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Case Report

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First Case Report of Early Neonatal Acute Laryngitis Due to *Neisseria subflava*

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To the Editor

We recently reported in this journal a rare case of laryngomalacia associated with upper respiratory tract infection by *Corynebacterium kroppenstedtii* in the early neonatal period. In the present report, an infant was hospitalized with hoarseness from the early postnatal period and diagnosed as having acute vocal cord (laryngitis) inflammation caused by an extremely rare infection of *Neisseria subflava*. Similar to our previous report, we dilated the larynx and used a laryngoscope normally used by neonatologists to observe the larynx. The red inflamed areas of the larynx and yellow secretions from the respiratory tract were directly sampled and cultured to identify the causative organism. Because we are keenly aware of the importance of this rare but basic technique of "sampling from the lesion itself", we would like to report the present case to the same journal.

Summary

A normal-term boy was born in good vigor and without respiratory distress by vaginal delivery. However, from about 6 hours after birth, he began to sound hoarse. He also showed mild forced breathing at rest, so we observed the area around his larynx with a laryngoscope and found redness near the glottis and purulent discharge from the airways. We collected samples from the same site and identified *Neisseria subflava* as a result of bacterial culture. Subsequent bronchial fibers copy showed secondary pharyngomalacia and laryngeal edema, which were alleviated by use of antibiotics for 1 week and high-flow nasal cannula therapy for about 1 month. *N. subflava*, which is considered a so-called "commensal bacterium", can also be a causative bacterium of opportunistic infections. Therefore, in the case of newborns with upper respiratory tract symptoms, it is important to observe the vicinity of the larynx under direct vision. Furthermore, in addition to searching for tracheobronchomalacia, bronchial fibers copy can be usedto confirm the presence or absence of pharyngomalacia.

Introduction

N. subflava, unlike the pathogens *N. gonorrrhea* and *N. meningitis* in the genus *Neisseria*, is considered to be one of the normal bacterial flora in the upper respiratory tract and urethra in adults and is a bacterium that "coexists" with the host. However, this bacterium is reported to be pathologic in most people with underlying disease [1, 2]. As far as we can determine, there are only two reports of infectious diseases caused by this bacterium in pediatrics, especially in the neonatal period: sepsis reported by Rivacoba et al. [3] and meningitis reported by Tallo et al. [4]. We experienced a newborn male infant with acute laryngitis and mild pneumonia who developed hoarseness from 6 hours after birth and showed pharyngomalacia on bronchial fibers copy (BF). We used a laryngoscope that we usually use to assess the larynx and directly observed it to collect scratch samples from the inflamed area and airway secretions. Bacterial culture identified *N. subflava*, which was determined to be the causative bacterium. The etiology of *N. subflava* infection in adults has been reported to be mainly opportunistic in patients with underlying diseases [1, 2]. Few bacteria form the bacterial flora of the upper respiratory tract in the first several hours of life, and only a few species belong to the genus *Neisseria*. We report an extremely rare case of *N. subflava* as the causative agent of laryngeal infection in the neonatal period.

Case Report

The mother, a 42-year-old Japanese woman, gravida 2, para 1, with no signs of infection during pregnancy, gave birth to a boy by spontaneous delivery on the 5th day of the 39th week of pregnancy. His birth weight was 3510 g, and his Apgar score was 8 points at 1 minute and 9 points at 5 minutes. His pH of umbilical artery was 7.400, and no turbidity of the amniotic fluid was observed. Immediately after birth, the baby was crying

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well and had no respiratory problems. After that, as a healthy term infant, routine observation of his general condition was started on the cot. Around 6 hours after birth, this healthy boy suddenly became quiet. The volume of his crying decreased, and hoarseness was recognized. However, no respiratory problems were noted, so first breastfeeding was started.

