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Canine tonsillar polyps: characteristics, classification and review of the pathogenesis

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Abstract:	Canine tonsillar polyps are uncommon. We describe 14 tonsillar polyps dogs and review their classification and pathogenesis. All dogs were adult (3-13 years old). Females (10/14) were more affected than males (4/14). Most of the lesions were asymptomatic (10/14). All lesions were unilateral, pedunculated (9/14) or sessile (5/14), with a smooth (12/14) or papillary/verrucous surface (2/14). Histologically, polyps consisted or benign proliferation of lymphatic vessels, blood vessels, fibrous tissue and lymphoid tissue in variable proportions, with occasional adipose tissue (4/14). According to the main stromal components, polyps were categorized as lymphangiomatous (5/14), lymphangiolipomatous (2/14 lymphangiofibromatous (1/14), angiofibrolipomatous (1/14), angiofibrolipomatous (1/14), sthe pathogenesis of these polyps remains unclear, we propose to replace the term inflammatory tonsillar polyp by a morphological diagnosis based on the stromal characteristics of the lesions. Simple surgical excision was curative in the 9 cases with available follow-up information.

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1 Canine tonsillar polyps: characteristics, classification and

2 review of the pathogenesis

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20 Abstract

21	Canine tonsillar polyps are uncommon. We describe 14 tonsillar polyps in dogs
22	and review their classification and pathogenesis. All dogs were adult (3-13
23	years old). Females (10/14) were more affected than males (4/14). Most of the
24	lesions were asymptomatic (10/14). All lesions were unilateral, pedunculated
25	(9/14) or sessile (5/14), with a smooth (12/14) or papillary/verrucous surface
26	(2/14). Histologically, polyps consisted of benign proliferation of lymphatic
27	vessels, blood vessels, fibrous tissue and lymphoid tissue in variable
28	proportions, with occasional adipose tissue (4/14). According to the main
29	stromal components, polyps were categorized as lymphangiomatous (5/14),
30	lymphangiolipomatous (2/14), lymphangiofibromatous (2/14), angiofibromatous
31	(1/14), angiofibrolipomatous (1/14), lymphoid (2/14), and myxomatous (1/14).
32	As the pathogenesis of these polyps remains unclear, we propose to replace
33	the term inflammatory tonsillar polyp by a morphological diagnosis based on the
34	stromal characteristics of the lesions. Simple surgical excision was curative in
35	the 9 cases with available follow-up information.
36	Keywords: dog, hamartoma, oropharynx, pathogenesis, polyp, review, tonsil

37	Benign proliferative tonsillar lesions are infrequent in dogs. Only 10 canine
38	tonsillar polyps and an epithelial cyst have been reported, among 3 publications
39	and a conference proceeding. ^{3,5,11,13} Histologically, most of the lesions are
40	composed of mature fibrovascular stroma with multifocal aggregates of
41	lymphocytes and plasma cells, and have been defined as inflammatory
42	polyps. ^{11,20} Predominance of dilated lymphatic vessels within a dense
43	fibrovascular stroma have been described only rarely. ^{3,13}
44	Benign tonsillar polyps in humans are mostly considered hamartomatous
45	growths containing vascular, connective, lymphoid and fat tissue in variable
46	proportions. ^{7,8,12} As in dogs, human tonsillar polyps are infrequent but the real
47	incidence is unknown. ^{7,12} Histologically, polyps are recommended to be
48	classified according to the most prominent stromal component and, in contrast
49	to dogs, different histotypes have been reported including lymphangiomatous,
50	lymphangiectatic, fibrous or fibrolipomatous, lymphoid, fibroepithelial. ^{2,7,12,17}
51	The objective of this report is to describe the clinicopathological characteristics
52	of 14 tonsillar polyps in dogs, review their classification, and compare the
53	canine lesion to known pathogenesis in humans.
54	Our records included 402 canine cases with tonsillar histopathology from 1995
55	to 2020. From those, 14 were selected because the descriptions were
56	consistent with tonsillar polyps. Samples had been fixed in 10% neutral-buffered
57	formalin, processed routinely, and stained with hematoxylin and eosin.
58	Microscopic characteristics of each case were re-examined by two board-
59	certified pathologists (JM, GAR). Vascularization, edema, and degree of
60	inflammation were graded on a 0–3 scale (0, absent; 1, mild; 2, moderate; 3,
61	marked). Vascular spaces, lymphoid, fibrous and fat tissue were graded on a 0–

4 scale based on percent (0, absent; 1, 1–25%; 2, 26–50%; 3, 51-75%; 4 >75%
stroma). Clinical data and follow-up information were obtained through e-mail
and telephone interviews with the referring clinicians.

