Semilobar Holoprosencephaly with Congenital Oropharyngeal Stenosis in a Term Neonate

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Abstract

Background Holoprosencephaly (HPE) is often accompanied by a deficit in midline facial development; however, congenital oropharyngeal stenosis in neonates with HPE has not been reported before. We describe a case of a neonate with prenatally diagnosed semilobar HPE accompanied by congenital oropharyngeal stenosis.

Case Report The patient was born at 39 weeks of gestation and developed dyspnea shortly after. Laryngoscopic test revealed oropharyngeal stenosis. Nasal continuous positive airway pressure, high-flow nasal cannula, and nasopharyngeal airway did not resolve her dyspnea; tracheostomy was required.

Conclusion Neonates with HPE might be at higher risk of pharyngeal stenosis because of the functional and/or anatomical abnormalities. In the case of dyspnea in neonates with HPE, laryngoscopic evaluation should be considered.

Keywords
- holoprosencephaly
- oropharyngeal stenosis
- congenital pharyngeal stenosis

Holoprosencephaly (HPE) is a common developmental disorder that occurs in the human forebrain. The cause of HPE is thought to be because of a disturbance in the delicate balance of signals for the separation of the cerebral hemisphere.[1] HPE is classified into the following four types according to the severity of the abnormality of cleavage of the cerebral hemispheres and deep nuclear structures: alobar, semilobar, lobar, and middle interhemispheric variant or syntelencephaly.[2] Although HPE is often accompanied by a deficit in midline facial development, there has been no report on HPE with congenital oropharyngeal stenosis. Here, we report a case of HPE with congenital oropharyngeal stenosis, which resulted in respiratory distress.

Case Presentation

A 33-year-old pregnant woman (Gravida 1, Para 0) was referred to our hospital for fetal growth retardation and fetal ventriculomegaly at 30 weeks of gestation. She had no history of infections during pregnancy, medication, or any other chronic diseases. Her niece had a congenital abnormality, but the details were unclear. Prenatal sonographic findings revealed fetal growth retardation (−2.0 standard deviation [SD]), enlargement of the anterior and posterior horns of the bilateral lateral ventricles, fused lateral ventricles and thalami, and hypotelorism (binocular distance, 37.8 mm, < −2.0 SD). No other congenital malformations were found. Prenatal diagnosis was semilobar HPE. Amniocentesis was performed and the chromosomal karyotype was normal (46,XX). The course of pregnancy was uneventful. At 39 weeks of gestation, she had spontaneous labor and vaginal delivery.

A female baby of weight 2,172 g (−2.2 SD) was born. The Apgar scores at 1 and 5 minutes were 7 and 9 points, respectively. Her respiratory status was stable at birth and hence resuscitation was not required. She was transferred to the neonatal intensive care unit (NICU) for further examination.

In the NICU, the newborn's vital signs were within normal limits. Physical examinations showed microcephaly (head circumference, 29.7 cm; −2.6 SD), hypotelorism (magnetic

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resonance imaging [MRI] findings at 2 months: interocular distance, 10.1 mm, < -2.0 SD; binocular distance, 47.3 mm, < -2.0SD) and hypoplasia of nasal septum. Cleft lip, cleft palate, microstomia, and micrognathia were not found. Neurologically, she had normal tone and reflexes. Brain sonography and MRI findings were in line with her prenatal examinations. There were no abnormal findings in her blood tests, chest and abdominal X-rays, echocardiography, and abdominal sonography. We diagnosed semilobar HPE, which was consistent with her prenatal diagnosis.

On day 1 of life, the newborn developed dyspnea with stridor. Her breathing worsened gradually accompanied by retraction and hypercapnia; nasal continuous positive airway pressure (nCPAP) was initiated on day 4. On day 7, we performed a laryngoscopic evaluation of her upper airway. Her oropharyngeal lumen was narrow, plugged by secretion and opened slightly with labor only during inspiration (►**Fig. 1**). A diagnosis of oropharyngeal stenosis was made. We deemed the patient too small in size for nasopharyngeal airway (NPA) insertion. Her respiratory status was initially stabilized but deteriorated progressively, with nCPAP or high-flow nasal cannula rendered ineffective. We placed an NPA through the oropharyngeal stenotic portion on day 35, which resulted in the resolution of her dyspnea. However, an erosion of the wall of her oropharynx just above the larynx developed soon after because of the continuous use of the NPA, leading to difficulties in inserting an NPA consecutively. Furthermore, the NPA was easily obstructed by respiratory secretion. Frequent suction and washing of the NPA was required, rendering her breathing unstable. We successfully performed a tracheostomy on day 112 when her weight was 4,468 g. Consequently, her breathing became easy and stable.

