

Failure to Thrive Related to Nasal Encephalocele in a Toddler: A Diagnostic Challenge

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Abstract

Infants with an extremely low birth weight, who receive intensive unit care in the neonatal period may have severe unrecognized neurologic sequelae. We describe a 3-year-old boy, born preterm small for gestational age, who presented with food aversion, failure to thrive, and recurrent upper respiratory tract infections. Because of persistent rhinorrhea, nasal endoscopy was performed revealing a gray polypoid mass in the right nasal cavity. β -trace protein concentration in the nasal secretions confirmed cerebrospinal fluid (CSF) leakage. Magnetic resonance imaging showed perforation of the lamina cribrosa with a large nasal encephalocele. The clinical presentation of growth retardation, recurrent infections, hyponatremia, and hypoalbuminemia could be explained by persistent loss of CSF. Following surgical correction of the defect, gradual recovery of the overall condition, including catch-up growth occurred. Reconstruction of perinatal care in this patient revealed complicated nasotracheal intubation immediately after birth, providing an adequate explanation for an acquired perforation of the lamina cribrosa.

Keywords

- ▶ failure to thrive
- ▶ encephalocele
- ▶ lamina cribrosa
- ▶ neonatal intensive care
- ▶ nasotracheal intubation

Introduction

Preterm birth, particularly in combination with fetal growth retardation, has many short- and long-term neurologic complications. Follow-up programs for preterm born subjects have contributed to better recognition of sequelae and improved care for those with suboptimal neurodevelopment outcomes.

Failure to thrive is a generic description of reduced age-appropriate growth and (particularly physical) development, usually due to an underlying chronic condition or illness. The differential diagnosis is long, and it may be hard to confirm a specific cause and/or disease. Particularly in infants, the relationship between nutrition and growth and development with failure to thrive is often difficult to disentangle, especially when comorbidity due to preterm and/or small

for gestational age (SGA) birth is present. We describe an exceptional case of failure to thrive as a consequence of persistent nasal cerebrospinal fluid (CSF) leakage due to neonatally acquired perforation of the lamina cribrosa. The background and merits of analysis of β -trace protein as the diagnostic marker to confirm CSF leakage are discussed.

Case Report

Patient R was born at 25^{5/7} weeks gestational age by cesarean section, following a pregnancy complicated by hemolysis, elevated liver enzymes, and low platelet syndrome of the mother, which led to fetal growth retardation. A SGA boy, weighing 640 g was born with APGAR (appearance, pulse, grimace, activity, respiration) scores of 2, 4, and 5 after 1, 5,

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and 10 minutes, respectively. He was intubated immediately postpartum because of respiratory insufficiency. Subsequently, he was admitted at the neonatal intensive care unit where he stayed for more than 2 months because of preterm birth-related problems, such as respiratory failure and a patent ductus arteriosus. Ultrasound of the brain showed possible right-sided schizencephaly. This was not confirmed on a brain magnetic resonance imaging (MRI) performed at term. However, a cavum septum pellucidum was seen without description of further obvious abnormalities. Six months after birth, at a corrected age of 2 months, he was readmitted because of a rapidly progressive dyspnea. Multiple subglottic cysts were visualized on rigid laryngobronchoscopy. The largest cyst obstructed more than two-thirds of the tracheal lumen and was treated with laser immediately. After 3 subsequent days of treatment with steroids, he was successfully extubated and after another 2 days, he was discharged in stable condition. MRI of the neck showed no residual cysts. At a corrected age of 6 months, an outpatient appointment was made with the pediatric neurologist. Physical and neurological examination showed a normal head circumference, no hypertelorism or (other) facial dysmorphism, normal cranial nerve function, symmetric reflexes, and adequate coordination.

