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# Desaturation During Cry in the Neonatal Period

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## Case Presentation

A 10-day-old boy was addressed to our unit by his pediatrician for intermittent stridor associated with frequent episodes of desaturation while crying. Prenatal and perinatal periods were uneventful and the baby was born at term (41 weeks of gestation) to a primipara mother. Neonatal adaptation was good (Apgar score 8/9/10). The baby was small for gestational age with a weight of 2985 g (third to 10th percentile). A hoarse cry was present from the second day of life. He was exclusively breastfed without fatigue or perspiration during feeding. The weight gain was adequate (20 g per day). At 10 days of life, the physical examination demonstrated stridor with costal retraction and 86% oxygen saturation while crying (maximum 90 seconds), reason for which the child was hospitalized for further investigations.

## Hospital Course

During preliminary investigations, we performed a chest X-ray that was normal without signs of upper airway extrinsic compression. Cardiac investigation (electrocardiogram and echocardiography) demonstrated a patent foramen ovale. Endoscopy was performed, which excluded a vocal cord paralysis, a laryngomalacia, an extrinsic tracheal compression, or a bronchial tree anomaly. Endoscopy revealed discrete arytenoid inflammation indirectly suggesting gastro-esophageal reflux. During endoscopic visualization, breath-holding spells (BHS) occurred just after crying with total vocal cord collapse, oxygen desaturation to 80%, and cyanosis. He spontaneously recovered after 60 seconds. The oxycapnometry showed a $PCO_2$ mean value of 6.13 kPa, with a mean $PO_2$ value at 94%. Blood gas analysis, hemoglobin, electrolytes measurements, and blood iron level (iron = 26 μmol/L [8-33 μmol/L] and ferritin = 208 μg/L [11-342 μg/L]) were normal. Cerebral ultrasound and magnetic resonance imaging excluded structural lesions, such as Arnold Chiari type 1 malformation, a delay in myelination, or increased echogenicity on the ganglionic eminence. General and neurologic examinations showed normal muscle tone, strength, and posture, symmetric movements of all limbs, normal head circumference (35 cm, 25th percentile), and alertness appropriate for age. Evolution was marked by new episodes of crying followed by BHS with desaturation and cyanosis (30-60 seconds) without bradycardia or link with feeding period and with spontaneous recovery. Interestingly, the family history revealed that the father had symptoms compatible with BHS in early childhood (4 months of age). None other pathology was relevant in the family history.

Based on clinical examination and laboratory results, we concluded that the patient suffered from BHS, and we treated the gastro-esophageal reflux by milk thickening and proton pump inhibitors. He was discharged from the hospital after 9 days.

One week after discharge, we noticed that there was a reduction of symptoms, a disappearance of the stridor, and normalization of the child's voice. The nocturnal oxycapnometry was repeated 1 month after hospitalization and showed neither desaturation nor hypercapnia. The patient was followed-up in our outpatient clinic over a 9-month period. At the end of the first month of follow-up, the parents decided to stop the gastro-esophageal reflux treatment. Additionally, the patient was diagnosed for a galactose-6-phosphate dehydrogenase deficiency on the usual neonatal

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screening without favism or anemia. All symptoms of BHS stopped at 5 months of age.

## Final Diagnosis

Breath-holding spells.