At age 2 days, the boy required treatment for jaundice, and he was admitted to the NICU for phototherapy. Distinct hoarseness was noted when he cried. Although no inspiratory or expiratory wheezing was present, mild labored breathing and mild retraction were observed. After confirming that there was no dyspnea or inspiratory wheezing, when the patient was 3 days old, we performed laryngoscopy to observe the area near the larynx, paying attention to laryngeal spasms. Redness around the epiglottis, swelling of the laryngeal folds, and purulent, highly viscous secretions from the trachea were noted. We collected samples by scraping the secretions and flared areas with a swab under direct vision. We diagnosed this finding as acute laryngitis (vocal cordites) and started intravenous administration of ampicillin sodium 100 mg/kg/day and gentamicin 5 mg/kg/day. His C-reactive protein (CRP) leveled off at a maximum of 6.61 mg/dL at 2 days of ageand remained at that level for about 2 days before declining. The antibiotics were administered for 7 days and then stopped, with no subsequent relapse of inflammation. *Neisseria subflava* was isolated from the specimen obtained near the larynx. Squamous epithelial cells and neutrophils were found in the smear. Only coagulase-negative *Staphylococcus* was isolated in bacterial cultures obtained at the same site 1 week after the end of treatment.

BF was performed at 8 days of age to clarify the cause of the hoarseness. Pharyngeal collapse with hyperemia, edema, and glossoptosis near the larynx were noted (Figure 1). As a result, high-flow nasal cannula (HFNC) therapy was started on the same day to help prevent pharyngeal collapse. The infant wore the HFNC 24 hours/day for 2 weeks. Thereafter, HFNC therapy was changed to half a day for 3 weeks and then was completely withdrawn. BF was repeated at the age of 43 days, and redness, swelling, and pharyngeal collapse around the larynx were confirmed to have disappeared (Figure 2).

He was discharged from the hospital at the age of 44 days and was followed as an outpatient (Figure 3). After that, the patient developed upper respiratory tract infection several times, but hoarseness did not reappear, and the patient was immediately relieved by administration of an antitussive expectorant as an outpatient. Currently, the patient is 9 months old, has no symptoms of upper airway stenosis, and is growing steadily.

Discussion

Surprisingly few papers have examined the formation of bacterial flora in the upper respiratory tract of newborns early after birth [5-8]. They mainly examined flora to show the neonatal period as a division of childhood, or the studies spanned a wide range of years from the neonatal period to adulthood. Moreover, examination of the formation of bacterial flora in this report focusing on *N. subflava*, as one of the isolated genera of *Neisseria*, is beyond the scope of our investigation.

Suzuki et al. examined swab specimens of the larynx, retropharyngeal wall, palatine tonsils, and nasal cavities of infants immediately after birth and at 3, 6, 9, 12, and 24 hours later and at ages 2 and 4 days. Up to 3 hours after birth, no bacteria were isolated, but bacteria began to be detected in 20% of infants from 6 hours after birth. Then, at 24 hours after birth, some bacteria were detected in all infants. Gram-negative bacteria accounted

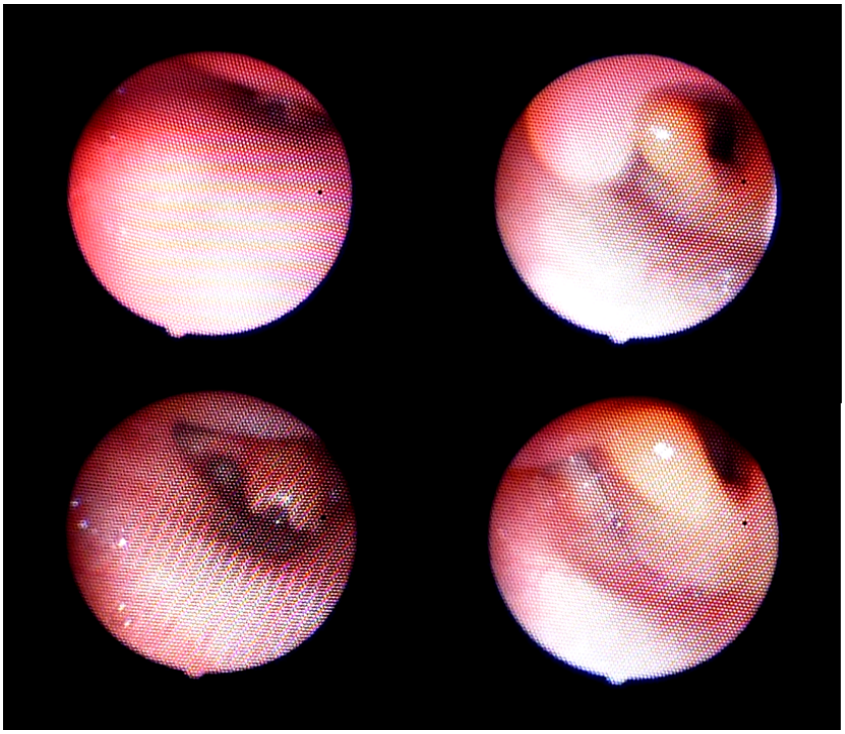

Figure 1: Laryngo-bronchial fiberscope findings on 8 days after birth.This is the finding on the 6th day after the start of antibiotics. Severe collapse of the pharynx was confirmed. Significant edema remains in the epiglottis and redness still remains. No abnormalities in tracheal or bronchial structure or function were observed.

