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

3

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8

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11

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**13 Abstract**

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

## 31 Introduction

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

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

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

59

## 60 **Materials and Methods**

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

66 CT imaging was done using a 16-slice MDCT scanner (MX 8000 IDT, Philips Medical Systems,  
67 Cleveland, USA). CT series to examine bone were obtained using axial acquisition, 120kVp, 120-  
68 240mAs, 0.75-1.5 mm slice thickness, 80-256mm field of view, and 512x512 or 768x768 matrix (pixel  
69 size 0.12-0.17mm), and were reconstructed using a high frequency algorithm. CT series to examine  
70 soft tissues were obtained using axial acquisition, 120kVp, 120-240mAs, 1.5-3.0 mm slice thickness,  
71 80-250mm field of view, and 512x512 or 768x768 matrix (pixel size 0.12-0.4mm) and were  
72 reconstructed using a medium frequency ('soft tissue') algorithm. Post-contrast CT images were  
73 obtained 60s after the start of rapid manual intravenous injection of 2ml/kg bolus of iohexol  
74 (Omnipaque 300, GE Healthcare, Oslo, Norway). Transverse CT images were reviewed with reference  
75 to extent of osseous bulla involvement (overall size and thickening), site of the polyp, and size of the  
76 retropharyngeal lymph nodes. The maximum diameter of the polyp and width of rim enhancement  
77 (if present) of the polyp were recorded. In post-contrast images, the extent of enhancement around  
78 the periphery of the polyp was estimated subjectively using a scale of 0-4 (0, absent; 1, <25%; 2, 25-  
79 50%; 3, 50-75%; 4, >75% rim enhanced). Pre- and post- contrast Hounsfield units (HU) were also  
80 recorded for each polyp by taking the median HU of a circular region of interest (ROI) placed in the  
81 center of the polyp in three consecutive images. Rim enhancement was quantified by taking the

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

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

87 For histological examination, biopsy specimens were fixed in 10% neutral-buffered formalin,  
88 processed into paraffin wax, and 4 $\mu$ m sections were stained with hematoxylin and eosin (H&E).

89 Archived histologic samples were reviewed by SLP with reference to the core stroma, the superficial  
90 stroma, and the epithelium. Differentiation between the core and superficial stroma was

91 determined by viewing the whole polyp under low magnification (4X) and defining the outermost

92 10% of the stroma as the superficial stroma. A pre-determined set of variables were then assessed in

93 each of these zones. The epithelium was assessed for cellular classification and the degree of

94 epithelial injury, including both erosion and ulceration, was estimated subjectively using a scale of 0-

95 3 (0, no signs of injury; 1, 1-10%; 2, 11-50%; 3, >50% epithelium injured). The core stroma and

96 superficial stroma were each assessed for vascularization, edema, hemorrhage, and degree of

97 inflammatory infiltrate. Vascularization, edema and degree of inflammatory infiltrate were all

98 graded on a 0-3 scale (0, absent; 1, mild; 2, moderate; 3, marked). Hemorrhage was also graded on a

99 0-3 scale based on percent (0, no signs of hemorrhage; 1, 1-10%; 2, 11-50%; 3, >50% stroma affected

100 by hemorrhage).

101 Statistical testing was done by CRL using SPSS Statistics version 19 (IBM Corporation, Chicago, IL).

102 Differences in median grades of histologic features of core stroma and superficial stroma of polyps

103 were tested using the Wilcoxon Signed-Rank test. Associations between attenuation values in CT

104 images and median grades of histologic features of core stroma and superficial stroma of polyps

105 were tested using Spearman's rank-order correlation coefficient. Results with  $p < 0.05$  were

106 considered significant.