65 Clinical and macroscopic data are shown in Table 1. Age of the dogs ranged from 3 to 13 years (mean 9.3). Females (10/14) were more affected than males 66 (4/14). All patients presented with a unilateral, variably sized polyp emerging 67 from the surface of palatine tonsil. Polyps were located on the right (6/14), left 68 (4/14), or unreported (4/14). Most dogs were asymptomatic; only 4/12 (33%) 69 cases showed clinical signs consisting of mouth bleeding (case 7), cough (case 70 10), retching (case 10,14) and dyspnea (case 13). Follow-up information was 71 available in 9/14 (64%) cases, none of which showed local recurrence after 72 simple surgical excision. 73

Nine of 14 (67%) polyps were pedunculated and 5/14 (36%) were sessile. The total length of the polyps ranged from 1 cm to 3.8 cm (mean, 1.93 cm) and the diameter from 0.3 to 1.4 cm (mean, 0.69 cm). Polyps showed a smooth (12/14), papillary (1/14) or verrucous (1/14) surface. Cut section was white to yellow and varied from soft and spongy (9/14) to firm and fibrous (4/14) to gelatinous (1/14).

Polyps were categorized into different histological subtypes according to the
main constituents of their stroma. Histologic characteristics of each case are
shown in Supplemental Table S1.

Seven of 14 polyps (57%) were diagnosed as lymphangiomatous. Lesions
showed a highly vascularized stroma with abundant dilated endothelial-lined
cavities and interconnected vascular channels, compatible with lymphatic

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86	vessels (Figs. 1, 2). Lymphatics were empty or filled by eosinophilic fluid, and
87	were separated by hypocellular, dense fibrovascular tissue occupying <50% of
88	the stroma (Fig. 2). In 2/14 lesions, 25-50% of the stroma was infiltrated by
89	adipose tissue and were subclassified as lymphangiolipomatous (Supplemental
90	Fig. S1). Expanded subepithelial lymphoid follicles were multifocally present
91	(Supplemental Fig. S2). Polyps were covered by stratified squamous epithelium
92	with mild to moderate irregular hyperplasia (Supplemental Figs. S2-S4).
93	Multifocally, the stroma elevated the surface forming small nodular projections
94	and, in one case, causing a verrucous appearance (Supplemental Fig. S4).
95	Acute necrotic changes including fibrinoid necrosis of blood vessel walls and
96	intravascular fibrin thrombi were rarely seen (case 1; Supplemental Fig. S5),
97	without associated clinical signs.
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107 variable-sized follicular structures with reactive germinal centers surrounding a

108 fibrovascular core (Figs. 5, 6). The presence of reticular epithelium

- transmigrated by large numbers of lymphocytes was more abundant in
- 110 lymphoid polyps than in other histological subtypes (Fig. 5 inset).

Finally, one of 14 cases (7%) was categorized as myxomatous (case 14). The
stroma was occupied by severe hypocellular myxomatous edema containing
few interspersed spindle cells without atypia on loose fibrovascular stroma
(Figs. 7, 8). At the base of the polyp, the vascular density was increased (Fig.
9). The surface epithelium showed moderate hyperplasia, intracellular and
intercellular edema, and occasional intraepithelial vesicles (Fig. 7 inset).

All polyps showed a mild to moderate inflammation with multifocal infiltrates of lymphocytes and plasma cells, with occasional presence of neutrophils (Fig. 8 and Supplemental Figs. S1, S6).

Ten cases of canine tonsillar polyps were previously reported ^{3,11,13} and 14 are 120 described herein. Although tonsillar polyps mainly affect adult dogs, they can 121 affect dogs as young as 3 years (case 9).^{3,11,13} Human lymphangiomatous 122 polyps are more frequent in young adults, while lymphoid polyps commonly 123 affect children.^{2,7,8,12} No sex predisposition has been reported for canine or 124 125 human tonsillar polyps, except for the lymphoid subtype which is more common in males.^{2,7,8,11,12} In dogs, females were more affected than males but the 126 overall numbers were too few to determine a sex predilection. All tonsillar 127 polyps reported in dogs were unilateral without side predilection.^{3,11,13} In 128 humans, most polyps are unilateral but bilateral involvement has been rarely 129 observed.^{6-8,12} Canine tonsillar polyps are mostly asymptomatic. Only 8/22 130 (36%) dogs, including the 12 with clinical information in this series, showed 131 clinical signs of lethargy, chronic dyspnea, coughing, gagging, retching or 132 episodes of oral bleeding.^{3,11,13} Human tonsillar polyps might be asymptomatic 133 or associated with dysphagia, dyspnea, foreign body sensation, sore throat, 134 tonsillitis and cough, depending on the size of the lesion.^{7,8,12} 135

136	Canine and human tonsillar polyps can present as pedunculated or sessile
137	masses with smooth or papillary surface. ^{3,7,8,11-13} Canine tonsillar polyps in this
138	series were mostly pedunculated with smooth surface. This contrast with
139	observations from the previously reported case series in which only 3/8 polyps
140	were pedunculated. ¹¹
141	As in humans, the stroma of canine tonsillar polyps was composed by variable
142	proportions of lymphatic and blood vessels, fibrous tissue, lymphoid tissue, and
143	occasionally fat tissue, leading to different histomorphology that allow their
144	classification into different histological subtypes. ^{2,7,8,12}
145	Lymphangiomatous polyps were the most common histological subtype in this
146	case series. They show identical features to those previously reported in an
147	adult dog and in humans. ^{7,13} These type of polyps have also been referred as
148	tonsillar lymphangiomas by human pathologists. ¹² However, tonsillar
149	lymphangiomatous polyps have smaller lymphatic spaces and more fibrous and
150	lymphoid stromal elements than lymphangiomas found elsewhere. ¹² Canine
151	lymphangiomas usually affect the skin of young dogs, and involvement of
152	internal tissues is rare and mostly associated to a lymphangiomatosis syndrome
153	with systemic involvement. ¹⁶