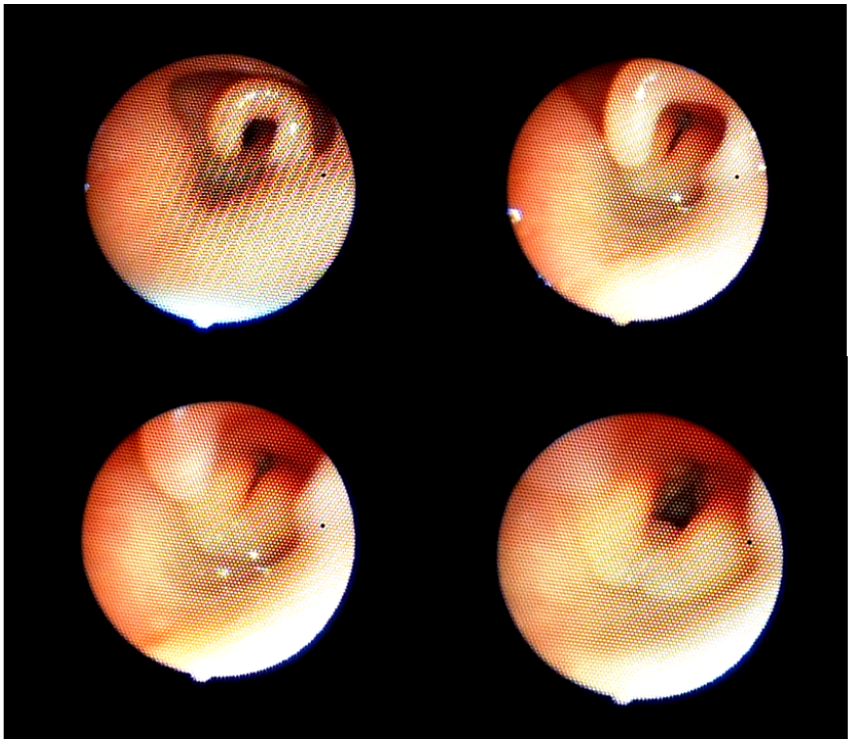

Figure 2: Laryngo-bronchial fiberscope findings on 43 days after birth.Compared with figure 1, pharyngeal collapse has been improved and inflammation of epiglottis was clearly reduced.

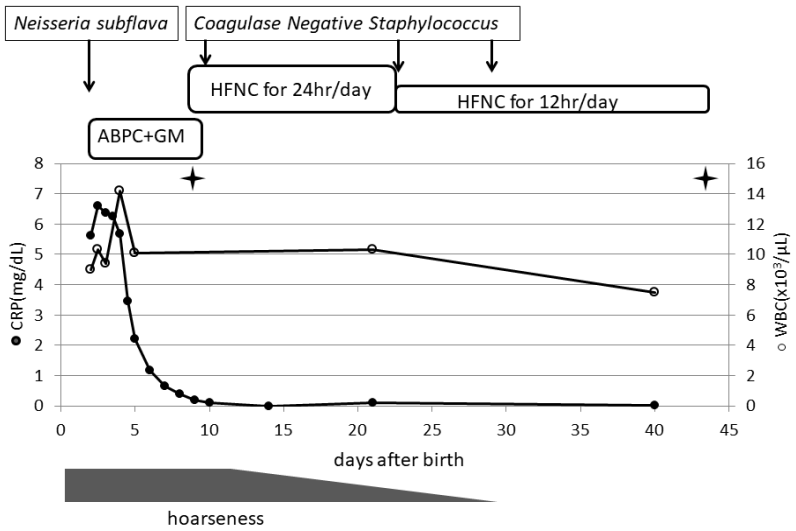

Figure 3: Clinical course of the patient**:** ✦ Laryngo-bronchial fiberscope, ABPC: aminobenzil penicillin, GM: gentamicin, HFNC: high flow nasal cannula, ↓: bacterial culture around the epiglottis.

for about 6.2% of the total and the genus *Neisseria* for about 5%. The isolation of species of the *Neisseria* genus increased to just over 18% after the neonatal period. They pointed out a causal relationship with the establishment of the bacterial flora in newborns from about 6 hours after birth because the timing almost coincided with the start of oral feeding.