107

108 **Results**

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

114 *Clinical Findings*

115 Ten cats were male (9 neutered) and 12 were female (all neutered). Their median age at the time of  
116 diagnosis was 4 years (range 3 months – 16 years). There were 14 domestic shorthair cats, and one  
117 cat of each of eight other breeds. Median duration of clinical signs was 2 months (range 2 weeks – 4  
118 years). All cats were referred for investigation of respiratory signs and/or signs of otitis. The  
119 prevalence of individual clinical signs was otorrhea in 12 (55%) cats, visible aural or oral mass in 11  
120 (50%), head shaking and/or ear scratching in 11 (50%), stertor in 10 (45%), head tilt in 7 (32%), ataxia  
121 in 6 (27%), dyspnea in 6 (27%), nasal discharge in 5 (23%), Horner's syndrome in 5 (23%), sneezing in  
122 4 (18%), dysphagia in 3 (14%), nystagmus in 3 (14%), and cough in 3 (14%).

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

130 *CT Imaging findings*

131 In non-contrast CT images acquired to examine osseous structures, thickening of the tympanic bulla  
132 was observed in all 15 cats with a polyp in the tympanic cavity; in 12 of these cats osseous thickening  
133 was regular; in 3 it was irregular. The tympanic cavity was enlarged compared to the contralateral in  
134 8 (53%) of these cats.

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

#### 147 *Histologic findings*

148 Of 22 polyps examined histologically, 17 (77%) had a pseudostratified columnar ciliated epithelium  
149 (4 with regions of stratified squamous epithelium), 2 (9%) had entirely stratified squamous  
150 epithelium, 2 (9%) had pseudostratified columnar (non-ciliated) epithelium, and 1 (5%) had a  
151 pseudostratified cuboidal ciliated epithelium. All polyps showed variable degrees of epithelial injury.  
152 Median grade for epithelial injury was 2 (range 1-3). All but one polyp contained lymphoid follicles.  
153 The core stroma of polyps could be distinguished from the superficial stroma on low-power  
154 microscopic examination of whole polyps. For core stroma, median grades were 1 (range 1-2) for  
155 vascularization, 0 (range 0-1) for hemorrhage, 2 (range 1-3) for edema, and 1 (range 1-2) for

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

#### 161 *CT-Histologic correlation*

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

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

173

#### 174 **Discussion**

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

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

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

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

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

226 In the present study, positive correlations were found between the grade of inflammation in the  
227 core stroma and the pre-contrast HU of polyps, and between the grade of inflammation in the  
228 superficial stroma of polyps and the degree of rim enhancement observed in post-contrast CT  
229 images. Hence it appears that inflammation is the major determinant of contrast medium  
230 accumulation in feline nasopharyngeal polyps, and the tendency for inflammation to affect  
231 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

CT features	Histologic features (grade)								
	Core stroma				Superficial stroma				Epithelial injury
	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&gt;0.2