The histomorphology of angiofibromatous polyps in our series is similar to those described by Lucke et al¹¹ as canine tonsillar inflammatory polyps, and to the stroma of canine and feline nasopharyngeal and middle ear polyps.^{9,15} In contrast to tonsillar polyps, nasopharyngeal and middle ear polyps are usually partially covered by pseudostratified ciliated columnar epithelium and the stromal core and peduncle are less vascularized.^{9,15} The main differential diagnosis considered for angiofibromatous and angiofibrolipomatous polyps

was angiofibroma. Due to the lack of infiltrative growth, the stromal fat 161 162 infiltration, and the lower cellularity in these polyps when compared to canine 163 nasal angiofibromas, this diagnosis was excluded.⁴ 164 One polyp was classified as myxomatous. To the best of our knowledge, such histological appearance has not been described in human or canine tonsillar 165 166 polyps. The highly edematous appearance of this polyp might be secondary to inflammation, as suggested for similar stromal changes in nasopharyngeal and 167 laryngeal canine and feline polyps.^{9,18,19} 168 169 The pathogenesis of benign tonsillar polyps is unclear. While an inflammatory origin has been suggested for canine lesions, the most accepted theory in 170 human pathology considers these polyps as hamartomas.^{2,7,8,11,12,20} This is 171 further supported by the evidence of a disorganized distribution of fibronectin 172 173 and collagens I and III within the stroma of tonsillar polyps regardless of their 174 histomorphology.¹ Therefore, tonsillar hamartomas could present a variable 175 histologic spectrum including polyps with fibrous/fibrovascular, lymphangiomatous, lymphoid and/or, more rarely, lipomatous 176 appearances.^{2,7,8,12} A second theory involves chronic inflammatory hyperplasia 177 with irreversible lymphatic obstruction and lymphangiectasia, eventually causing 178 mucosal prolapse and formation of a polyp.^{8,12} Evidence against this 179 explanation is that chronic tonsillitis occurs more commonly than polyps, and 180 many patients with polyps lack a history of tonsillitis.^{7,8,12} A clinical history of 181 previous episodes of tonsillitis was not indicated in any of our cases or those 182 previously reported.^{3,11,13} Partial polyp torsion with subsequent 183 lymphangiectasia and acute inflammatory and necrotic changes is possible in 184 lesions with a long peduncle, as observed in our series (case 1). 185

186	As in humans, the pathogenesis of canine tonsillar polyps may involve a
187	multistep process with an initial hamartomatous growth followed by secondary
188	inflammatory and degenerative changes. ^{1,12} Secondary chronic inflammation in
189	human tonsillar polyps causes stromal remodeling and lymphoid hyperplasia,
190	occasionally producing lymphoid polyps. ^{1,2,12} These are characterized by a
191	stroma composed predominantly of lymphoid tissue (>80%) organized in
192	follicles around a fibrovascular core, similar to that observed in cases 12 and
193	13. ^{1,2} To the best of our knowledge, tonsillar lymphoid polyps have not been
194	previously described in veterinary medicine.
195	Fat tissue was present in 4 of the lesions and, when occupying >25% of the
196	stroma, the term lipomatous was added to the morphological diagnosis.
197	Adipose tissue infiltration within some polyps probably reflects chronic
198	degenerative and metaplastic stromal changes.7,10,14
199	In conclusion, canine tonsillar polyps are benign unilateral and usually
200	asymptomatic lesions of adult dogs, with excellent response to surgical
201	resection. They are composed of lymphatics, blood vessels, fibrous, lymphoid
202	and fat tissue in variable proportions, producing different histomorphology. As in
203	humans, a hamartomatous origin with superimposed inflammatory changes
204	may be considered. We propose replacing the term inflammatory tonsillar polyp
205	with morphological diagnoses based on the stromal characteristics.

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Declaration of Conflicting Interests 211

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266

Figure legends

267	Figures 1-4. Polyps, tonsil, dog. Figures 1-2. Lymphangiomatous polyp, case
268	No. 1. Figure 1. Pedunculated polyp with numerous dilated vascular cavities in
269	the stroma. Large aggregates of lymphocytes are within the subepithelial space.
270	Hematoxylin and eosin (HE). Figure 2. Dilated lymphatic vessels with
271	occasional valves are present amid scant fibrous stroma. HE. Figures 3-4.
272	Angiofibrolipomatous polyp, case No 8. Sessile polyp with abundant fibrous
273	stroma that multifocally contains adipose tissue. Numerous congested blood
274	vessels are concentrated in the stromal core. HE.
275	
276	Figures 5-9. Polyps, tonsil, dog. Figures 5-6. Lymphoid polyp, case No. 13.
277	Figure 5. Sessile polyp with stroma composed of large hyperplastic lymphoid
278	follicles surrounding a fibrovascular core. Inset: the polyp is covered by stratified
279	epithelium and tonsillar reticular epithelium transmigrated by lymphocytes. HE.
280	Figure 6. Secondary antigen-polarized lymphoid follicles with expanded
281	germinal centers surrounded by a thin mantle zone. Inset: germinal centers
282	contain tingible-body macrophages. HE. Figures 7-9. Myxomatous polyp, case
283	No. 14. Figure 7. Pedunculated polyp with severely edematous stroma and a
284	fibrovascular pedicle. A transition line between the two areas is seen
285	(arrowheads). Inset: Intraepithelial and subepithelial vesicles containing
286	edema. HE. Figure 8. Edematous stroma contains small numbers of spindle
287	cells and mild multifocal to diffuse mononuclear inflammatory infiltrates. HE.
288	Figure 9. Fibrovascular pedicle with numerous congested blood vessels and
289	empty lymphatic vessels at the base. HE.

