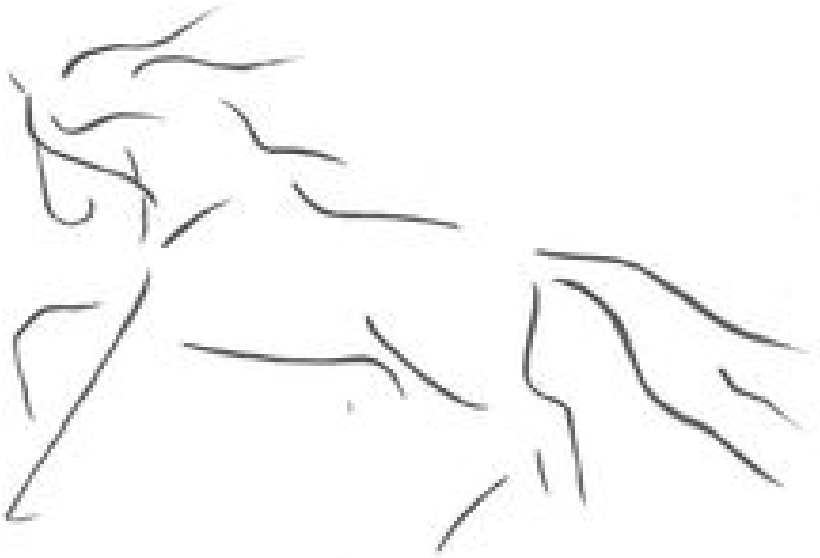
“King of the Wind”

(Malik el Hawaa)



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Introduction

Cleft palate, or palatoschisis, is a congenital defect that occurs in foals that appears to be due to the partial or complete failure of closure of the lateral palatal folds along midline during embryologic development [1,2,4-9]. Closure of midline typically occurs in the rostrad-to-caudad direction around the 47th day of gestation [1,5-9]. Incomplete closure of the palatal folds may involve the soft palate, hard palate, or both. Typically, involvement of the hard palate will decrease the chances of a successful recovery and may lead to a poorer prognosis [1,6,8,9]. In previous studies, cleft palate has had a prevalence of 0.04 to 0.2% of foals most commonly affecting the caudal half to two-thirds of the soft palate [2,5-8]. Other than euthanasia, treatment options include medical management or surgical correction with management of associated problems. The capability of the owner and extensiveness of the defect further dictates the treatment options due to associated complications with cleft palate repair [2,5,8].

History and Presentation

Malik el Hawaa is an approximately 18-month-old Arabian stallion that was presented to Mississippi State University College of Veterinary Medicine Equine services on January 8, 2017 for assessment of a previously diagnosed cleft palate due to a prolonged history of nasal discharge from both nostrils. Hawaa was diagnosed with cleft palate as a foal and presented to MSU-CVM for endoscopic and radiographic evaluation of the defect to further characterize the lesion and enable surgical planning. On presentation, Hawaa was very bright, alert, and responsive with an elevated heart rate (60 beats per minute) and respiratory rate (40 breaths per minute), along with a temperature of 99 degrees Fahrenheit. His heart and lungs auscultated normally and all other vital parameters were within normal limits.

Hawaa was sedated for endoscopy with a combination of 10mg detomidine and 10mg butorphanol to relax him and to allow for proper visualization of the defect. Copious feed material and mucoid debris were appreciated in the nasal cavity and the pharynx. The cleft could be visualized on endoscopy and was determined to involve the caudal third of the soft palate only with an asymmetrical aperture opening to the right. Although the defect was extensive, the soft palate was shown to have a sufficient amount of tissue for surgical closure. While visualizing the area, lymphoid hyperplasia could also be appreciated throughout the dorsal aspect of the pharynx, which is consistent with Hawaa's age and disease process.

Along with endoscopy, skull radiographs were requested to further examine for congenital abnormalities and to determine the best surgical approach for closure. No other congenital abnormalities were observed and adequate images were obtained of the larynx to best enable a surgical approach for a laryngotomy. Hawaa was then discharged and sent home with instructions to monitor nasal discharge and for any signs of aspiration pneumonia. His owners were informed that due to the rarity of his diagnosis, surgical complications are numerous and multiple procedures may be warranted to fully close the defect.

On February 8, 2017 Hawaa returned to MSU-CVM for surgical repair of his cleft palate. Hawaa appeared to be very nervous and was stalled immediately upon presentation to acclimate to his surroundings. His vital parameters were within normal limits (pulse of 48 beats per minute and respiratory rate of 28 breaths per minute). A rectal temperature was unobtainable due to his temperament. His heart and lungs auscultated normally, but there was moderate bilateral nasal discharge noted on physical exam. Hawaa was once again sedated (5mg detomidine and 5mg butorphanol) in preparation for placement of a tracheostomy.

A ventral midline incision of the middle third of the trachea was blocked with lidocaine and an approximately 10cm longitudinal incision was made to expose two tracheal rings. A horizontal incision was then made between the two tracheal rings encompassing approximately 40% of their circumference and a stainless steel self-retaining tracheostomy trochar was inserted to maintain a patent airway. This site was also be used for inhalant anesthesia during the surgical procedure the following day to allow access to the laryngotomy site.