## Discussion

Breath-holding spells correspond to an episode of change in behavior after a stimulus such as anger or pain and is characterized by sudden repetitive cyanosis, apnea, modification in postural tone, or rarely tonic-clonic activity without neuronal damage.[1] Benign BHS are described in up to 27% of healthy children, whereas severe BHS are less frequent with occurrence varying between 0.1% and 4.6%. BHS diagnosis is more frequent in boys than girls with a peak age of onset between 6 months and 4 years of age. Complete disappearance is seen at the age of 6 years.[2] Two different forms of BHS are described in the literature: the pallid and the cyanotic forms. The pallid form is a loss of consciousness associated with apnea, pallor, and diaphoresis possibly because of changes in the cardiovascular system such as an extreme bradycardia, and even a few seconds of asystole.[3] Minor trauma is the most common etiology. In the cyanotic form, the child is usually angry and the initial cry is followed by a breath-hold after forced expiration with cyanosis and apnea. However, the pathophysiology of both forms is not fully understood.[4,5] In our case, the age where BHS occurred was not within the classical age frame and presentation was not compatible with the cyanotic form. Before 6 months of age, these events have been currently reported as apparent life-threatening events (ALTE). Recently, the Academy of Paediatrics proposed a new terminology for ALTE. ALTE was substituted with brief resolved unexplained event (BRUE).[6] BRUE concerns children under the age of 1 year that present with a short single resolved event. BRUE occurs in 1% of healthy children and 50% of these cases show severe episode without associated etiology.[7-10] The repetitive nature of the events in patients suffering from BHS excludes the diagnosis of BRUE. In our patient, BHS neonatal cases are rarely described in the literature and are a difficult diagnosis. To our knowledge, there are only very few case reports of neonatal BHS. Singh[7] described a case of neonatal BHS in a 20-day-old infant. The authors based their diagnosis on the typical history and clinical presentation with a confirmation between the third and the fifth weeks of life. Breukels et al[8] reported a case of BHS in 3-day-old newborn with a positive family history of BHS whose diagnosis was established at 4 months of life. The symptomatology persisted for 4 months and the prescribed iron supplementation did not show any beneficial effect. Bhat and Ali[9] described a case of neonatal BHS with the first episode also detected on the third day of life and treated with iron supplementation. Total recovery occurred at 4 months of life. In our case, symptoms started at 2 days of life, diagnosis was determined during the third week of life, with a complete spontaneous recovery at 5 months of life. Seizure, cerebral anomalies (Arnold Chiari malformation, myelination anomalies), cardiac anomalies (long QT syndrome or Brugada syndrome), vasovagal syncope, infectious diseases, vocal cord palsy, and laryngospasm were not seen. We retained BHS diagnosis only after having excluded other etiologies.[6]

The presence of a hoarse voice at birth, stridor, and sporadic arrest in respiration incited us to perform a large number of examinations. These investigations allowed us to exclude upper airway pathology (laryngomalacia), tracheal anomalies (abnormal vascular ring), or a cerebral etiology (Arnold Chiari type 1, abnormal myelinization, or epileptic syndrome). Only the laryngotracheal endoscopy revealed anomalies with periodic respiratory arrest or desaturation during crying that correlated with the typical clinical observations of BHS diagnosis. In our case, BHS was observed and recorded during this examination and might be due to a disagreeable stimulus during the procedure that led to crying. Physical examination, film of events, and observation with cardiac and respiratory monitoring are the standard noninvasive investigations conducted to validate a diagnosis of BHS. The clinical course of BHS is generally benign and a complete spontaneous resolution is expected. In our case, the familial history suggests a genetic association with BHS. Attention to familial history is indeed required to exclude genetic factors, which account for one third of cases of BHS[11] and for familial dysautonomia.[12]

From a therapeutic perspective, iron supplementation was proposed due to its possible interplay with catecholamine metabolism and in the functioning of enzymes or neurotransmitters of the central nervous system.[13] In addition to limited side effects, this treatment is suitable for children of all ages suffering from BHS since they were described to be more prone to iron deficiency anemia.[14] Other off-label treatments have been prescribed for patients with important and iterative BHS, such as Piracetam, a cyclic derivate of the GABA molecule, or the implantation of cardiac pacemakers.[3,15]

In conclusion, this case report demonstrates that BHS diagnosis has to be evoked even in the neonatal period. Clinical history and complete examination are essential to diagnose BHS. Spontaneous resolution of symptoms can be expected without drug treatment (aside from iron supplementation). Although there were no adverse

outcomes resulting from delay in diagnosis, the fact remains that the cost incurred from long hospitalization and parental stress could be avoided with correct, early diagnosis. Description of neonatal cases and a better knowledge of this entity are important and may help physicians correctly diagnose BHS.

## Author Contributions

CS: Drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
KAS: Drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
CMK: Manuscript revision; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
IL: Manuscript revision; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
ST: Drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
RC: Manuscript revision; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
CBA: Manuscript revision; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.
IRM: Drafted the manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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