2	review of the pathogenesis
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Commented [JLC1]: please state their initials, in parentheses.
Commented [JM2R2]: Initials have been added

Commented [JLC3]: Table 1. Instead of revision (3 uses), I suggest "examination" or "checkup".

Commented [JM4R4]: The term revision has been replaced by examination in the R2 version of Table 1.

86	Seven of 14 polyps (57%) were diagnosed as lymphangiomatous. Lesions
87	showed a highly vascularized stroma with abundant dilated endothelial-lined
88	cavities and interconnected vascular channels, compatibles with lymphatic
89	vessels (Figs. 1, 2). Lymphatics were empty or filled by eosinophilic fluid, and
90	were separated by hypocellular, dense fibrovascular tissue occupying <50% of
91	the stroma (Fig. 2). In 2/14 lesions, 25-50% of the stroma was infiltrated by
92	adipose tissue and were subclassified as lymphangiolipomatous (Supplemental
93	Fig. S1). Expanded subepithelial lymphoid follicles were multifocally present
94	(Supplemental Fig. S2). Polyps were covered by stratified squamous epithelium
95	with mild to moderate irregular hyperplasia (Supplemental Figs. S2-S4).
96	Multifocally, the stroma elevated the surface forming small nodular projections
97	and, in one case, causing a verrucous appearance (Supplemental Fig. S4).
98	Acute necrotic changes including fibrinoid necrosis of blood vessel walls and
99	intravascular fibrin thrombi were rarely seen (case 1 <u>;</u>) (Supplemental Fig. S5),
99 100	intravascular fibrin thrombi were rarely seen (case 1;) (Supplemental Fig. S5), without associated clinical signs.
100	without associated clinical signs.
100 101	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous,
100 101 102	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 <u>of the 4/4 polyps</u> ,
100 101 102 103	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 of the 4/4 polyps, lymphatics predominated and were categorized as lymphangiofibromatous
100 101 102 103 104	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 of the 4/4 polyps, lymphatics predominated and were categorized as lymphangiofibromatous (Supplemental Fig. S6). The <u>remaining-other 2 of these /</u> 4 polyps showed a
100 101 102 103 104 105	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 of the 4/4 polyps, lymphatics predominated and were categorized as lymphangiofibromatous (Supplemental Fig. S6). The remaining other 2 of these /4 polyps showed a predominance of blood vessels and were classified as angiofibromatous (1/4) or
100 101 102 103 104 105 106	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 of the 4/4 polyps, lymphatics predominated and were categorized as lymphangiofibromatous (Supplemental Fig. S6). The remaining other 2 of these /4 polyps showed a predominance of blood vessels and were classified as angiofibromatous (1/4) or angiofibrolipomatous (1/4), if based on adipose tissue occupying more than
100 101 102 103 104 105 106 107	without associated clinical signs. Four of 14 cases (29%) showed a predominantly fibrous stroma with numerous, slightly-dilated and non-anastomosing vessels. In 2 of the 4/4 polyps, lymphatics predominated and were categorized as lymphangiofibromatous (Supplemental Fig. S6). The remaining other 2 of these /4 polyps showed a predominance of blood vessels and were classified as angiofibromatous (1/4) or angiofibrolipomatous (1/4), if based on adipose tissue occupying more than >25% of the stroma was infiltrated by adipose tissue (Figs. 3, 4).

