Association of clinical signs with endoscopic findings in horses with nasopharyngeal cicatrix syndrome: 118 cases (2003–2008)

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Objective—To characterize the associations between clinical signs of nasopharyngeal cicatrix syndrome (NCS) and endoscopic findings in horses.

Design—Retrospective, case-control study.

Animals—239 horses (118 case horses and 121 control horses).

Procedures—Medical records of horses that had an endoscopic evaluation of the upper airway performed between January 2003 and December 2008 were reviewed. Clinical signs and the appearance and anatomic locations of lesions identified during endoscopic evaluation were reviewed and recorded for each horse. The associations between clinical signs and endoscopic findings were evaluated by the use of a prospective logistic model that used a Bayesian method for inference and was implemented by a Markov chain Monte Carlo method.

Results—Nasal discharge was associated with acute inflammation of the pharynx and larynx. Exercise intolerance was associated with circumferential pharyngeal lesions. Respiratory noise was associated with chronic scarring of the pharynx, a combination of pharyngeal and laryngeal scarring, and circumferential scarring of the pharynx. Respiratory distress was associated with acute inflammation of all portions of the airway, especially when there was preexisting scarring and narrowing of the airway by ≥ 50%. Cough did not have any significant association with NCS, compared with results in control horses.

Conclusions and Clinical Relevance—Associations between the endoscopic appearance of NCS lesions and relevant clinical signs will help practitioners identify horses with NCS and allow them to select appropriate treatment. (J Am Vet Med Assoc 2012;240:734–739)
endoscopy from January 2003 to December 2008 were searched by use of the computerized Veterinary Medical Information System. Horses were considered for the analysis if the medical record was available and complete, endoscopy of the upper airway was performed, and the endoscopic images were available and of adequate quality for evaluation.

Case horses were defined as horses that had endoscopic findings consistent with NCS, which included scarring and inflammation of the pharynx, larynx, or trachea. Horses with clinical signs of respiratory or pharyngeal dysfunction were chosen as a clinically relevant control population for comparison of clinical signs in horses without NCS with clinical signs in horses with NCS. The control group was chosen from the remaining list of horses that met the study inclusion criteria but for which there were no endoscopic findings consistent with NCS. To minimize selection bias and potential bias associated with the date of admission to the Texas Veterinary Medical Center, every third horse was selected from the list. The list underwent 1.5 iterations to attain a number of control horses approximately equal to the number of case horses.

**Medical records review**—Age, sex, and breed were recorded for all case and control horses. Clinical signs were ascertained from the recorded history, the primary problem at the time of initial examination, and physical examination findings. Clinical signs included nasal discharge, cough, exercise intolerance, respiratory noise, and respiratory distress. Endoscopic images were evaluated, and abnormalities were recorded. For the endoscopic evaluation, acute inflammation was defined as erythema, swelling, or the presence of a diphtheritic-type membrane on any surface of the pharynx or larynx (Figure 1). Chronic inflammation was defined as any weblike or circumferential scarring on the surfaces of the pharynx or trachea and deformation of the larynx or salpingopharyngeal openings (Figures 2–4). For the purposes of this study, laryngeal referred to the arytenoid cartilages, vocal folds, epiglottis, and aryepiglottic folds; pharyngeal referred to the dorsal and lateral surfaces of the pharynx and the dorsal surface of the soft palate. The term circumferential scar referred to a continuous scar that included the dorsal, lateral, and ventral pharynx (dorsal soft palate; Figure 3), and obstruction referred to scarring, deformation, or inflammation that reduced the cross-sectional area of the airway by ≥ 50%.

**Statistical analysis**—A Bayesian logistic regression model was used for analysis. The first model compared case horses with control horses. Briefly, the approximate probability of the patient being a case horse was modeled as a Bernoulli distribution:

\[ Y_i = \text{Bernoulli}(\mu_i) \]

where \( Y_i \) is the probability of the patient being a case horse and \( \mu_i \) is the Bernoulli parameter.
The logit of the Bernoulli parameter was then modeled as a linear function of the predictors:

$$\text{Logit}(\mu_i) = \beta_1 \cdot \text{factor}_1 + \beta_2 \cdot \text{factor}_2 + \ldots$$

where $\beta_1$ is a regression coefficient for factor 1, $\beta_2$ is a regression coefficient for factor 2, and so on.