On February 9, 2017 Hawaa was sedated with butorphanol and xylazine, then general anesthesia was induced using ketamine and diazepam followed by maintenance with isoflurane in oxygen. A laryngotomy approach was used to visualize the defect with the added use of laparoscope through the cricotracheal space and endoscope passed through the ventral meatus to further improve visualization and decrease interference with instruments. Although these tools were beneficial, the increased difficulty with access and visibility towards the caudal end of the cleft warranted an extension of the incision caudally to allow creation of a pharyngotomy. The pharyngotomy allowed access to the most caudal edge of the defect and facilitated additional closure of the defect.

Barbed, self-retaining V-loc suture on a cutting needle was used to facilitate a tight closure of the defect, which was approximated to involve 60% of the soft palate with no hard palate involvement. Due to the increased difficulty of access and visualization, only approximately 70% of the defect could be closed with the most rostral and caudal aspects still open. The surgical site was copiously lavaged with fluids to facilitate draining of blood, blood clots, and any other remaining fluids from the site. The pharyngotomy site and subcutaneous tissues were closed with simple continuous patterns and the skin was apposed with surgical

staples. The laryngotomy site was left to heal by second intention to allow proper drainage of the incision and the tracheostomy was retained for the post-operative period.

Post-operatively, Hawaa recovered well from surgery and was place on broad spectrum antimicrobials (Ceftiofur – Naxel 2.2 mg/kg IV twice daily and Ceftiofur – Excede 6.6 mg/kg IM once) to reduce the risk of infection and to manage any chronic pneumonia that may have been associated with his cleft palate. He was also given various anti-inflammatory drugs (Dimethyl Sulfoxide – 1 pint in 5 mL lactated ringer's solution once, Flunixin meglumine – 1.1 mg/kg IV twice daily, and throat spray – 10 mL locally in laryngotomy site twice daily) to decrease inflammation from surgery and provide some level of comfort. Hawaa was also kept on intravenous fluids to maintain gastrointestinal motility and supplement oral intake. He was kept on a mostly pelleted mash diet to reduce the amount of stemmy plant material passing through his surgical site causing irritation. Hawaa was sent home on February 13, 2017 with instructions for post-operative medications, care of his surgical sites, feed and water supplementation, and recommendation for a recheck 2 weeks post-surgery.

On March 1, 2017 Hawaa returned for endoscopic evaluation of his previous surgical repair. Endoscopy was performed on March 2, which revealed the improved closure of the soft palate with a 50% reduction in the cleft. However, the caudle margin remained unopposed. . No feed material was noted in the nasopharynx, which was a significant improvement from initial presentation. A second soft palate repair was performed on March 3rd via the previous laryngotomy and pharyngotomy sites. Due to the friable nature of the tissue, closure of the remaining defect was unsuccessful. The suture material was unable to stay in place and after 80 minutes of attempted closure the surgery was terminated due to the friability of the tissue.

Post-operatively, Hawaa's tracheostomy was removed and the site was left to heal by second intention. Once again, Hawaa was placed on antimicrobial therapy and anti-inflammatories to facilitate comfort and maintain a patent airway post-surgery. Hawaa was discharged on March 4th with further instructions for post-operative medications, surgical site upkeep, and recommendation for return in 3 months to reassess the healing of his soft palate. Malik el Hawaa's owners have not yet scheduled a time for his recheck, but he is doing well at home without any major complications.

Pathophysiology (Anatomical Considerations)

The exact etiology of cleft palate defect in the horse in unknown and not well understood, but suggested causes in other domestic species include genetic factors, exposure to teratogens, environmental or hormonal factors, nutrition, vitamin and mineral deficiencies, metabolic interactions, infections, traumatic mechanical factors, exposure to ionizing radiation, and administration of corticosteroids or tranquilizers during pregnancy [1,5,8,9]. Cleft palates in cattle and swine have been associated with the ingestion of toxic plants, including lupine species, wild parsnip, poison hemlock, and wild tobacco tree [5,8]. While cleft palate is rare in the horse, it seems probable that one or more of these factors may also be responsible for the defect during early embryologic development in the equine species.

Diagnostic Approach/Considerations

Diagnosis of cleft palate in the horse is generally achieved via thorough history, clinical signs, and endoscopic examination of the nasopharynx and upper airway [1,2,5,6,8,9]. Radiographs may also be beneficial to look for any other congenital abnormalities [8]. In one study, the palatal defects were classified as symmetrical or asymmetrical, and the defect length was classified as

mild, moderate, extensive, or not specified [2]. Clinical signs associated with cleft palate are numerous and may include bilateral, persistent milk drainage from the nostrils after nursing, coughing, signs of aspiration pneumonia, recurrent respiratory infections, malnutrition and slow growth, ill-thrift, abnormal noise from the proximal portion of the airway during exercise, chronic submandibular lymphadenopathy, tracheal contamination with feed material or mucous, dysphagia, tachypnea, tachycardia, and pyrexia [1-3,5-6,8-9]. Of these, the most common clinical sign on initial presentation is dysphagia with bilateral nasal discharge of milk immediately after nursing [6,8,9].