111 fibrovascular core (Figs. 5, 6). The presence of reticular epithelium

- 112 transmigrated by large numbers of lymphocytes was more abundant in
- 113 lymphoid polyps than in other histological subtypes (Fig. 5 inset).
- 114 Finally, one of 14 cases (7%) was categorized as myxomatous (case 14). The
- stroma was occupied by severe hypocellular myxomatous edema containing
- 116 few interspersed spindle cells without atypia on loose fibrovascular stroma
- 117 (Figs. 7, 8). At the base of the polyp, the vascular density was increased (Fig.
- 118 9). The surface epithelium showed moderate hyperplasia, intracellular and
- intercellular edema, and occasional intraepithelial vesicles (Fig. 7 inset).
- All polyps showed a mild to moderate inflammation with multifocal infiltrates of
- 121 lymphocytes and plasma cells, with occasional presence of neutrophils (Fig. 8
- and Supplemental Figs. S1, S6).
- 123 Considering the 10Ten cases of canine tonsillar polyps were previously
- 124 reported <u>3,11,13</u> and the 14 are described herein, there have been 24 canine
- 125 tonsillar polyps informed.^{3,11,13} Although tonsillar polyps mainly affect adult
- dogs, they can affect patients dogs as young as 3_-years_-old (case 9).^{3,11,13}
- 127 Human lymphangiomatous polyps are more frequent in young adults, while
- 128 lymphoid polyps commonly affect children.^{2,7,8,12} No sex predisposition has been
- reported for canine or human tonsillar polyps, except for the lymphoid subtype
- 130 which is more common in males.^{2,7,8,11,12} This report includes too few cases to
- 131 determine if there was a sex predilection in dogs, but females were more
- affected than males but the overall numbers were too few to determine a sex
- 133 predilection. All tonsillar polyps reported in dogs are-were unilateral without side
- 134 predilection.^{3,11,13} In humans, most polyps are unilateral but bilateral
- involvement has been rarely observed.^{6-8,12} Canine tonsillar polyps are mostly

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asymptomatic. Only 8/22 (36.36%) patientsdogs, including the 12 with clinical
information in this series, have-showedn clinical signs of lethargy, chronic
dyspnea, coughing, gagging, retching and or episodes of oral bleeding.^{3,11,13}
Human tonsillar polyps might be asymptomatic or associated with dysphagia,
dyspnea, foreign body sensation, sore throat, tonsillitis and cough, depending
on the size of the lesion.^{7,8,12}

Canine and human tonsillar polyps can present as pedunculated or sessile masses with smooth or papillary surface.^{3,7,8,11-13} Canine tonsillar polyps in this series were mostly pedunculated with smooth surface. This contrast with observations from the previously reported case series in which only 3/8 polyps were pedunculated.¹¹

As in humans, the stroma of canine tonsillar polyps is was composed by 147 variable proportions of lymphatic and blood vessels, fibrous tissue, lymphoid 148 149 tissue, and occasionally fat tissue, leading to different histomorphology that justify-allow their classification into different histological subtypes.^{2,7,8,12} 150 151 Lymphangiomatous polyps were the most common histological subtype in this case series. They show identical features to those previously reported in an 152 153 adult dog and in peoplehumans.^{7,13} These type of polyps have also been 154 referred as tonsillar lymphangiomas by human pathologists.¹² However, tonsillar lymphangiomatous polyps show have not as largesmaller lymphatic spaces and 155 more fibrous and lymphoid stromal elements than lymphangiomas found 156 157 elsewhere.¹² Canine lymphangiomas usually affect the skin of young dogs, and involvement of internal tissues is very-rare and mostly associated to a 158

159 lymphangiomatosis syndrome with systemic involvement.¹⁶

160 The histomorphology of angiofibromatous polyps in our series is similar to those described by Lucke et al¹¹ as canine tonsillar inflammatory polyps, and to the 161 stroma of canine and feline nasopharyngeal and middle ear polyps.^{9,15} In 162 contrast to tonsillar polyps, nasopharyngeal and middle ear polyps these are 163 usually partially covered by pseudostratified ciliated columnar epithelium and 164 the stromal core and peduncle are less vascularized.9,15 The main differential 165 diagnosis considered for angiofibromatous and angiofibrolipomatous polyps 166 was angiofibroma. Due to the lack of infiltrative growth, the stromal fat 167 infiltration, and the lower cellularity in these polyps when compared to canine 168 169 nasal angiofibromas, this diagnosis was excluded.⁴ 170 One polyp was classified as myxomatous. To the best of our knowledge, such histological appearance has not been described in human or canine tonsillar 171 polyps. The highly edematous appearance of this polyp might be secondary to 172 inflammation, as suggested for similar stromal changes in nasopharyngeal and 173 laryngeal canine and feline polyps.9,18,19 174 The pathogenesis of benign tonsillar polyps is unclear. While an inflammatory 175 origin has been suggested for canine lesions, the most accepted theory in 176 human pathology defends considers these polyps to be considered as 177 hamartomas.^{2,7,8,11,12,20} This is further supported by the evidence of a 178 179 disorganized pattern of distribution of fibronectin and collagens I and III within 180 the stroma of tonsillar polyps regardless of their histomorphology.¹ Therefore, tonsillar hamartomas could present a variable histologic spectrum including 181 182 polyps with fibrous/fibrovascular, lymphangiomatous, lymphoid and/or, more rarely, lipomatous appearances.^{2,7,8,12} A second theory involves chronic 183 inflammatory hyperplasia with irreversible lymphatic obstruction and 184

185 lymphangiectasia, eventually causing mucosal prolapse and formation of a polyp.^{8,12} Evidence against this explanation is that chronic tonsillitis occurs more 186 commonly than polyps, and many patients with polyps lack a history of 187 tonsillitis.7,8,12 None of our cases or those previously reported presented with A 188 clinical history of previous episodes of tonsillitis was not indicated in any of our 189 cases or those previously reported.^{3,11,13} Partial polyp torsion with subsequent 190 lymphangiectasia and acute inflammatory and necrotic changes is possible in 191 lesions with a long peduncle, as observed in our series (case 1). 192 193 As in humans-beings, the pathogenesis of canine tonsillar polyps may involve a multistep process with an initial hamartomatous growth followed by secondary 194 195 inflammatory and degenerative changes.^{1,12} Secondary chronic inflammation in human tonsillar polyps causes stromal 196 remodeling and lymphoid hyperplasia, occasionally producing lymphoid 197 198 polyps.^{1,2,12} These are characterized by a stroma composed predominantly of lymphoid tissue (>80%) organized in follicles around a fibrovascular core, 199

similar to that observed in cases 12 and 13.^{1,2} To the best of our knowledge,

tonsillar lymphoid polyps have not been previously described in veterinarymedicine.

