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STANDARD ARTICLE

Upper digestive tract abnormalities in dogs with chronic idiopathic lymphoplasmacytic rhinitis

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Abstract

Background: Chronic idiopathic lymphoplasmacytic rhinitis (CILPR) is a common inflammatory disorder of unknown etiology affecting the nasal cavity of dogs. The diagnosis is made by exclusion of other causes of nasal disease and specific therapeutic protocols are lacking. In human medicine, a relationship between CILPR and gastrointestinal clinical signs has been postulated, and remission of respiratory signs after clinical trials with medications for gastrointestinal disorders has been observed.

Objectives: To describe history, clinical presentation, endoscopic and histopathologic concurrent respiratory and digestive tract abnormalities, and to evaluate improvement of respiratory signs after treatment for gastrointestinal signs.

Animals: Twenty-five dogs with CILPR.

Methods: Prospective study. For inclusion, following information had to be available: respiratory and digestive clinical signs, airway and digestive tract endoscopic abnormalities, histologic evaluation of respiratory and gastrointestinal tract biopsy specimens, and clinical response to different treatment strategies.

Results: Twenty-two dogs had endoscopic gastrointestinal lesions, whereas 13 dogs had concurrent gastrointestinal signs. Most esophageal and duodenal endoscopic abnormalities were classified as moderate or severe. Respiratory and gastrointestinal tract histologic evaluation identified mostly chronic inflammation. Remission or marked improvement of respiratory signs was observed in the majority of dogs treated only for gastrointestinal signs up to 12 months after endoscopy. No significant associations between treatments and follow-up information were found.

Conclusion and Clinical Importance: Nasal and upper digestive tract abnormalities coexist in some dogs with CILPR. Lack of standardized therapeutic protocols suggests caution when interpreting improvement in nasal clinical signs. Additional studies are needed to explore the possibility of a cause-effect relationship between the 2 processes.

KEYWORDS

clinical signs, endoscopy, follow-up, treatment, vomiting

Abbreviations: BCS, body condition score; CILPR, chronic idiopathic lymphoplasmacytic rhinitis; GERD, gastroesophageal reflux disease.

1 | INTRODUCTION

Chronic idiopathic lymphoplasmacytic rhinitis (CILPR) is a common inflammatory disorder of the nasal cavity in dogs.[1-4] It is characterized by nonpathognomonic clinical signs, including unilateral or bilateral nasal discharge, epistaxis, reverse sneezing, stridor, and inspiratory dyspnea.[1,2,4,5] Diagnosis usually is based on histopathologic identification of infiltrating plasma cells and lymphocytes in the nasal mucosa and exclusion of other underlying diseases.[2,6] The etiology of CILPR remains unknown. Several hypotheses have been proposed, such as innate immunity and hypersensitivity, odontogenic causes, and bacterial or fungal infection.[1-3,7] Moreover, CILPR is not only a diagnostic but also a therapeutic challenge for clinicians. No specific protocols are available for treating the disease, and only a single clinical trial has been reported.[8] In human medicine, CILPR remains a major problem of public health worldwide.[9] Many studies have postulated a relationship between CILPR and gastrointestinal clinical signs such as those related to gastroesophageal reflux disease (GERD).[10-12] However, it is difficult to establish a direct relationship between CILPR and GERD, because both entities are highly prevalent, which makes it likely for them to coexist independently.[13] Gastroesophageal reflux disease can affect the nasal cavity directly by introduction of acid, pepsin, and gastric contents into the nasal cavity, or indirectly by stimulating the autonomic nervous system.[14,15] As frequently reported, the respiratory clinical signs can be the only clinical manifestation of GERD in humans, confusing the clinician about the correct diagnosis.[16-20] However in these cases, remission of respiratory clinical signs after a clinical trial with PO proton-pump inhibitors, prokinetics, diet, or some combination of these may confirm the diagnosis.[16,18-21] It is thought that GERD also occurs in dogs because the clinical findings and response to treatment are similar to those reported in humans.[22-28] It has been observed in brachycephalic and nonbrachycephalic dogs, and may be more common than previously suspected.[29,30] Although the approach to diagnosis of GERD has improved recently,[31] specific diagnostic criteria are still lacking and a tentative diagnosis is made if clinical signs and endoscopic findings suggestive of esophageal involvement are present, other esophageal and extra-esophageal diseases have been ruled out, and response to treatment is adequate.[22,23] Most dogs with clinical signs related to GERD, however, do not have identifiable endoscopic mucosal lesions or other evidence of gastroesophageal reflux.[32]