The second model defined a 4-level classification for stage of disease among horses (none, acute, chronic, and acute and chronic). The probability of a patient having each clinical sign was modeled by use of a logistic model similar to the 1 used to model the stage of disease. Horses with no lesions formed the baseline or referent group. Modeling involved the use of a Bayesian method of inference, vague prior beliefs, and Markov chain Monte Carlo implementation. Markov chain Monte Carlo implementation was performed by use of a commercially available software package. Prior beliefs included a broad normal distribution with a mean of 0 and a precision of 0.0001 for the regression coefficients ($\beta$s). Convergence was evaluated by visual examination of the history plots of the 2 chains and visual examination of the Brooks, Gelman, and Rubin statistics. For parameter estimation, the initial 1,000 iterations were discarded to allow for convergence, then every 10th iteration was retained until 5,000 iterations had been saved.

For all analyses, odds ratios were considered significant if the 95% Bayesian confidence interval excluded 1. For all analyses, values of $P \leq 0.05$ were considered significant.

**Results**

**Horses**—A total of 1,236 horses had endoscopy of the upper airway performed during the study period, of which 118 had endoscopic findings consistent with NCS and were classified as case horses. Of the 1,118 horses that did not have endoscopic findings consistent with NCS, 121 were selected as control horses. Case horses ranged in age from 4 to 28 years (mean, 14.2 years; median, 16 years). Control horses ranged in age from 0 to 29 years (mean, 8.7 years; median, 14.6 years). Of the 118 case horses, 64 (54%) were geldings, 51 (43%) were mares, and 3 (3%) were stallions. This distribution did not differ significantly from that of the control horses. Quarter Horse was the most common breed represented in both the case ($n = 79$ [67%]) and control ($62$ [51%]) groups, followed by mixed, Thoroughbred, Paint, Arabian, and other breeds. However, evaluation of the breed composition of the case and control groups revealed that breed representation was not equal between the 2 groups.

**Clinical signs**—The most common clinical sign among the 118 case horses was respiratory noise ($n = 76$ [64%]), followed by nasal discharge ($70$ [59%]), cough ($37$ [31%]), exercise intolerance ($34$ [29%]), and respiratory distress ($27$ [23%]). Five horses had none of these clinical signs, and NCS was identified as an incidental finding during endoscopic evaluation for another purpose. The majority ($n = 82$ [69%]) of case horses had > 1 clinical sign. Other clinical signs in the case horses included epistaxis ($n = 3$), dysphagia (3), weight loss (3), dysphonia (2), lethargy (2), colic (2), and lymphadenopathy (1), collapse (1), and fever (1). For 4 horses, a respiratory noise or cough was observed only when the horse’s neck was flexed.

The most common clinical sign among the 121 control horses was respiratory noise ($n = 47$ [39%]), followed by nasal discharge ($42$ [35%]), respiratory noise ($34$ [28%]), exercise intolerance ($31$ [26%]), epistaxis ($17$ [14%]), and respiratory distress ($8$ [7%]). Similar to the
case horses, many control horses had > 1 clinical sign. Other clinical signs in the control horses included fever
(n = 5), dysphagia (4), atrophy of the masseter muscle (3), ptyalism (2), weight loss (1), anorexia (1), retropharyngeal abscess (1), tachypnea (1), head shaking (1), and intraluminal esophageal obstruction (1).

Endoscopic findings—Nearly all of the 118 horses (n = 115 [97%]) with NCS had pharyngeal involvement, and of these, 57 (50%) had circumferential scarring. Additionally, the larynx was affected in 107 (91%) case horses. Images of the proximal portion of the trachea were available for examination for only 47 case horses, of which 31 (66%) had evidence of inflammation and scarring. Forty-two (36%) case horses had rostral displacement of the palatopharyngeal arch. Forty-six (39%) case horses had airway obstruction (pharyngeal obstruction, n = 9; laryngeal obstruction, 37) secondary to NCS, and 7 (6%) had ulcerated nasal mucosa.