²⁰³ Fat tissue was present in 4 of the lesions and, when occupying >25% of the

stroma, the term lipomatous was added to the morphological diagnosis.

Adipose tissue infiltration within some polyps probably reflects chronic

206 degenerative and metaplastic stromal changes.^{7,10,14}

207 In conclusion, canine tonsillar polyps are benign unilateral and usually

asymptomatic lesions of adult dogs, with excellent response to surgical

- 209 resection. They are composed by of lymphatics, blood vessels, fibrous,
- 210 lymphoid and fat tissue in variable proportions, producing different
- histomorphology. As in humans, an hamartomatous origin with superimposed
- inflammatory changes should may be considered regarding the pathogenesis.
- 213 We propose replacing the term inflammatory tonsillar polyp to be replaced
- 214 bywith morphological diagnoses based on the stromal characteristics.

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279 Figure legends

280 Figures 1-4. Polyps, tonsil, dog. Figures 1-2. Lymphangiomatous polyp, case 281 No. 1. Figure 1. Pedunculated polyp with a stroma with numerous dilated vascular cavities in the stroma. Large aggregates of lymphocytes are within the 282 subepithelial space. Hematoxylin and eosin (HE). Figure 2. Dilated lymphatic 283 284 vessels with occasional valves on are present amid scantree fibrous stroma. HE. Figures 3-4. Angiofibrolipomatous polyp, case No 8. Sessile polyp with 285 286 abundant fibrous stroma that multifocally infiltrated bycontains adipose tissue. 287 and nNumerous congestedive blood vessels are concentrated at in the stromal core. HE. 288

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Figures 5-9. Polyps, tonsil, dog. Figures 5-6. Lymphoid polyp, case No. 13. 290 Figure 5. Sessile polyp with stroma composed of large hyperplastic lymphoid 291 follicles surrounding a fibrovascular core. Inset: the polyp is covered by stratified 292 epithelium and tonsillar reticular epithelium transmigrated by lymphocytes. HE. 293 Figure 6. Secondary antigen-polarized lymphoid follicles with expanded 294 295 germinal centers surrounded by a thin mantle zone. Inset: germinal centers 296 contain tingible-body macrophages. HE. Figures 7-9. Myxomatous polyp, case No. 14. Figure 7. Pedunculated polyp with severely edematous stroma and a 297 fibrovascular pedicle. A transition line between both the two areas is seen 298 (arrowheads). Inset: Intraepithelial and subepithelial vesicles containing 299 edema. HE. Figure 8. Edematous stroma contains small numbers of spindle 300 cells and mild multifocal to diffuse mononuclear inflammatory infiltrates. HE. 301 302 Inset: Intraepithelial and subepithelial vesicles containing edema. Figure 9.

303 Fibrovascular pedicle with numerous congested ive blood vessels and empty

304 lymphatic vessels at the base. HE.

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Table
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Clinical
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Case	Breed	Age	Sex	Type of polyp	Clinical signs	Side	Macroscopic appearance ^a	Outcome
-	Poodle	13 y	п	Lymphangiomatous	Incidental finding during intubation (n/s surgery)	ת	2,8 x 1,4-0,45 cm, pedunculated, smooth surface	No recurrence nsd
N	Yorkshire Terrier	7 y	Σ	Lymphangiomatous	Incidental finding during annual examination	-	1 x 0,3 cm, pedunculated, smooth surface	No recurrence nsd
ω	Catalan Sheepdog	11 y	п	Lymphangiolipomatous	Incidental finding n/s reason	ת	1,4 x 0,8-0,6 cm, sessile, smooth surface	No recurrence after 7 mo; death by unrelated causes
4	Scottish Terrier	10 y	п	Lymphangiomatous	Unknown	n/s	1,2 x0,3-0,1, pedunculated, smooth surface	Unknown
ഗ	Mongrel	10 y	Σ	Lymphangiomatous	Incidental finding during annual examination	ת	2,4 x 0,4 cm, pedunculated, smooth surface	No recurrence 3 mo.; missing after that
0	Mongrel	9 y	П	Lymphangiolipomatous	Unknown	F	2,4x 1,1- 0,4 cm, pedunculated, smooth surface	Unknown
7	Fox Terrier	11 y	Σ	Lymphangiomatous	Recurrent episodes of oral bleeding	n/s	1,4 x 0,8-0,3 cm, pedunculated, verrucous surface	Unknown
8	Maltese	12 y	п	Angiofibrolipomatous	Incidental finding during intubation (dental cleaning)	ਸ	3 x 1 cm., sessile, smooth surface	No recurrence after 8 mo.; no more follow-up
9	Labrador Retriever	3 y	п	Lymphangiofibromatous	Incidental finding during intubation (n/s surgery)		1,6 x 1, sessile with smooth surface	Unknown
10	Barbone	13 y	п	Angiofibromatous	Cough, retching	F	1 x 0,4-0,2 cm, pedunculated, papillary surface	No recurrence after 2 mo.; no more follow-up
1 1	Miniature Schnauzer	9 y	п	Lymphangiofibromatous	Incidental finding during annual examination	n/s	1,5 x 0,5-0,2 cm, pedunculated, smooth surface	No recurrence
12	Mongrel	7 y	п	Lymphoid	Incidental finding n/s reason	ת	1,5 x 0,6 cm, sessile, smooth surface	No recurrence after 2 y; death by unrelated causes
13	Mongrel	7 y	П	Lymphoid	Progressive dyspnea 3 mo.	n/s	1,3 x 0,5 sessile, smooth surface	Unknown
14	Mongrel	8 y	Σ	Myxomatous	Retching	ת	2,1 x 0,9-0,5 cm, pedunculated, smooth surface	No recurrence nsd