To our knowledge, no information exists about a possible association between CILPR and gastrointestinal clinical signs in dogs. Thus, our prospective study was designed to: (1) describe the history, clinical presentation, concurrent endoscopic and histopathologic respiratory, and digestive abnormalities in a population of dogs with CILPR, and (2) evaluate improvement of respiratory signs in dogs that received treatment for gastrointestinal signs.

2 | MATERIALS AND METHODS

Client-owned dogs with chronic upper respiratory clinical signs lasting for at least 3 weeks and a presumptive diagnosis of CILPR that presented to different referral clinics of northwest Italy over a 2-year period (2015-2017) were considered for enrollment. At admission, each dog's case history was obtained from the owner, as well as information about previous diagnostic evaluation, and response to specific treatments. A clinical examination was performed, body weight was recorded, and 9-point body condition score (BCS) was assigned. In addition, a case-based diagnostic evaluation, including survey skull radiographs, thoracic radiographs, and bronchoalveolar lavage, was carried out to complete the previous diagnostic evaluation and rule out specific upper and lower respiratory diseases as potential causes of the upper respiratory clinical signs.[2,4] Upon owner consent to diagnostic and therapeutic procedures, dogs underwent endoscopic evaluation of the airways (nares, rhinopharynx, trachea, and bronchi) and upper digestive tract (oropharynx, esophagus, stomach, and duodenum). All endoscopic procedures were performed in standardized fashion by one of the authors (E. B.).[33-35] Rigid (2.7 mm × 18 cm, 30°; mod. 64029, Karl Storz Endoscopia Italia S.r.l., Verona, Italy) and flexible video endoscopes (6.0 mm × 103 cm; EG-1840, Pentax Italia S.r.l., Milano, Italy; 7.8 mm × 140 cm, mod. PV-SG 28-140, Karl Storz Endoscopia Italia S.r.l.; 5.0 mm × 55 cm fiberscope; Olympus BF-P40, Olympus Medical Systems Europe GmbH, Hamburg, Germany) were used. Images and video clips were acquired using video recording devices (Pinnacle Studio 21.5; Corel Corporation, Ottawa, Canada; Tele Pack Vet X Led, Karl Storz Endoscopia Italia S.r.l.). Mucosal biopsy specimens from the nasal cavity, stomach, and duodenum were submitted for histologic evaluation by a single pathologist. A presumptive diagnosis of CILPR was made based on histopathologic identification of infiltrating plasma cells and lymphocytes in the nasal mucosa and exclusion of other underlying diseases, as described elsewhere.[2,4] The severity of nasal endoscopic abnormalities was subjectively classified as normal (no evidence of abnormalities), mild (mild focal or diffuse hyperemia or edema, mild accumulation of mucoid secretions, mild mucosal hyperplasia), or moderate to severe (marked diffuse hyperemia or edema, abundant accumulation of mucoid or mucopurulent secretions, marked mucosal or polypoid hyperplasia, mucosal erosions, presence of necrotic turbinates). The severity of gastrointestinal endoscopic abnormalities was subjectively classified as normal (no evidence of abnormalities), mild, or moderate to severe. The following mucosal variables were evaluated: dyschromia, hyperemia, edema, follicular changes, hypertrophy or granularity, and erosion or ulcers. Video documentation for each dog was independently reviewed by 2 authors (E. B., P. G.) in a blinded, separate fashion to subjectively classify the severity of the endoscopic lesions. A discussion to reach consensus was done only in cases of divergent opinion.