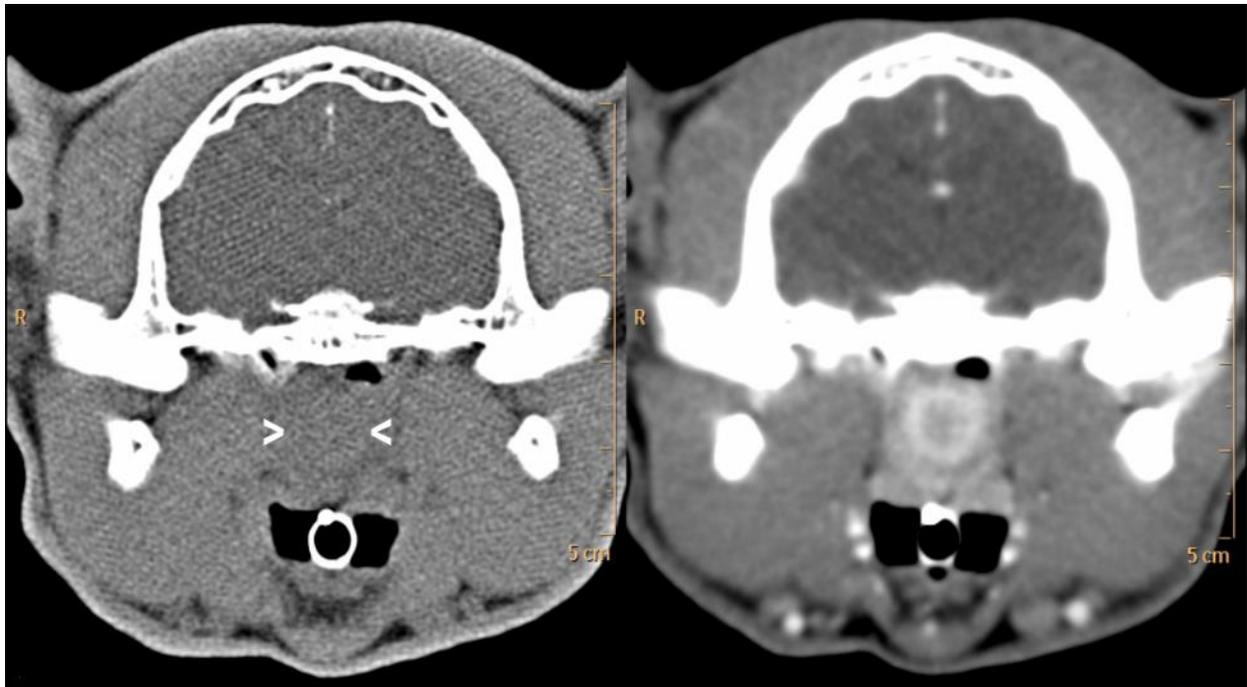
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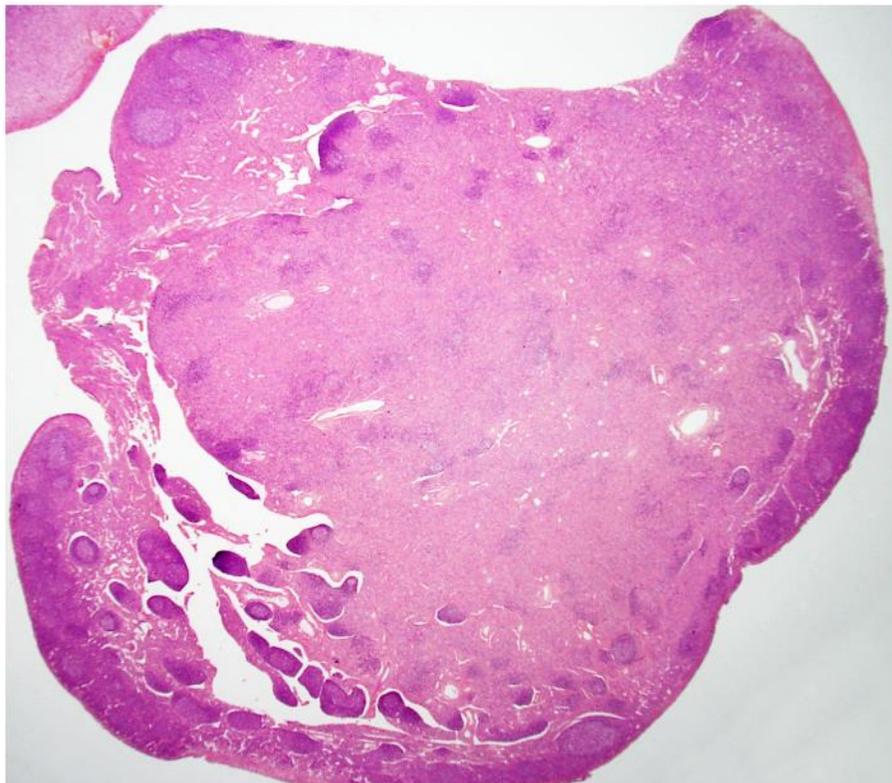
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- 283

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)