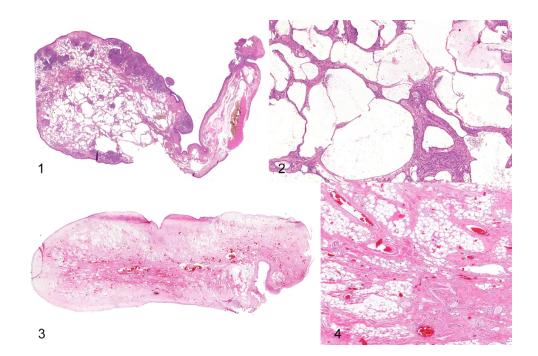
^a Measures are expressed as total length of the polyp x diameter of the polyp – diameter of the pedicle. Abbreviations: M, male; F, female; R, right; L, left; n/s, not specified; n/a, not applicable; nsd, not specified duration.

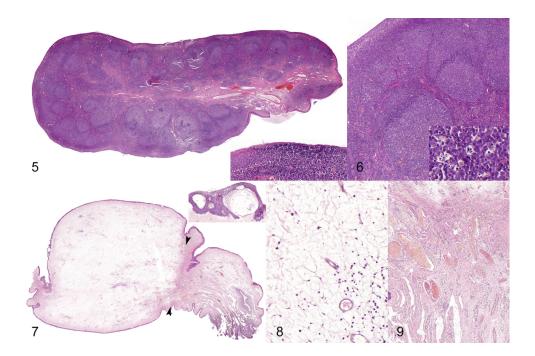
n/s, not specified; n/a, not applicable; nsd, not specified duration. ^a Measures are expressed as total length of the polyp x diameter of the polyp – diameter of the pedicle. Abbreviations: M, male; F, female; R, right; L, left; Case Table 1. Clinical and macroscopic characteristics of canine tonsillar polyps $\stackrel{\frown}{=}$ 4 3 10 3 ശ ω ~ ດ S 4 ω N Breed Mongrel Mongre Schnauzer Terrier Sheepdog Miniature Barbone Retriever Mongrel Scottish Catalan Poodle Mongrel Labrador Maltese Fox Terrier Mongrel Terrier Yorkshire 11 y 11 V Age 8 Y 9 y 13 y 9 y 10 y 10 y 7 7 7 y ω < 12 y 7 y 13 y Sex Type of polyp \leq П П П П П П \leq П \leq П П \leq П Myxomatous Lymphangiomatous Lymphangiomatous Lymphangiomatous Lymphoid Lymphangiolipomatous Lymphangiomatous Lymphangiolipomatous Lymphangiomatous Lymphoid Lymphangiofibromatous Angiofibromatous Lymphangiofibromatous Angiofibrolipomatous Unknown annual annual intubation (n/s surgery) Retching mo. Progressive dyspnea 3 Cough, retching Incidental finding during intubation (dental cleaning) bleeding Incidental finding during Unknown reason annual intubation (n/s surgery) **Clinical signs** reason revisionexamination Incidental finding during Incidental finding during revisionexamination Incidental finding n/s revisionexamination Incidental finding during Incidental finding n/s Recurrent episodes of oral Incidental finding during Side n/s n/s n/s n/s ע ע ע ע ת ע Macroscopic appearance^a smooth surface papillary surface 3 x 1 cm., sessile, smooth smooth surface smooth surface smooth surface smooth surface 2,1 x 0,9-0,5 cm, pedunculated, surface surface surface verrucous surface smooth surface 2,4x 1,1- 0,4 cm, pedunculated, 2,4 x 0,4 cm, pedunculated smooth surface 1 x 0,3 cm, pedunculated, pedunculated, smooth surface 2,8 x 1,4-0,45 cm surface 1,3 x 0,5 sessile, smooth 1,5 x 0,6 cm, sessile, smooth 1,5 x 0,5-0,2 cm, pedunculated, 1 x 0,4-0,2 cm, pedunculated, 1,4 x 0,8-0,3 cm, pedunculated 1,2 x0,3-0,1, pedunculated 1,4 x 0,8-0,6 cm, sessile, 1,6 x 1, sessile with smooth No recurrence nsd No recurrence Unknown Outcome Unknowr No recurrence after 2 y; no more follow-up No recurrence after 2 mo.; Unknown no more follow-up No recurrence after 8 mo.; Unknown Unknown death by unrelated causes missing after that No recurrence 3 mo.; No recurrence after 7 mo; No recurrence nsd No recurrence nsd