Histologic examination of nasal mucosal biopsy specimens was assessed based on a previously proposed histologic nasal inflammation scoring system.[36] The lesions were graded as absent, mild, moderate, or severe. Histologic examination of gastroduodenal mucosal biopsy specimens was performed according to a quantitative simplified scoring system.[37] The lesions were graded as absent, mild, moderate, or severe.

Based on the severity of clinical signs, endoscopic abnormalities, and histopathologic results in each dog, selected medications were allowed. For respiratory clinical signs only, systemic (prednisolone) or

topical (fluticasone, betamethasone) glucocorticoids, antibiotics (enrofloxacin, amoxicillin-clavulanic acid), or mucolytics (acetylcysteine, ambroxole) could have been prescribed to dogs, whereas for digestive clinical signs only H2 antagonists (ranitidine), protonpump inhibitors (omeprazole, pantoprazole, esomeprazole) or hydrolyzed protein diets could have been prescribed. In cases of digestive clinical signs or endoscopic abnormalities, gastrointestinal medications as the only therapeutic strategy were recommended.

Efficacy of the treatments was assessed by re-examination of the dogs by the attending clinician at 15 days, and 2, 3, 6, and 12 months after endoscopy. Information on remission, marked improvement, persistence, worsening, or relapse of respiratory clinical signs during or after cessation of treatment was recorded. Marked improvement was defined as sporadic respiratory signs less than once monthly. Worsening was defined as the presence of new respiratory signs, any increase in severity or frequency of previous respiratory signs or both.

2.1 | Statistical analysis

Statistical analyses were performed using the free software environment for statistical computing (R, version 3.6.1, available at: https://www.r-project.org; RStudio, version 1.2.1335; available at: https://rstudio.com). Continuous variables were expressed as median (minimum and maximum) or percentage. The following variables were dichotomized: sex (male versus female), breed (breed versus mixed breed), respiratory clinical signs (sneezing versus not sneezing), gastrointestinal clinical signs (vomiting versus not vomiting), treatment strategies (treatments only for gastrointestinal signs versus treatments for respiratory signs or combination of treatments for both respiratory and gastrointestinal signs), and follow-up information. Fisher's exact test was used to detect associations between sex or breed and respiratory or gastrointestinal signs and severity of endoscopic or histologic abnormalities. The Wilcoxon-Mann-Whitney test was used to detect associations between age or weight and respiratory or gastrointestinal signs. The Chi-squared test was used to detect associations between BCS and respiratory or gastrointestinal signs and severity of endoscopic or histologic abnormalities. The Kruskal-Wallis test was used to detect associations between age or weight and severity of endoscopic or histologic abnormalities. Associations between severity of nasal and gastrointestinal endoscopic abnormalities, severity of nasal and gastrointestinal histologic abnormalities, severity of nasal endoscopic and histologic abnormalities, and severity of gastrointestinal endoscopic and histologic abnormalities, treatment strategies, and follow-up information were evaluated using Fisher's exact test. Values of $P < .05$ were considered significant.

3 | RESULTS

Twenty-five dogs with CILPR were included in the study, subdivided as follow: 10 mixed breed dogs (40%), 4 Jack Russell terriers (16%), 3 Labrador retrievers (12%), 2 Golden retrievers (8%), 2 Dachshunds (8%), 1 Pinscher (4%), 1 Akita Inu (4%), 1 Poodle (4%), and 1 English Setter (4%). Thirteen (52%) dogs were male (2 neutered) and 12 (48%) were female (9 spayed). The median age was 7.2 years (range, 1-12). The median body weight was 16 kg (range, 2.5-42). The median BCS was 5.6 (range, 4-8). Table 1 shows all presenting respiratory clinical signs. Sneezing (20 dogs, 80%) was most common, followed by nasal discharge (16 dogs, 64%), which was serous (6 dogs, 37.5%), mucoid (6 dogs, 37.5%), or purulent (4 dogs, 25%). Thirteen dogs (52%) had gastrointestinal clinical signs in addition to respiratory clinical signs (Table 1). Gastrointestinal clinical signs were intermittent (up to once weekly) or sporadic (less than once monthly) in 12 dogs (48%), and in the remaining dog (4%) occurred on a daily basis.