Our patient cried normally with sufficient voice volume immediately after birth. However, from the time of his first breastfeeding around 6 hours after birth, although it would not be appropriate to say that the infant was "not doing well", he apparently became quiet, hoarseness was recognized, and the volume of his voice decreased. No cyanosis or choke was observed during feeding. In the examination of vaginal cultures of normal pregnant women, the main bacterial flora are *Lactobacillus* and *Staphylococcus epidermidis*, and *Neisseria* is hardly isolated [9]. Laboratory findings of the vaginal culture of the mother in our case suggested that postnatal infection was more likely than intrauterine infection. As we reported previously [10], we dilated the larynx and observed the vicinity of the larynx with a laryngoscope. Redness from the epiglottis to the vocal cords and purulent discharge from the trachea were found, a sample was collected under visual observation, and *N. subflava* was cultured. This type of sample collection is not possible with the pharyngeal and nasal cultures that are usually performed when a baby is admitted to the NICU. If a

lesion near the larynx is suspected due to hoarseness or stridor, we reconfirm that it is important to dilate the larynx and use an appropriate method to collect samples under visual observation with the laryngoscope to determine the presence or absence of infectious disease.

To our knowledge, there are only two reports of neonatal infections by *N. subflava* [3,4]. Among the genus *Neisseria*, this bacterium, which is listed as a *Neisseria* species that coexists with the normal bacterial flora, rarely threatens the human body as a pathogen [1,2].

As a causative agent of respiratory infections, *N. catarrhalis* has been proven as *Moraxella catarrhalis* in laryngitis, tracheitis, pneumonia, sinusitis, etc. [11]. In addition, although several types of symbiotic *Neisseria* spp. have been reported, the present case is the first report of an infectious disease by *N. subflava* in the laryngeal area. Reports of this bacterium as a pathogenic bacterium are occasionally found in endocarditis, meningitis, and sepsis. In the respiratory system, the symbiotic *Neisseria* genus comprises nearly 20% of the indigenous bacteria after the neonatal period, so it is difficult to conclude that it is the causative bacterium. *Streptococcus* is the main bacterial species detected in the neonatal period, which makes it additionally difficult to consider *N. subflava* as the pathogenic bacterium. The sepsis and meningitis in the above two reports are hematogenous infections, and if the sites are not otherwise contaminated, they are usually sterile, so it would seem to be easy to determine the causative organism.

Although this normal-acting infant did not appear to be doing poorly, he became calm, was hoarse when crying, the volume of his voice decreased, his CRP level increased, and BF findings showed laryngitis that improved with antibiotics. Furthermore, as this *N. subflava* was isolated from the swab sample of the lesion collected under direct vision, we can reasonably conclude that it was the causative bacterium. The reason for the lack of stridor in this infant was that the pharyngomalacia was present on the oral side of the larynx, so even if there was laryngeal edema, inflammation of the vocal cords, or swelling, the negative pressure was released at the obstructed part of the airway upstream of these findings, and it is expected that the flow velocity in the lower respiratory tract would be reduced. After the infant was treated with HFNC therapy, a follow-up BF performed about 1 month later confirmed improvement of the pharyngomalacia and disappearance of the inflammatory reaction in the vocal cords. We presumed that his recovery was quick because the infection caused by *N. subflava* was the primary lesion and the cause of the secondary airway stenosis.

Conclusion

A newborn baby who was asymptomatic immediately after birth showed hoarseness and diminished voice volume in the early neonatal period. We were able to diagnose acute laryngitis due to *N. subflava* by direct visual observation with a laryngoscope and collection of a sample. Due to the complication of secondary pharyngomalacia, only hoarseness and no inspiratory stridor were observed. Further, BF is an indispensable method to determine airway condition even in the early neonatal stage.

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