Discussion

To our knowledge, this is the first report of HPE with congenital oropharyngeal stenosis, which is a very rare condition. Previously, Kawashiro et al reported on congenital pharyngeal stenosis.[3] The authors categorized anatomical stenosis into the following three types: type 1 was associated with mandibular hypoplasia (e.g., Pierre Robin syndrome); type 2 was associated with mandibulofacial dysostosis (e.g., Apert syndrome and Crouzon syndrome); and type 3 was associated with structural abnormalities (e.g., abnormal proliferation of pharyngeal wall tissues). To date, no firm conclusions about the pathogenesis congenital pharyngeal stenosis have been drawn because of the scarcity of reports on this condition. However, we postulate that congenital pharyngeal stenosis could be because of the various causes including abnormal neuromuscular factors and anatomical stenosis. In this case, laryngoscopic evaluation of upper airway revealed a narrowing of the oropharyngeal lumen which opened slightly only during inspiration. We did not find other common etiologies of dyspnea such as respiratory distress syndrome, transient tachypnea of the newborn, pulmonary air leak, rhinostenosis, choanal stenosis, and laryngomalacia. In addition, we did not observe any mass lesion that was pressing on her oropharynx. Two possible etiologies/mechanisms that could have resulted in the patient's oropharyngeal stenosis are functional pharyngeal stenosis caused by neurogenic factors associated with HPE, and anatomical pharyngeal stenosis caused by mandibulofacial dysostosis with hypotelorism and hypoplasia of nasal septum. Neonates with HPE might be at higher risk of pharyngeal stenosis because of functional and/or anatomical abnormalities. In the case of dyspnea with HPE, pharyngeal stenosis may not be evaluated sufficiently.

The effect of nCPAP, HFNC, and NPA on our patient was temporary. The air pressure of nCPAP and HFNC seemed to be insufficient to open the patient's oropharynx. For the NPA, the tip was needed to be placed in the small space between the narrow segment of the patient's oropharynx and the epiglottis. It was challenging to keep the NPA at the suitable position because of movements of the patient. As a result, erosion occurred in the wall of her oropharynx. Although Kawashiro et al recommended uvula splitting as an alternative treatment, we were unable to use this option because the newborn's physique was too small to tolerate such a procedure. Instead, a tracheostomy was performed to resolve her problem.

In summary, we experienced a case of HPE with congenital oropharyngeal stenosis which resulted in respiratory distress. In the case of dyspnea with HPE, laryngoscopic test should be considered for the evaluation of pharyngeal stenosis.

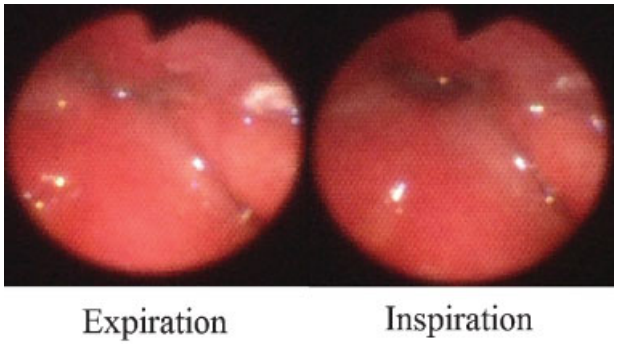

Fig. 1 Laryngoscopic findings of the oropharynx. We looked down the patient's oropharynx from the posterior nasal cavity. Her oropharyngeal lumen was narrow, plugged by secretion, and opened slightly with labor only during inspiration.

Conflict of Interest

The authors declare no conflict of interest.

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