A significant association between age and respiratory clinical signs was found (median age 9 years, $P < .04$). Distribution of clinical signs among sex, breed, and BCS is shown in Table 2.

No abnormalities were found on abdominal ultrasonography performed in dogs with vomiting and anorexia before referral. Previous symptomatic treatments for respiratory clinical signs had failed in 22 (84%) dogs. The remaining 4 (16%) dogs had not received any treatment. Seven of these 21 dogs (33.3%) were treated using a single antibiotic (amoxicillin-clavulanic acid 12.5 mg/kg PO q12h, doxycycline 5 mg/kg PO q12h or marbofloxacin 2 mg/kg PO q24h for 1-2 weeks), 6 dogs (28.6%) with a combination of antibiotic and systemic glucocorticoids (prednisone or prednisolone at an initial dosage of 1 mg/kg PO q24h for 7-10 days, then tapered to 0.5 mg/kg PO q48h for 2-3 weeks), 5 dogs (23.8%) with nonsteroidal anti-inflammatory drugs (meloxicam 0.1 mg/kg or carprofen 1 mg/kg PO q24h for 2-3 weeks), 2 dogs (9.5%) with mucolytics (acetylcysteine 50 mg of a 2% solution nebulized over 30 minutes q12h for 1 week),

TABLE 1 Presenting respiratory and gastrointestinal clinical signs in 25 dogs with chronic idiopathic rhinitis

Presenting clinical signs	Number of dogs (%)
Sneezing	7 (28%)
Sneezing, nasal discharge	10 (40%)
Sneezing, nasal discharge, stertor	2 (8%)
Sneezing, nasal discharge, epistaxis	1 (4%)
Nasal discharge, reverse sneezing	1 (4%)
Nasal discharge, stertor	2 (8%)
Reverse sneezing and stertor	1 (4%)
Reverse sneezing	1 (4%)
Sporadic, nonproductive cough	8 (32%)
Vomiting	7 (53.8%)
Vomiting, anorexia, repeated swallowing, and eructation	2 (15.4%)
Vomiting, retching, and borborygmus	1 (7.7%)
Vomiting, hypersalivation, and episodic praying position	1 (7.7%)
Anorexia, repeated swallowing, and eructation	1 (7.7%)
Retching and borborygmus	1 (7.7%)

TABLE 2 Distribution of respiratory and digestive clinical signs and severity of endoscopic and histologic abnormalities among sex, breed, and BCS in 25 dogs with chronic idiopathic rhinitis

	RS Sneezing/not sneezing	DS Vomiting/not vomiting	ENA M/S	EGA N/MD/M/S	EDA N/MD/M/S	HNA M/MD/S	HGA N/MD/M	HDA MD/M/S
Sex	*P* = .32	*P* = 1	*P* = .43	*P* = .16	*P* = .17	*P* = .31	*P* = .18	*P* = 1
F	11/1	5/1	6/6	0/8/3/1	0/3/4/0	3/8/1	2/9/1	6/2/1
ML	9/4	6/1	9/4	4/6/3/0	3/1/3/2	7/5/1	0/9/4	7/4/1
Breed	*P* = .61	*P* = .19	*P* = .44	*P* = .51	*P* = .32	*P* = .71	*P* = .54	*P* = 1
MB	9/1	4/2	5/5	3/5/2/0	2/3/2/0	4/6/0	1/6/3	5/2/1
P	11/4	7/0	10/5	1/9/4/1	1/1/5/2	6/7/2	1/12/2	8/4/1
BCS	*P* = .59	*P* = .19	*P* = .15	*P* = .58	*P* = .35	*P* = .32	*P* = .76	*P* = .85
4	3/0	1/0	1/2	0/2/1/0	0/1/2/0	0/3/0	0/2/1	1/1/1
5	9/3	8/1	9/3	4/4/3/1	3/1/3/2	7/5/0	1/8/3	7/4/1
6	4/1	1/0	4/1	0/5/0/0	0/2/1/0	1/3/1	0/4/1	3/1/0
7	3/0	1/0	1/2	0/2/1/0	—	1/1/1	1/2/0	1/0/0
8	1/1	0/1	0/2	0/1/1/0	—	1/1/0	0/2/0	1/0/0