The 2nd year of life was characterized by regular visits to our outpatient clinic and several clinical admissions for respiratory tract infections. Concomitant persistent food refusal was interpreted as a recognized complication of infants who failed to get accustomed to normal oral feeding in the neonatal period as a result of prolonged intubation and tube feeding. No signs of chronic upper airway obstruction such as dyspnea or obstructive sleep apnea were found. A diagnosis of failure to thrive following preterm and SGA birth with recurrent (upper) respiratory tract infections and food aversion seemed to offer a good explanation for the clinical condition. Catch-up growth was absent, which was attributed to food aversion. Logopedic support had little effect. Further investigations to exclude immune deficiencies or gastrointestinal malabsorption revealed that sodium and albumin were in the low range of normal value. On one occasion, a very low serum sodium (122 mmol/L; normal 136–146 mmol/L) was measured during clinical admission for bronchiolitis. In search for an explanation of (external) sodium or albumin loss, no evidence of gastrointestinal, renal, or skin disorders was found. During subsequent outpatient consultation with the ear, nose, and throat specialist, a gray polypoid mass was seen in the right nasal cavity from which clear liquid seeped. A subsequent brain MRI showed a large right-sided frontoethmoidal encephalocele, protruding into the nasal cavity (► Fig. 1). Revision of the first MRI at term age showed a small protrusion of the right gyrus orbitalis (► Fig. 2). Careful reconstruction of the procedure of placement of the nasotracheal tube directly after birth revealed that intubation was difficult as a result of a cleft soft palate and was complicated by nasopharyngeal bleeding.

With an endoscopic transnasal procedure, the encephalocele was resected and the frontoethmoidal defect was closed. In the period thereafter, CSF leakage stopped, respiratory infections disappeared, and serum sodium and albumin normalized. With psychological support, gradual increase of food intake was obtained leading to sustained catch-up

growth. At the age of 5 years, approximately 2 years after closure of the encephalocele, his corrected height increased from -3 standard deviation (SD) to -1.5 SD and his corrected weight for length from -4 to -1.2 SD, that is, both within the normal range. Neurodevelopmental outcome at the age of 4 years showed that gross motor function and active language were somewhat below age-adjusted average, other mental and motor functions were age adequate. His right-sided sense of smell seemed inadequate. MRI at that age showed right frontal basal protrusion of the brain with distortion of the gyrus rectus (► Fig. 3).

Analysis of β -trace Protein as a Diagnostic Marker of CSF Rhinorrhea

Laboratory testing of the liquid from his nasal cavity showed a β -trace protein concentration of 14.7 mg/L, confirming CSF leakage. The use of β -trace protein as a diagnostic marker of CSF (e.g., in case of suspected leakage) is based on its high concentration as compared with other body fluids and secretions. β -trace protein can be detected in serum, although in a concentration $35\times$ lower than in CSF, whereas in normal nasal secretion, the β -trace protein concentration is even $130\times$ lower than in CSF.¹ Moreover, β -trace protein is absent in tear fluid. These concentrations distinguish β -trace protein from markers such as prealbumin and immunoglobulin G concentration. State-of-art quantification of β -trace protein concentration is done by nephelometric assay (N latex β -trace protein; a lyophilized reagent for Behring nephelometer systems, Dade Behring, Marburg, Germany) with high sensitivity and specificity in a reduced time span.

Polystyrene particles are coated with immunoaffinity antibodies from rabbits against human β -trace protein, which agglutinate in the presence of sample β -trace protein. This results in an increased light scattering, which can be measured and translated to a concentration. To define the results, they are compared with a calibration line, which is made up by a sample only containing human β -trace. In a diluted sample of 1:100, the detection range is 0.25 to 15.8 mg/L with the advantage that only tiny samples are needed; 5 μ L is recommended.^{2,3}

Discussion

In retrospect, this patient acquired a lamina cribrosa perforation due to complicated nasotracheal intubation directly after extreme preterm birth with fetal growth retardation. Nasal encephaloceles are rare but severe complications that may remain unrecognized for a prolonged period of time. The coronal MRI (► Fig. 1B) shows an anterior skull base defect at the lamina cribrosa on the right side. This is a parasagittal, off-midline unilateral defect. From an embryological point of view, congenital frontoethmoidal encephaloceles should herniate through a midline skull defect, often at the site of the foramen cecum and surrounded by nasal and ethmoidal bones.⁴ In our case, the skull defect is transethmoidal and parasagittal, and must therefore be iatrogenic. The enlargement is due to secondary herniation of intracranial content, as can be seen in the figures.

