



Association between follicular tracheitis and gastroesophageal reflux



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ABSTRACT

Objective: Follicular tracheitis (also known as tracheal cobblestoning) is an entity that is poorly described and of unclear significance. The objective of this study was to better define follicular tracheitis and determine the association between the clinical finding of follicular tracheitis on bronchoscopy and objective evidence of gastroesophageal reflux disease.

Methods: Retrospective chart review of children with recurrent croup having undergone a rigid bronchoscopy and an investigation for gastroesophageal reflux between 2001 and 2013.

Results: 117 children with recurrent croup children age 6–144 months were included in the study. Follicular tracheitis was noted on 41% of all bronchoscopies. Fifty-nine percent of all children who underwent bronchoscopy were diagnosed with gastroesophageal reflux on at least one investigation. Forty-nine of 117 children underwent a pH probe study, and 51% were found to have evidence of reflux on this study. Nine children were diagnosed with eosinophilic esophagitis. Three patients underwent a biopsy of the follicular tracheitis lesions, which revealed chronic inflammation. There was no evidence of an association between findings of follicular tracheitis and a positive test for gastroesophageal reflux ($p = 0.52$) or a positive pH probe study ($p = 0.64$). There was no association between follicular tracheitis and subglottic stenosis ($p = 0.33$) or an history of asthma and/or atopy ($p = 0.19$).

Conclusion: In children with recurrent croup, follicular tracheitis remains an unspecific finding associated with an inflammatory disorder of unknown etiology.

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1. Introduction

Recurrent croup, defined as two or more episodes of croup within a lifetime, is a common pediatric disorder that affects approximately 6.4% of children [1]. Otolaryngologists are frequently consulted to evaluate these children in order to rule-out underlying anatomical anomaly, which could lead to a predisposition to recurrent croup. While anatomical anomalies are detected in up to 97% [2] of children, the vast majority of these anomalies are mild and do not require any treatment [3–5]. Additionally, there is evidence that a large proportion of these children suffer from

underlying inflammatory disorders such as asthma [6,7], atopy [8] and gastroesophageal reflux [9,10].

Follicular tracheitis, also known as tracheal cobblestoning, is a poorly understood entity that is commonly encountered during pediatric bronchoscopy. It has been described by Dave et al. [11] as “inflammatory irritation with a nodular or lumpy appearance of the tracheal wall mucosa”. A recent study reported a prevalence of 38.8% in children aged 0–6 years old undergoing a non-airway elective surgical procedure [11] and 33% of children undergoing a bronchoscopy for airway symptoms [12]. While it is hypothesized to be associated with inflammation, such as that due to a respiratory tract infection, pulmonary aspiration or gastroesophageal reflux disease (GERD), there currently is no evidence to confirm such an association.

The objective of this study was to further characterize follicular tracheitis in children having undergone a diagnostic bronchoscopy for recurrent croup and determine whether it is associated with objective findings of gastroesophageal reflux on investigations.

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2. Methods

2.1. Ethical considerations

Institutional review board approval was obtained from the University of Utah.

2.2. Study design and setting

A retrospective case series of all children having undergone a rigid bronchoscopy for recurrent croup between 2001 and 2013 at a single tertiary pediatric institution was performed.

2.3. Participants

Inclusion criteria were any child age 0–18 years old with two or more episode of croup in one year or three or more lifetime episodes of croup who had undergone a rigid bronchoscopy and objective evaluation for gastroesophageal reflux at our tertiary care pediatric institution. Children were excluded if they had a known underlying airway anomaly diagnosis preceding development of recurrent croup, had persistent stridor at rest, had not undergone a formal airway endoscopy in the operating room or had not undergone any objective evaluation for gastroesophageal reflux.

2.4. Variables

Data retrospectively gathered from the children's chart included patient's age, gender, gestational age at birth, past medical history, age at time of endoscopy, findings on endoscopy according to the written operative report and results of studies evaluating gastroesophageal reflux.

A diagnosis of GERD was defined as a positive result on any of the following investigations: 24-h pH probe, esophageal biopsy and/or upper gastrointestinal radiographic study. On these studies, a diagnosis of GERD was made if a child had a pH less than four for more than four percent of the 24-h pH probe study duration, if reflux was visualized by the radiologist during the upper gastrointestinal radiographic study or if the esophageal biopsy revealed esophagitis, intraepithelial eosinophilic infiltration or squamous hyperplasia.