Abbreviations: BCS, body condition score; DS, digestive signs; EDA, severity of endoscopic duodenal abnormalities; EGA, severity of endoscopic gastric abnormalities; ENA, severity of endoscopic nasal abnormalities; F, female; HDA, severity of histologic duodenal abnormalities; HGA, severity of histologic gastric abnormalities; HNA, severity of histologic nasal abnormalities; M, moderate; MB, mixed breed; MD, mild; ML, male; N, normal; P, purebred; RS, respiratory signs; S, severe.

TABLE 3 Nasopharyngeal and gastrointestinal endoscopic abnormalities in dogs with chronic idiopathic rhinitis

Endoscopic site	Endoscopic findings	n/*t*
Nasal cavity	Bilateral diffuse hyperemia	25/25 (100%)
Nasal cavity	Bilateral diffuse edema	18/25 (72%)
Nasal cavity	Bilateral accumulation of mucoid secretions	12/25 (48%)
Nasal cavity	Bilateral accumulation of mucopurulent secretions	2/25 (8%)
Pharynx	Diffuse hyperemia and edema	2/25 (8%)
Esophagus	Hyperemia and erosions in the caudal thoracic esophagus	1/22 (4.5%)
Stomach	Hyperemia and edema	9/22 (40.9%)
Duodenum	Diffuse hyperemia and edema	1/22 (4.5%)
Stomach (1) + Duodenum (2)	Diffuse hyperemia and edema (1, 2), increased granularity (2), erosion (2)	12/22 (54.5%)

Note: n/*t* = number of dogs (%) with a particular endoscopic finding/total number of dogs with nasal or gastrointestinal endoscopic lesions.

and 1 dog (4.8%) with topical glucocorticoids (fluticasone 2 sprays q24h for 2 weeks). Gastrointestinal clinical signs did not worsen while dogs were receiving glucocorticoids or nonsteroidal anti-inflammatory drugs. Except for deworming, none of the 13 dogs with gastrointestinal clinical signs had received previous symptomatic treatment. Twenty-one dogs (84%) were fed a commercial maintenance diet, and 4 dogs (16%) a home-prepared diets with different protein and carbohydrate sources.

TABLE 4 Nasal and gastrointestinal histopathology findings in 25 dogs with chronic idiopathic rhinitis

Anatomical district	Histopathology findings	n/*t*
Nasal cavity	Bilateral lymphocytic-plasmacytic inflammation	24/25 (96%)
	Neutrophilic superimposition	9/25 (36%)
	Eosinophilic infiltration	2/25 (8%)
	Hyperplasia	25/25 (100%)
	Squamous metaplasia	3/25 (12%)
	Erosive neutrophilic infiltration	1/25 (4%)
Stomach	Lymphocytic-plasmacytic inflammation	21/25 (84%)
	Neutrophilic superimposition	3/25 (12%)
	Eosinophilic infiltration	1/25 (4%)
	Fibrosis	4/25 (16%)
Duodenum	Lymphocytic-plasmacytic inflammation	19/21 (90.5%)
	Neutrophilic superimposition	5/21 (23.8%)
	Eosinophilic infiltration	2/21 (9.5%)
	Villus stunting	11/21 (52.4%)
	Crypt dilatation	7/21 (33.3%)
	Lacteal dilatation	1/21 (4.8%)

Note: n/*t* = number of dogs (%) with the histopathology finding/total number of dogs in which nasal or gastrointestinal histopathology was considered adequate.

Other than slight opacification, pathological changes were not observed in radiographs of the nasal cavities. Thoracic radiographs were normal in all dogs. Nasopharyngeal endoscopic abnormalities are

shown in Table 3 and were classified as moderate to severe in all dogs. Laryngeal function was normal in all dogs. No tracheal or bronchial endoscopic abnormalities were observed. Bronchoalveolar lavage cytology was performed in dogs with cough and was normal.