Among the 121 control horses, 57 (47%) had no endoscopic abnormalities of the upper airway during the time they were resting. In the other 64 (53%) control horses, a variety of endoscopic abnormalities were identified, including left laryngeal hemiplegia (n = 12 [19%]), disease of the auditory tube diverticula (guttural pouches; including empyema, tympany, mycosis, and retropharyngeal abscess [15 [23%]]), dorsal displacement of the soft palate (11 [17%]), epiglottic entrapment (6 [9%]), cleft palate (4 [6%]), drainage from the nasomaxillary opening (3 [5%]), subepiglottic cyst (2 [3%]), petechiation (2 [3%]), and epiglottic malformation, ethmoid hematomata, foreign body, trauma, and laceration of the soft palate (1 [2%] each).

Associations between clinical signs and endoscopic findings—Horses that had endoscopic evidence of acute NCS were significantly more likely to have clinical signs of nasal discharge and respiratory distress than were control horses (Table 1). Similarly, horses that had endoscopic evidence of chronic NCS were more likely to make a respiratory noise and have respiratory distress than were control horses.

The odds ratios for the association of clinical signs with various anatomic locations of pathological lesions identified via endoscopy were determined for horses with NCS (Table 2). Horses with pharyngeal lesions were significantly more likely to have respiratory noise than were horses without pharyngeal lesions. Horses with lesions in both the pharynx and larynx were more likely to have nasal discharge, respiratory noise, and respiratory distress than were horses without lesions in the pharynx or larynx. Horses with pharyngeal and laryngeal obstruction had increased risk of respiratory distress, and horses with circumferential scarring had increased risk of exercise intolerance, respiratory noise, and respiratory distress. There were insufficient numbers of horses with pathological lesions in the nasal passages or trachea for analysis.

Discussion

The identification of associations between clinical signs and specific diseases or pathological lesions allows veterinary practitioners to consider differential diagnoses and develop effective diagnostic plans and therapeutic interventions. To our knowledge, prior to the present study, there were no reports of the associations between clinical signs and endoscopic findings in horses with NCS. Findings of the present study revealed differences in the clinical signs in horses with NCS and those in control horses and differences in clinical signs in case horses with various lesions of NCS. These findings may help practitioners in geographic regions...

Table 1—Odds ratios (95% confidence interval) for various clinical signs in 118 horses with acute NCS, chronic NCS, or acute and chronic NCS, compared with those clinical signs in 121 control horses.

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Acute NCS (n = 93)</th>
<th>Chronic NCS (n = 114)</th>
<th>Acute and chronic NCS (n = 88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal discharge</td>
<td>3.51 (1.42–7.46)</td>
<td>0.86 (0.34–1.74)</td>
<td>2.63 (1.43–4.41)</td>
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<tr>
<td>Cough</td>
<td>0.72 (0.28–1.5)</td>
<td>1.27 (0.51–2.59)</td>
<td>0.81 (0.42–1.38)</td>
</tr>
<tr>
<td>Exercise intolerance</td>
<td>0.87 (0.33–0.88)</td>
<td>1.68 (0.63–3.49)</td>
<td>1.25 (0.63–2.23)</td>
</tr>
<tr>
<td>Respiratory noise</td>
<td>1.52 (0.61–3.14)</td>
<td>4.14 (1.73–9.59)</td>
<td>5.63 (2.97–9.85)</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>5.65 (1.16–11.18)</td>
<td>2.01 (0.33–6.62)</td>
<td>7.62 (2.50–20.27)</td>
</tr>
</tbody>
</table>

*Odds ratio is significant (P = 0.05).

Table 2—Odds ratios (95% confidence interval) for the association of clinical signs with the location or type of pathological lesions identified during endoscopic evaluation of the upper airway of 118 horses with NCS.