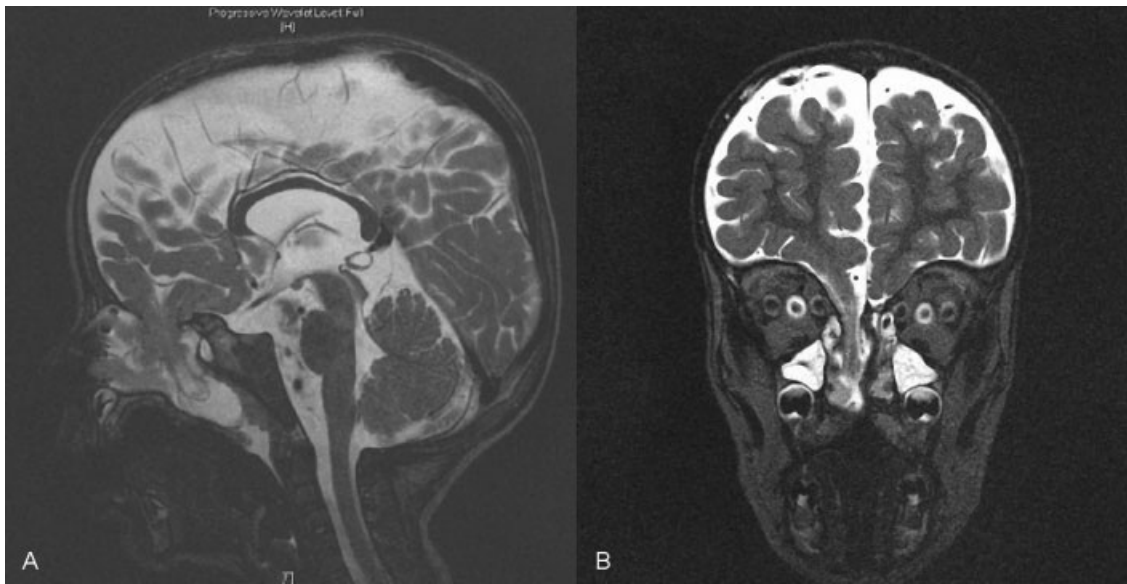


Fig. 1 (A) Parasagittal T1 and (B) coronal-weighted magnetic resonance images at the age of 3 years, where a nasal encephalocele is seen.

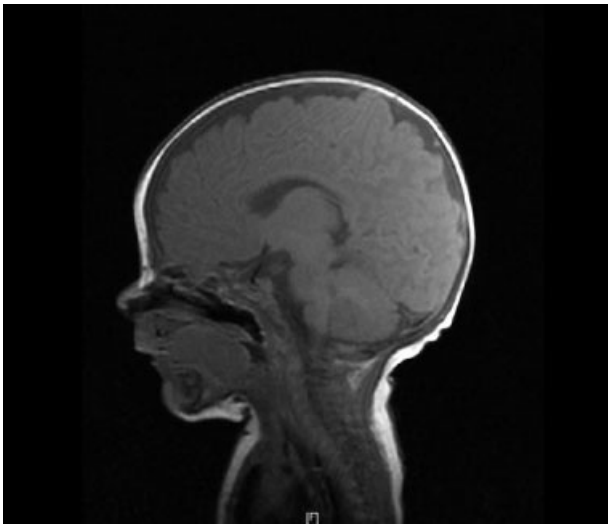


Fig. 2 Parasagittal T1-weighted magnetic resonance image at term age.

The relation of preterm SGA birth with subsequent (difficult) nutrition hampered catch-up growth. Recurrent respiratory tract infections for prolonged periods of time seemed to provide an adequate explanation of failure to thrive.