Overall, 22 dogs (88%) had endoscopic gastrointestinal lesions. Of these, 10 dogs (45.5%) had gastrointestinal clinical signs. The remaining 3 dogs (23.1%) with gastrointestinal clinical signs had no endoscopic digestive abnormalities, whereas 12 dogs (54.5%) without gastrointestinal clinical signs had endoscopic digestive abnormalities. Gastrointestinal endoscopic abnormalities are shown in Table 3. All esophageal abnormalities were classified as moderate to severe; gastric abnormalities were mild in 14 dogs (66.7%) and moderate to severe in 7 dogs (33.3%); intestinal abnormalities were mild in 4 dogs (30.8%) and moderate to severe in 9 dogs (69.2%).

With regard to nasal biopsy specimens, tissue quality was classified as adequate in all cases. The overall severity of lesions was graded as mild, moderate, or severe in 10 (40%), 13 (52%), and 2 (8%) dogs, respectively. With regard to gastrointestinal biopsy specimens, tissue quality was classified as inadequate for duodenal specimens from 4 dogs. The overall severity of gastric lesions was graded as mild or moderate in 18 (72%) and 5 (20%) dogs, respectively. No lesions were found in 2 (8%) dogs. The overall severity of duodenal lesions was graded as mild, moderate, or severe in 13 (61.9%), 6 (28.6%), and 2 (9.5%) dogs, respectively. Nasal and gastrointestinal histopathology results are shown in Table 4. No significant associations were found between signalment and severity of endoscopic or histologic abnormalities or between severity of endoscopic and histologic abnormalities. Distribution of severity of endoscopic and histologic abnormalities according to sex, breed and BCS, and scores is shown in Tables 2 and 5, respectively.

In 23 dogs (92%), different treatments were prescribed after endoscopic examination. For the remaining 2 dogs, this information was not recorded. Three treatment groups were identified. The first group included 5 dogs (21.7%) treated only with medications for respiratory clinical signs. All 5 dogs received glucocorticoids and antibiotics. In addition, 2 dogs received mucolytics. The second group included 7 dogs (30.4%) treated only for gastrointestinal clinical signs. Of these dogs, 4 (17.4%) received protonpump inhibitors or H2 antagonists and 3 (13%) received hydrolyzed protein diets. The third group included 11 dogs (47.8%) treated for both respiratory and gastrointestinal clinical signs. All of these dogs received glucocorticoids, antibiotics, H2 antagonists, and hydrolyzed protein diets. All treatments lasted from a few days to 1 month and were interrupted within 1 month of endoscopy. Follow-up information on respiratory clinical signs is shown in Table 6. Nine dogs (53.8%) showed remission of gastrointestinal signs within 2 months after endoscopy. For the remaining 4 dogs, this information was not recorded. No significant associations between treatment strategies and follow-up information on respiratory clinical signs were found.

TABLE 5 Distribution of severity of endoscopic and histologic abnormalities among scores

	EGA N/MD/M/S	EDA N/MD/M/S	HNA MD/M/S	HGA N/MD/M	HDA MD/M/S
ENA	*P* = .76	*P* = .26	*P* = .95	—	—
M	2/9/3/1	1/3/6/2	6/8/1		
S	2/5/3/0	2/1/1/0	4/5/1		
HNA	—	—	—	*P* = .12	*P* = .47
MD				1/8/1	6/3/0
M				0/9/4	5/3/2
S				1/1/0	2/0/0
EGA	—	—	—	*P* = .63	—
N				0/2/2	
MD				2/10/2	
M				0/5/1	
S				0/1/0	
EDA	—	—	—	—	*P* = .85
N					1/1/1
MD					2/2/0
M					4/2/1
S					1/1/0

Abbreviations: EDA, severity of endoscopic duodenal abnormalities; EGA, severity of endoscopic gastric abnormalities; ENA, severity of endoscopic nasal abnormalities; HDA, severity of histologic duodenal abnormalities; HGA, severity of histologic gastric abnormalities; HNA, severity of histologic nasal abnormalities; M, moderate; MD, mild; N, normal; S, severe.