<table>
<thead>
<tr>
<th>Clinical sign (No. of horses)</th>
<th>Location or type of NCS lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pharynx</td>
</tr>
<tr>
<td>Nasal discharge (70)</td>
<td>2.56 (0.69–6.70)</td>
</tr>
<tr>
<td>Cough (37)</td>
<td>2.82 (0.78–7.80)</td>
</tr>
<tr>
<td>Exercise intolerance (34)</td>
<td>1.64 (0.38–4.40)</td>
</tr>
<tr>
<td>Respiratory noise (76)</td>
<td>1.67 (1.71–17.28)</td>
</tr>
<tr>
<td>Respiratory distress (27)</td>
<td>2.65 (0.15–10.74)</td>
</tr>
</tbody>
</table>

For each comparison, the referent group was horses with NCS that did not have pathological lesions at a particular location or did not have a particular type of pathological lesion.

See Table 1 for remainder of key.
where NCS is prevalent and may also help guide further research into the etiopathogenesis of this syndrome.

Compared with results for the control horses, horses with NCS were more likely to have respiratory noise or respiratory distress. Horses with NCS may have inflammation, pharyngeal scarring, pharyngeal narrowing, arytenoid chondritis, and laryngeal dysfunction. These changes likely decrease tissue compliance and narrow the airway lumen. Given the typical changes in the upper airway associated with NCS, it is not surprising that airway dynamics would become altered over time in such a way as to cause respiratory noise, especially at increased respiratory rates. Progressive narrowing of the upper airway would logically lead to respiratory distress because higher pressure is required to inspire and expire air through an obstructed or poorly compliant airway. The findings of the present study indicated that NCS is an important differential diagnosis for horses making respiratory noise or in respiratory distress, especially in geographic areas where NCS is prevalent.

Upper airway endoscopy of case horses revealed lesions in multiple sites of the upper airway, including the nasal passages, pharynx, larynx, and proximal portion of the trachea. Images of the nasal passages and trachea were available in only a small number of cases, precluding their inclusion in statistical analysis. However, these sites should be critically examined in any horse for which NCS is a differential diagnosis.

Clinical signs in case horses were associated with the phase of the syndrome (acute vs chronic) and with the anatomical location of lesions. Nasal discharge was significantly associated with the acute phase of NCS and with pathological lesions in the pharynx and larynx. These findings were anticipated because mucosal irritation is a nonspecific trigger for serous and mucous secretions. In case horses, respiratory distress was associated with acute NCS (alone or concurrent with chronic changes). Active inflammation of the upper airways may disable a horse’s ability to compensate for chronic airway narrowing and may explain why some horses with major chronic changes of the airways go into acute respiratory distress. Upper airway inflammation was also associated with concurrent airway obstruction of the larynx and pharynx and with circumferential scarring. These findings were also anticipated because severe narrowing and loss of compliance of the upper airway would increase the pressure required to move air through the upper airway.

Respiratory noise in case horses was significantly associated with chronic scarring of the airway. Because scar tissue changes both the compliance and shape of the airway, it is likely that the dynamics of airflow are altered, which leads to turbulence and respiratory noise. Interestingly, increased respiratory noise was associated with pharyngeal scarring and not specifically with inflammation or deformation of the larynx and arytenoid cartilages. This finding was unexpected because many of the horses with arytenoid changes also appeared to have laryngeal dysfunction similar to laryngeal hemiplegia, which is a cause of exercise-associated respiratory noise in horses. Moreover, it has been our clinical experience that many horses admitted to a veterinary hospital with respiratory noise and respiratory distress due to NCS have laryngeal involvement that results in airway occlusion. It is probable that the lack of an association between laryngeal lesions and respiratory noise and respiratory distress in the present study was attributable to the fact that few horses had laryngeal lesions without concurrent pharyngeal involvement. Conversely, there were many case horses with only pharyngeal lesions. This disproportion in the data may have affected the statistical analysis and diminished the actual importance of laryngeal damage in NCS.

Exercise intolerance was reported in similar proportions in case (29%) and control (25%) horses. Exercise intolerance is a nonspecific clinical finding that may develop secondary to abnormalities of the musculoskeletal, neurologic, or cardiovascular systems as well as the respiratory system. The airway in horses that have exercise intolerance is often examined endoscopically because exercise intolerance is commonly caused by upper and lower airway diseases. Exercise intolerance in case horses was also not associated with laryngeal lesions, which are expected to have a profound effect on airflow, especially with increased respiratory rates during exercise. Because exercise intolerance is subjective assessment, it may have been underreported or overreported, especially in horses not used for competitive performance purposes. Additionally, exercise intolerance was a common finding in the control horses, which may have biased the results in assessing this clinical sign in case horses.

