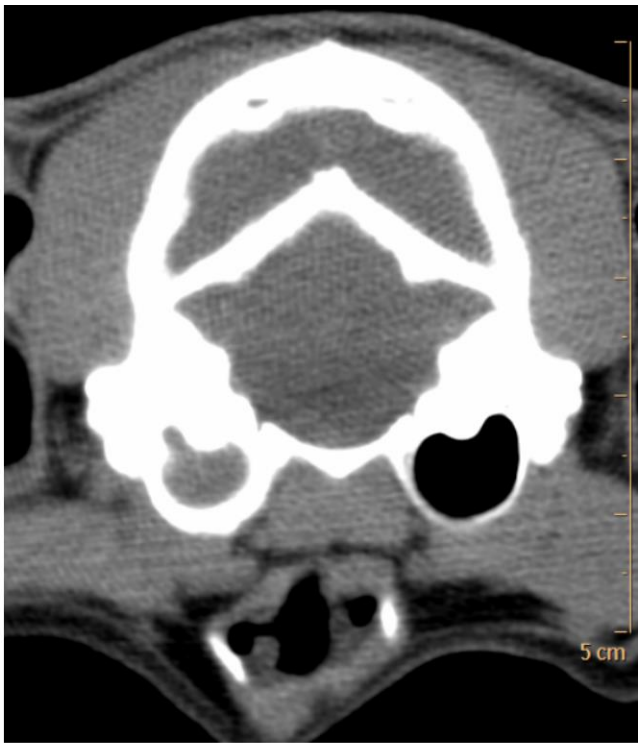
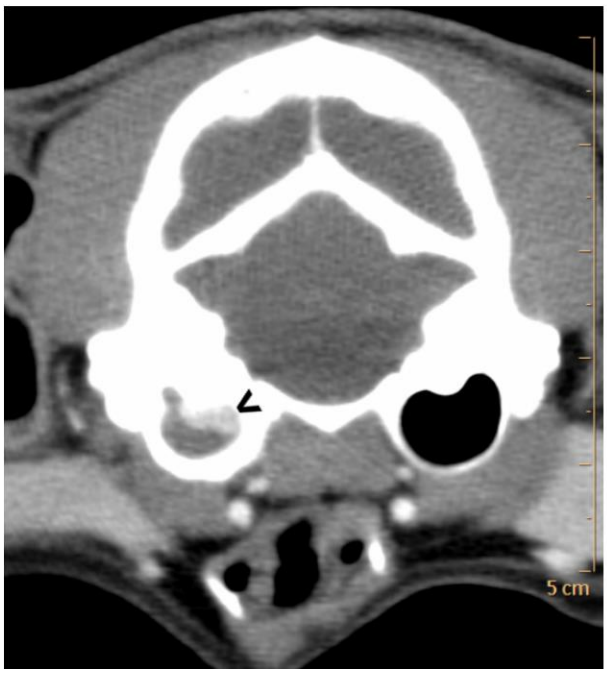
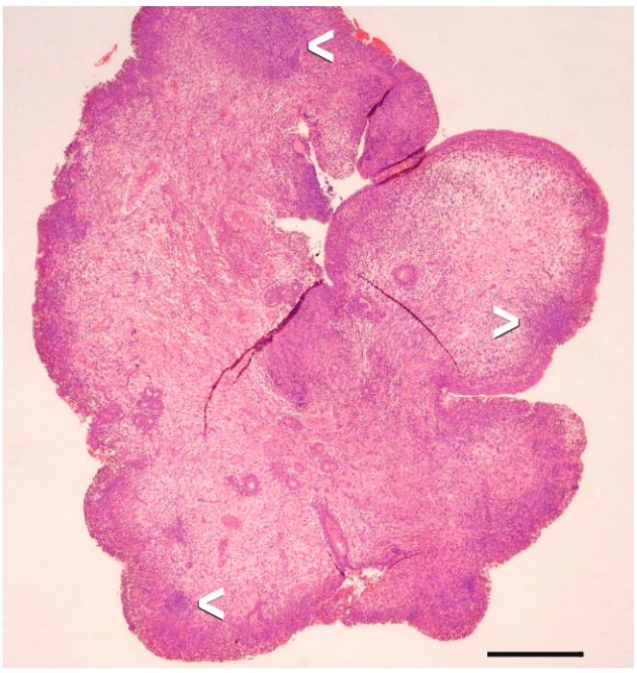
Figure 3. A 10 year old domestic short haired cat with a nasopharyngeal polyp within the right tympanic cavity. A) CT image obtained using high frequency reconstruction algorithm suitable for examination of bones shows slight thickening of the right bulla and soft tissue content. B) Pre- and (C) post-contrast CT images show an artifactual increase in apparent thickness of the bulla.[18] Localised contrast accumulation is evident only on the dorsomedial aspect of the bulla (black arrowhead). D) Corresponding histologic section of the polyp shows marked inflammatory infiltrate, including multiple lymphoid follicles (white arrowheads), in the superficial stroma. This histologic feature is associated with presence of a contrast-enhancing rim in CT images. Hence, in this instance it appears likely that enhancement of the rim of this polyp has been partially masked by the artifactual thickening of the bulla. Bar = 1mm (H&E stain)







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