TABLE 6 Follow-up information on respiratory clinical signs of dogs with chronic idiopathic rhinitis

Treatment groups	15 days n = 22	2 months n = 22	3 months n = 22	6 months n = 21	12 months n = 15
Medications for respiratory clinical signs only	R (-)	R 2	R (2)	R (2)	R (3)
	MI (5)	MI (2)	MI (2)	MI (1)	MI (-)
	P (-)	P (1)	P (-)	P (-)	P (-)
	RP (-)	RP (-)	RP (1)	RP (-)	RP (-)
	W (-)	W (-)	W (-)	W (2)	W (2)
Medications for gastrointestinal clinical signs only	R (3)	R (4)	R (4)	R (3)	R (2)
	MI (3)	MI (3)	MI (3)	MI (2)	MI (2)
	P (1)	P (-)	P (-)	P (-)	P (-)
	RP (-)	RP (-)	RP (-)	RP (1)	RP (2)
	W (-)	W (-)	W (-)	W (-)	W (-)
Medications for respiratory and gastrointestinal clinical signs	R (1)	R (2)	R (2)	R (3)	R (1)
	MI (4)	MI (2)	MI (2)	MI (3)	MI (-)
	P (5)	P (5)	P (4)	P (2)	P (2)
	RP (-)	RP (1)	RP (1)	RP (1)	RP (-)
	W (-)	W (-)	W (1)	W (1)	W (1)

Abbreviations: (n), number of dogs with a specific follow-up information; MI, marked improvement; n, number of dogs in which follow-up information is available; P, persistence; R, remission; RP, relapse; W, worsening.

4 | DISCUSSION

We aimed to explore the concurrent presence of upper respiratory and digestive endoscopic and histopathologic abnormalities in a population of dogs with a presumptive diagnosis of CILPR. In addition, the response to different treatments and eventual improvement in respiratory clinical signs during treatment for gastrointestinal clinical signs is reported.

Consistent with previous observations, middle-aged to old dogs of any sex, breed, or size were affected by idiopathic rhinitis.[2,4] Sneezing associated with different types of chronic discharge was the most commonly recorded respiratory sign. The mucopurulent nature of the nasal discharge found in the majority of dogs reported here likely reflects the chronicity of inflammation. Indeed, bacterial culture of nasal samples often yields minimal to no growth and response to antibiotic treatment is poor,[2,4,38] as observed in our study. Coughing normally is associated with lower respiratory tract disease,[39,40] but it also has been reported in dogs with idiopathic rhinitis.[38] In affected humans, rhinitis is considered a frequent extra-esophageal sign of GERD.[19,41-43] In our study, 8 dogs had a history of sporadic, nonproductive cough. Pneumonia, bronchitis, or tracheal diseases were ruled out, and therefore coughing may have been a result of vomiting or GERD. However, cough secondary to pharyngitis caused by swallowing of irritant nasal secretions remains a possibility.[38] The most consistent findings on rhinoscopy were hyperemia, edema, and accumulation of mucoid material within the nasal passage, as previously reported.[2,4,44] Chronic idiopathic lymphoplasmacytic rhinitis is difficult to differentiate from fungal rhinitis by radiography or endoscopy because both can cause turbinate destruction.[2] However, turbinate destruction tends to be less severe in dogs with CILPR compared with dogs with fungal rhinitis.[45] In addition to turbinate destruction, mass-like lesions mimicking nasal neoplasia can be visualized rhinoscopically.[2,46] Computed tomography is more sensitive and specific than is radiography or endoscopy in differentiating CILPR, nasal neoplasia, and fungal rhinitis.[2] Turbinate destruction or mass-like lesions were not detected in our study, however.