Bronchoscopic findings considered consistent with airway inflammation and suggestive of GERD included arytenoid and posterior glottis edema, tracheal folliculitis, subglottic or tracheal edema and blunting of the carina. Subglottic stenosis was evaluated according to the Myer–Cotton grading system [6].

2.5. Analysis

All statistical analysis was performed using Stata version 12.0 IC. Association between follicular tracheitis and GERD was calculated using the chi-square test for categorical variable. Association between other anomalies on rigid bronchoscopy and GERD was also evaluated using chi-square test.

3. Results

Out of 235 children that underwent a rigid bronchoscopy for recurrent croup by a pediatric otolaryngologist, 117 children also

Table 1

Crude analysis of odds ratio for significant abnormality by possible risk factor.

Risk factors	No follicular tracheitis n = 69 (%)	Follicular tracheitis present n = 48 (%)	p-Value
Gender (M/F)	49/20 (71.0/29.0)	34/14 (70.8/29.2)	0.98
Mean Age (in mos)	45.1	49.2	0.46
Age < 3 y.o.	35 (50.7)	15 (31.3)	0.04
Prematurity	14 (20.3)	13 (27.1)	0.39
History of GERD	27 (39.1)	16 (33.3)	0.52
Hx of asthma/atopy	26 (37.7)	24 (50.0)	0.19
Concomitant T&A	12 (17.4)	14 (29.2)	0.13
Chronic cough	17 (26.6)	12 (29.3)	0.76
Subglottic stenosis	23 (33.3)	12 (25.0)	0.33

had an objective evaluation for GERD and were included in the analysis. There were 83 boys and 34 girls. Endoscopy was performed by five academic pediatric otolaryngologists on children between 6 and 144 months of age with a mean of 47 months. Indications for rigid bronchoscopy were two or more episodes of croup. Rigid bronchoscopy was performed concurrently to myringotomy and tube insertion; and or adenoidectomy; and or tonsillectomy in 40/117 children (34.2%).

The overall prevalence of follicular tracheitis in the entire cohort of children with recurrent croup was 96/235 (41%) and 48/117 (41%) in children meeting inclusion criteria for this study. Children with follicular tracheitis were more likely to be over 3 years old ($p = 0.04$). There was no association between gender and follicular tracheitis ($p = 0.98$). The mean age in children without follicular tracheitis was 45 months and that of children with follicular tracheitis 49 months ($p = 0.46$). Characteristics of the children with and without follicular tracheitis can be found in [Table 1](#).

Investigations performed to evaluate for GERD included an esophagoscopy with biopsy in 107 patients, a pH probe study in 49 patients and an upper gastrointestinal radiologic study in 14 patients. Forty-six (46/107) children had an abnormal esophageal biopsy including 9 children with eosinophilic esophagitis, 15 children with intraepithelial eosinophils, 13 children with squamous hyperplasia and 9 children with non-eosinophilic esophagitis. Twenty-five of forty-nine (51%) who underwent a 24-h pH probe study had GERD and 9/14 (64%) radiographic studies showed evidence of reflux. Sixty-nine (59%) children had evidence of GERD on pH probe, upper gastrointestinal study and/or esophagoscopy. In children with evidence of GERD on objective testing, 30 (43.5%) had follicular tracheitis, while 37.5% of children without evidence of GERD had follicular tracheitis ($p = 0.52$). Parents of 43/117 children (37%) reported complaints that were considered consistent with GERD such as frequent regurgitation or vomiting. There was no association between reported symptoms of GERD and a positive investigation ($p = 0.52$).

There was no evidence of an association between follicular tracheitis and GERD on any objective testing ($p = 0.52$), including a positive pH probe study ($p = 0.64$). Data on the association between follicular tracheitis and GERD for the different tests can be found in [Table 2](#).

Other findings suggestive of GERD on bronchoscopy included arytenoid edema in 10/117 children (9%) and subglottic edema in six children (5.1%). There was no evidence of an association between arytenoid edema and GERD ($p = 0.46$) or subglottic edema

Table 2

Association between follicular tracheitis and gastroesophageal reflux on objective testing.

	Upper gastrointestinal study (n = 14)	pH Probe (n = 49)	Esophageal biopsy (n = 107)	Any test (n = 117)
Follicular tracheitis present (n = 48)	2/6 (33.3%)	11/20 (55.0%)	22/45 (48.9%)	30/48 (62.5%)
Follicular tracheitis absent (n = 69)	7/8 (87.5%)	14/29 (48.3%)	24/62 (38.7%)	39/69 (56.5%)
p-Value	0.06	0.64	0.29	0.52

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