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death by unrelated causes

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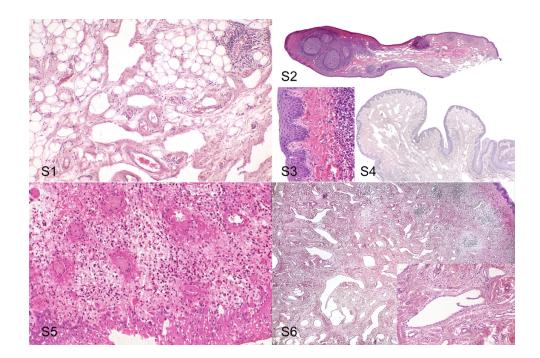




) } }	Vessel		Vascular	Fibrous	ר } ₽	Lymphoid	7 2 2 2 2		Inflammation	on	7
Case	density	vessei type	spaces	tissue	Гd	tissue	Euema -		Distribution		
								00.00		0010	
-	ω	lymphatic >> blood	4	_	0	<u> </u>		N	MF	ĻP, N	Lymphangiomatous
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ω	ω	lymphatic >> blood	ω		N		Ν	1,5	MF	L, P > N	Lymphangiolipomatous
4	ω	lymphatic >> blood	ω	N	0		_	1, 5	MF	Ľ Þ	Lymphangiomatous
Сī	ω	lymphatic >> blood	4	C	0	-		1,5	MF	Ļ P	Lymphangiomatous
6	ω	lymphatic >> blood	ω	_	N	0	<u> </u>	1,5	MF	Ļ	Lymphangiolipomatous
7	ω	lymphatic >> blood	ω	N	0	<u> </u>	<u>د</u>	1,5	MF	Ļ P	Lymphangiomatous
8	N	blood > lymphatic	–	ω	N	0	_	1,5	MF	Ļ P	Angiofibrolipomatous
9	ယ	lymphatic > blood	N	ω	0	0		Ν	MF to D	Ļ P	Lymphangiofibromatous
10	N	blood > lymphatic	–	ω	<u> </u>	-	0	_	MF	Ļ P	Angiofibromatous
11	N	Lymphatic > blood	N	ω	0	-	0	N	MF	Ļ P	Lymphangiofibromatous
12	N	lymphatics & blood	-	-	0	4	0	Ν		Ļ P	Lymphoid
13	-	lymphatics & blood	-	-	0	4	Ν	-		Ļ P	Lymphoid
14	N	blood > lymphatic	N	ω	0	0	ω	-	MF to D	L, P > N, H	L, P > N, H Myxomatous

Supplemental Table 1. Histologic characteristics of canine tonsillar polyps

Abbreviations: D, diffuse; H, histiocytes; L, lymphocytes; MF, multifocal; N, neutrophils; P, plasma cells. Vascularization, edema, and degree of inflammation were graded on a 0–3 scale (0, absent; 1, mild; 2, moderate; 3, marked). Vascular spaces, lymphoid, fibrous and fat tissue were graded on a 0–4 scale based on percent (0, absent; 1, 1–25%; 2, 26–50%; 3, 51-75%; 4 >75% stroma).



1	Supplemental Figures S1-6. Polyps, tonsil, dog. Figure S1.
2	Lymphangiolipomatous polyp, case No. 6. The stroma is severely infiltrated by
3	adipose tissue with empty dilated lymphatic vessels, few blood vessels and
4	multifocal small lymphoplasmacytic aggregates. HE. Figures S2, S3.
5	Lymphangiomatous polyp, case No. 2. Figure S2. Pedunculate polyp with
6	fibrovascular pedicle and subepithelial lymphoid hyperplasia. Secondary
7	hyperplastic follicles show expanded germinal centers surrounded by a thin
8	mantle zone and antigen-related polarity. HE. Figure S3. Polyp covered by
9	irregular hyperplastic stratified epithelium separated from the stromal core by a
10	band of fibrous tissue. HE. Figure S4. Lymphangiomatous polyp, case 7. The
11	surface is multifocally elevated producing a verrucous appearance. HE. Figure
12	S5. Lymphangiomatous polyp, case 1. Acute necrosis at the base of the polyp
13	with fibrinoid necrosis of blood vessel walls. HE. Figure S6.
14	Lymphangiofibromatous polyp, case No. 9. The stroma shows abundant fibrous
15	tissue with numerous lymphatic vessels. There are multifocal aggregates of
16	inflammatory cells. Inset: detail of lymphatic vessels with valves, lined by
17	flattened endothelium. HE