College of Human Medicine
MICHIGAN STATE UNIVERSITY

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Perinatal Ventriculomegaly in the Context of Bronchopulmonary Dysplasia and Pulmonary Hypertension: A Case Series

Michael Morrison[1], Jake Haver[1], Nina Shank MD[2], Michael Marian Bercu MD[2]

1. College of Human Medicine, Michigan State University

2. Division of Neurological Surgery, Corewell Health West Michigan, Grand Rapids, MI

Introduction

- Chronic cerebral hypoxia is often observed in anatomical changes of the neonatal and perinatal brain.
- There is increasing evidence mounting in the linkage between brain remodeling and pulmonary disease of prematurity[1-3].
- Cerebral hypoxia has been linked with inflammatory cytokine release resulting in increased permeability of the blood-cerebrospinal fluid (CSF) barrier and subsequent vasogenic edema and altered CSF flow dynamics[4].
- Highly prevalent in premature neonates, bronchopulmonary dysplasia (BPD) and persistent pulmonary hypertension (PHTN) present the ideal nidus for widespread chronic hypoxia[5,6].
- Hypoxia-inducible factors (HIFs) upregulated by hypoxia result in necrosis and damage to the choroid plexus and ependymal cells lining the ventricles[4,7-8].
- We present seven cases in which we hypothesize these neuroinflammatory mechanisms result in local destruction and increased permeability leading to vasogenic edema and ventriculomegaly.

Methods

- Literature reviewed: PubMed, Scopus, Google Scholar.
- Search modifiers included: *ventriculomegaly, hydrocephalus, hypoxia, ischemia, pulmonary hypertension, bronchopulmonary dysplasia, premature, neonatal, perinatal.*
- Articles were included based based on study relevance, language, format, and strength of evidence.
- Patient information was extracted retrospectively from a secure electronic medical record.

Case Series

- Seven neonates with severe respiratory complications developed ventriculomegaly.
- Six were delivered preterm.
- Most (5/7) were tracheostomy-ventilator dependent.
- Maternal risk factors: substance use, preeclampsia, hypertension, diabetes, poor prenatal care.
- Ventricular changes detected at birth or within first months.

Table 1. Details of Cases Included in Series

Patient (Age/Sex)	Gestational Age at Delivery	Birth Weight (kg)	Pulmonary History	Ventriculomegaly Onset	IVH (Grade)	Shunt
#1 2Y F	23w2d	0.60	BPD	Birth	IVH (Grades 3 and 4)	Y
#2 5Y M	26w2d	1.22	TBM, PHTN	Birth	IVH (Grade 1)	N
#3 3Y M	29w6d	0.74	NRDS, PHTN	4 months old	N/A	N
#4 8m M	35w0d	2.41	NRDS	3 months old)	N/A	N
#5 12m M	23w0d	0.42	BPD, PHTN	Birth	N/A	N
#6 4Y F	39w0d	4.19	LGM, NRDS	Birth	N/A	N
#7 5Y M	22w0d	0.53	NRDS, PHTN	Birth	IVH (Grades 1 and 3)	Y

***BPD, Bronchopulmonary dysplasia; IVH, Intraventricular hemorrhage; TBM, Tracheobronchomalacia; PHTN, Pulmonary hypertension; LGM, Larnygomalacia**

Discussion

- Long established is the relationship between premature birth with BPD and germinal matrix hemorrhage; however, little attention has been devoted to the role of chronic hypoxia in ventricular development.
- HIFs possess local neuroinflammatory activity on transcription factors at the blood-brain barrier.
- HIFs have been found to be elevated in rat studies in which chronic hypoxia resulted in increased local vascular permeability and insult to the choroid plexus[8].
- A study performed on dogs revealed increased radiolabeled albumin inside the basal cistern after inducing hypoxia in the cerebrum[7].
- Hypoxia has also been found to upregulate aquaporin channel activity in astrocytes and ependymal cells, resulting in decreased CSF outflow and subsequent hydrocephalus[9,10].
- From a clinical perspective, the findings in the cases and in animal models suggest that further attention must be allocated to the intracranial manifestations of premature pulmonary disease to ensure early recognition and the need for early neurosurgical intervention to improve quality of life and functional outcomes.

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