Despite his poor condition and persistent loss of proteins, the patient did not develop meningitis, although a direct portal of entry from the nasal cavity into the brain was present for almost 3 years. Resisting the option of nasal gastric tube feeding to improve his nutritional condition probably prevented potential severe complications from inadvertent (intrathecal) insertion of a feeding tube. The concealed subclinical course in our patient contrasts sharply with the prolonged initial neonatal resuscitation and rapid development of related ultrasound abnormalities, as reported in an older and a recent case of iatrogenic neonatal perfora-

tion of the lamina cribrosa.^{5,6} Failure to thrive is usually due to a shortage of calories, proteins, minerals, and other nutrients, resulting in physical growth that is significantly below the age-adjusted normal range.⁷ The list of possible causes is long, but in general, it can be categorized as (1) inadequate intake of nutrients, (2) loss or inadequate processing of nutrients, and (3) increase of caloric needs due to increased metabolism.⁷ In our patient, we concluded that failure to thrive was a result of food aversion, loss of nutrients (protein, minerals), and increased caloric need for catch-up growth, hence a combination of (1) to (3).

The improvement that occurred following closure of the lamina cribrosa supports the contribution of (2) and (3). This may also have supported the subsequent successful treatment of his food aversion. The concentration of β -trace protein in nasal secretions confirmed the suspicion of CSF leakage. The relation of external protein (albumin and globulin) loss with malnutrition and recurrent infections is well known. Yet, there is scarce literature regarding the relation of hyponatremia with prolonged CSF leakage. A case report in 2007 described an 18-month-old boy with liquorrhea and hyponatremia due to a congenital craniopharyngeal channel.⁸

In conclusion, a nasal encephalocele may develop as a result of unrecognized traumatic perforation of the lamina cribrosa during neonatal resuscitation. Following complicated nasotracheal intubation in very low birth weight newborns, the possibility of this complication should be realized. In absence of immediate clinical symptoms and signs, this condition may have a prolonged subclinical course. Other common complications of prolonged intensive care for preterm birth following intrauterine growth retardation may inadvertently be held responsible for this rare case of failure to thrive. Demonstration of β -trace protein concentration in nasal fluid, reconstruction of the neonatal history, and subsequent MRI led to a definitive diagnosis. We strongly

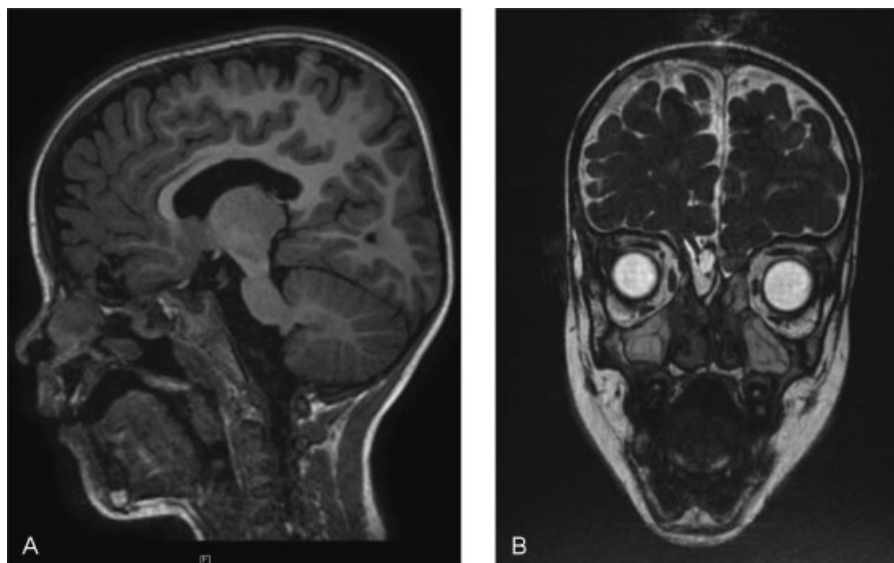


Fig. 3 (A) Parasagittal and (B) coronal magnetic resonance image 2 years after reconstruction.

recommend avoidance of nasal tube feeding and early nasal endoscopy when suspicion arises for nasal encephalocele.

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