**A**

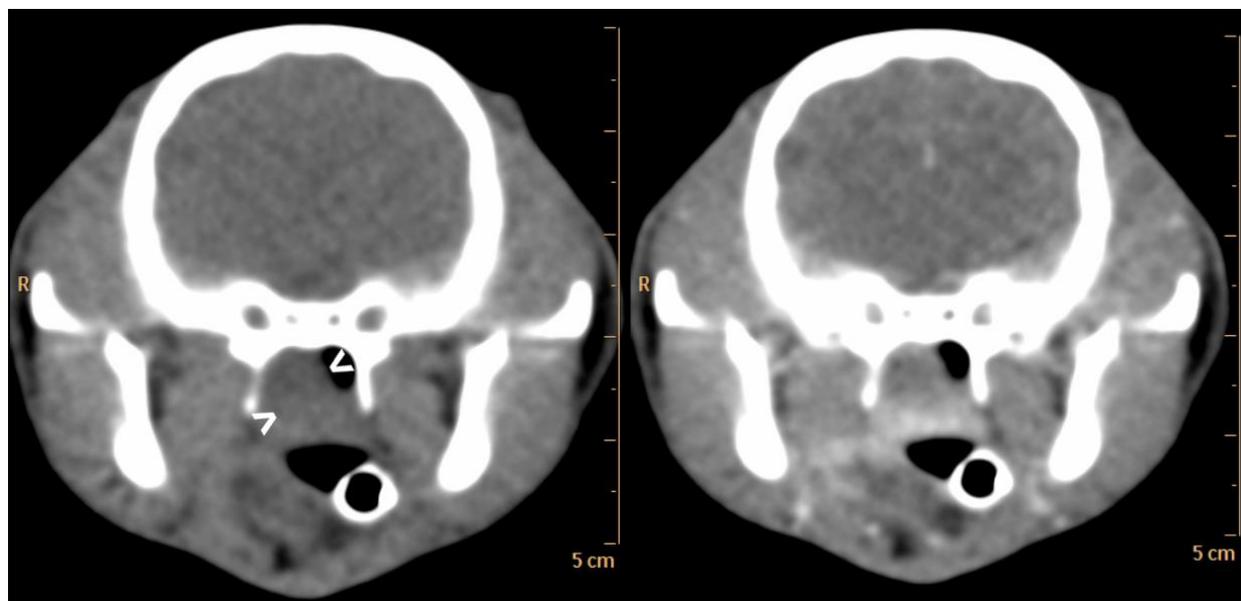


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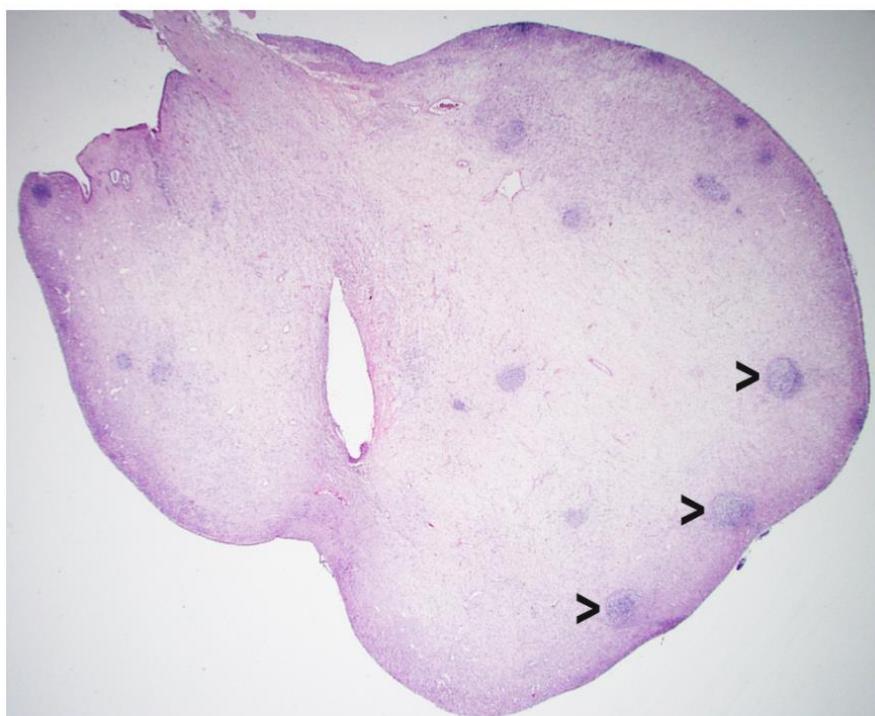
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296 Figure 2. Example of an edematous nasopharyngeal polyp in a 4 month old domestic short haired cat. A)  
297 The polyp (white arrowheads) has moderate attenuation (47HU) in pre-contrast CT image (at left) and is  
298 difficult to distinguish from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



A



B

304

305

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