On endoscopic examination, the scope should be passed through the nasal cavity medially along the ventral meatus and into the nasopharynx. The field of view may be small, but the margins of the soft palate and the epiglottis should be visualized and complete evaluation of the extent of the lesion should be appreciated [1,5]. The epiglottis may appear to be "dropped down" into the oropharynx between the two edges of the soft palate [9]. In diagnosis of cleft palate involving the hard palate, digital palpation or oral examination may be the only possibility with confirmation at surgery [8,9]. Radiographs of the thorax may indicate abnormalities such as lung consolidation and air bronchograms consistent with aspiration pneumonia and should be treated prior to surgical intervention [8].

Treatment and Management

There are few options for treatment of cleft palate. Euthanasia, medical management, surgical repair with management of complications, and no treatment are the only options available with euthanasia being the common. No treatment or medical management are generally less common due to the ill-thrift associated with the defect. Euthanasia occurs is approximately 50% of cases of cleft palate [1,2,5-9]. Surgical repair of the cleft palate, or palatoplasty, is considered

a salvage procedure and generally results in numerous complications often times followed by a second operation [1,9]. If surgery is elected, there are different surgical approaches that can be utilized, such as mandibular symphysiotomy, transoral, laryngotomy, pharyngotomy, bilateral buccotomy, or any combination of these approaches with mandibular symphysiotomy being the most common [1,4-9].

Surgical intervention is extremely difficult and is followed by numerous complications. Some of the complications are only associated with certain surgical approaches, but all of them end with complete or partial dehiscence of the repair. Complications of surgical repair include dehiscence of the caudal aspect of the soft palate, pneumonia, osteomyelitis of the mandible, salivary, oronasal, or oropharyngeal fistulas, incisional infections, continued dysphagia, ill-thrift, bilateral drainage from the nostrils, hypoglossal nerve damage, lack of sufficient palatal tissue resulting in high tension, lack of exposure of the surgical site, and euthanasia associated with these complications [1-3,5-9]. Post-operatively, foals are generally kept on broad spectrum antibiotics, non-steroidal anti-inflammatories, fluids, and opioids for analgesia [1,3,6]. Majority of cleft palate defects have been reported in foals less than 6 months of age, but some cleft palate defects have been diagnosed in horses up to 15 years of age [2,3,5-7].

In one adult horse, a new study has shown promising results for engraftment of cultured autologous mesenchymal stem cells (MSCs) at the site of surgical repair of a soft palate defect [4]. Cell therapy is gaining experience in human medicine, but has yet to be determined if it could become a clinical option for veterinary medicine. The mesenchymal stem cells were obtained via Jamshidi biopsy needle from the left tuber coxa 2 weeks before the surgical repair and implantation [4]. The MSCs were then cultured, incubated, characterized, and labelled with two chemical binding dyes (5-bromo-2-desoxymidine and chloromethybenzamido-Dil-derived) to

bind to the nucleus and cell membrane, respectively. A mandibular symphysiotomy approach was used on this horse. Once the defect was sutured closed, a 10 x 10^6 suspension of MSCs mixed with 10 mL of PBS were injected directly in to the soft palate near the suture line in 0.5 mL blebs using a 23-guage needle [4].

Fourteen days post-operatively, the horse was euthanized for reasons unrelated to the surgery [4]. After euthanasia, the soft palate was examined on a macroscopic scale and tissue samples were collected for evaluation. According to the study, macroscopic examination revealed 90% closure of the defect with normal apposition of the wound margins and wound healing. On microscopic examination, the MSCs had grown in a manner similar to that of natural soft palate tissue near the suture line [4]. These cells were said to be "located and integrated into the skeletal myocyte layers under the epithelium along the axis of skeletal myocytes". This study was done to investigate the possibility of labelled autologous mesenchymal stem cells to improve wound healing and participate in regeneration after surgical trauma [4]. The mechanism of stem cell integration in other organs in cell therapy is still not clear, but further research needs to be obtained to determine if stem cell therapy could become a clinical option in veterinary medicine. This study shows that MSCs can be integrated into soft palate tissue, but immunophenotypic analysis of the cells needs to be performed to confirm their identity [4].

Case Outcome

Although the prognosis of cleft palate defects are considered poor, some foals and horses may survive to perform their intended job. Hawaa underwent a tracheostomy, two surgical repairs via combined laryngotomy and phayrngotomy, and still had some dehiscence of the caudal edge of the cleft palate. Hawaa is scheduled to return to MSU-CVM in the near future for his 3-month post-operative recheck via endoscopy to determine the extent of healing of his cleft

palate repair and tracheotomy site. Hawaa's clinical signs upon presentation were not severe and most likely aided in a smoother recovery and decreased clinical signs post-operatively. Hopefully Hawaa is doing well at home and is able to train properly without any major complications.

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