In addition to respiratory clinical signs, half of the dogs reported here had gastrointestinal clinical signs, most of which were compatible with GERD.[30] However, in contrast to humans in whom clinical signs such as "heartburn" and acid eructation are considered indicative of GERD, clinical signs in dogs are less specific. Indeed, previous studies showed that only 20% to 25% of dogs with clinical signs suggesting gastroesophageal reflux had GERD.[31,32] This observation means that a reliable diagnosis of GERD in dogs should be based on pH measurement or histologic evaluation of esophageal samples.[30,47] Most dogs in our study (88%) had gastrointestinal endoscopic lesions. Interestingly, these lesions also were found in dogs with only upper respiratory clinical signs. Intermittent or sporadic gastrointestinal clinical signs unnoticed by the owners or a subclinical gastrointestinal process are possible explanations. Another interesting finding of our study is the coexistence of both nasal and gastrointestinal lymphoplasmacytic inflammation in approximately 80% of dogs with and without digestive clinical signs. Different hypotheses could be formulated. First, because the clinical utility of gastrointestinal histopathology has come under scrutiny because of a lack of correlation between clinical signs and response to treatment, gastrointestinal histopathology may not necessarily reflect clinical disease.[48,49] Second, because this type of inflammatory infiltrate is nonspecific, 2 distinct underlying pathologic processes of both the respiratory and digestive systems could be present.[2,4,37,48,50] Indeed, because dogs did not undergo a complete and

standardized evaluation for their gastrointestinal signs, coexistence of CILPR and chronic enteropathy is a possibility. Third, a primary digestive problem with secondary chronic exposure of the respiratory mucosa to acid reflux could not be ruled out.[16,19,42,51,52] However, if this were the case, a marked response to protonpump inhibitor treatment should have been observed. Moreover, because treatments were not standardized and not all dogs received protonpump inhibitors, firm conclusions about the improvement in observed nasal clinical signs cannot be drawn.

Current literature suggests that partial to almost complete response to glucocorticoids can be observed in some dogs with CILPR.[2,4,6] Instead, anti-inflammatory drugs and antibiotics have shown variable therapeutic effects.[2,4] Other treatment strategies include the combination of a glucocorticoid and a nonsteroidal anti-inflammatory drug;[8] a combination of glucocorticoids, cyclosporine and desensitization,[4] and use of antifungal medications and inhaled steroids.[2,53] In our study, all dogs that received previous symptomatic treatment for respiratory clinical signs failed to show resolution or sustained improvement. Whether the dose or length of prescribed drugs was inappropriate or a mechanism other than immune-mediated inflammation was responsible was not investigated. Interestingly, most of the dogs that received only a gastrointestinal therapeutic approach showed complete remission or sustained improvement of respiratory clinical signs up to 12 months after endoscopy. Moreover, according to information from the client, gastrointestinal signs resolved in the majority of the dogs. Based on these findings and observations from human medicine, the hypothesis that acid reflux could be a contributory cause of upper respiratory clinical signs, although not demonstrated, cannot be ruled out.[19,20,23,30,54] However, the same positive trend was observed in the remaining 2 groups, and the specific contribution of glucocorticoids, H2 antagonists or diets is not known, as well as a possible self-limiting nature of the gastrointestinal clinical signs.

Our study had some limitations, primarily related to relatively small sample size and lack of a standardized gastrointestinal diagnostic evaluation and therapeutic approach. Indeed, without this information, the clinical utility of some data presented here is unknown and cannot be adequately interpreted. Particularly, a link between improvement in respiratory clinical signs and the gastrointestinal therapeutic approach may not be present. Indeed, in the absence of a control population of dogs with other chronic non-CILPR disease, it is not possible to state that the high prevalence of endoscopic gastrointestinal abnormalities and clinical signs observed here is not at least partially associated with the selection of chronically sick dogs.

In conclusion, to our knowledge, no information exists about the concurrent endoscopic evaluation of both the upper airways and digestive system in dogs with CILPR. Our results suggest that in some dogs with nasal clinical signs, in which no primary disease could be identified, some gastrointestinal clinical signs, endoscopic lesions, and histopathologic abnormalities occur concurrently. In light of these findings, consideration should be given to the possibility of a cause-effect relationship between the 2 processes. However, additional studies are needed to explore the impact of gastrointestinal medications on respiratory clinical signs.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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