Cough was reported in approximately the same proportion of case (31%) and control (35%) horses. In case horses, cough was not associated with the phase of disease or a specific lesion location. This was not surprising because the cough reflex is a nonspecific protective response of the upper and lower airways to irritation. Also, similar to exercise intolerance, the common finding of cough in the control horses may have affected the analysis of this clinical sign in the case horses.

The study reported here has several limitations. As in all retrospective studies, the available information was limited to that recorded in the medical records, whereas a prospective study has the advantage of obtaining specific information on all animals. Although all records contained images from endoscopic examinations, the images were static and did not provide dynamic information about airflow function. Additionally, the images that were available for review were not the same views for all horses, which would have been helpful. Images of the trachea and nasal passages were not available for all cases, which limited the data available for analyzing associations at these anatomic locations. Similarly, many endoscopic examinations of horses with ethmoid hematomas included only images of the ethmoids and likely led to an underrepresentation of this lesion in the control population. A set of standard images for all horses undergoing upper airway endoscopy would have facilitated the investigation.
Potentially, case horses may have not been included in the present study because of miscoding or a lack of endoscopic images. The case and control populations were strictly defined, but because images were required for review, a sizeable number of cases may have been missed in the initial review process. The availability of a greater number of case horses may have strengthened some associations. Even though a large overall number of horses was examined in the present study, some of the subgroups had a relatively small number of horses. The fact that NCS is a common airway disorder in our geographic region may have also affected the results of the present study, and these results may not apply in areas where NCS in horses is less common.

Several conclusions can be drawn from the information obtained from the present study. In geographic regions where NCS is prevalent, horses that have respiratory distress are more likely to have NCS than other types of airway disease. For horses that have NCS and are in respiratory distress, pathological lesions are likely to affect multiple sites of the upper airway and will probably include both active inflammation and chronic scarring. Horses with NCS that have nasal discharge are more likely to have acute inflammation in the upper airway, which may respond to medical treatment or management changes. Respiratory noise secondary to NCS is less likely to resolve with surgical intervention, compared with respiratory noise caused by other conditions, because the pathological lesions are likely located in the pharynx. Laser and histioury reduction of cicatricial scarring have been performed, but long-lasting improvements in horses’ airway function were not observed if horses remained in the same environment. Because of the tendency for scar tissue to recur in the upper airway if horses’ environment is not changed, permanent tracheostomy has become the treatment of choice for horses with NCS that have circumferential scarring.

Nasopharyngeal cicatrix syndrome has a substantial economic impact on the horse industry in Texas because of the frequency with which it occurs. Despite long-standing awareness of NCS, many questions remain unanswered and further research to characterize and improve treatment for this condition is imperative. The distribution of lesions in the airways of horses with NCS supports inhalation of a direct irritant, allergen, or infectious agent as the cause. More research is needed to determine the specific geographic distribution, natural history, and risk factors associated with the development of NCS. This information will be vital in determining the etiopathogenesis of the cyclic inflammation and scar formation. More information is also needed about the pathophysiologic impact of causative agents on the respiratory tract, including any possible impact on the lower respiratory tract, of horses with NCS. This information will be critical for determining effective treatment, management, and preventive strategies for horses in NCS-prevalent areas.

The present study revealed associations between physical changes in the upper respiratory tracts of horses with NCS and the clinical signs of the disease by use of an unaffected control population for comparison. For veterinarians practicing in regions where horses develop NCS, the disease should be suspected in horses with cyclic nasal discharge. Additionally, horses with chronic NCS that have obstruction of the larynx or pharynx are at risk for developing respiratory distress should the airway become inflamed. Practitioners can use this information to advise horse owners of the risk of respiratory distress and potentially avoid a respiratory crisis by the performance of a permanent tracheostomy.


References