Annals of Clinical Case Reports

Case Report
Published: 10 Jun, 2023

An Infant with Subgaleal Hemorrhage, Hypoxic Ischemic Encephalopathy and Multiple Fractures – Iatrogenic or Genetic?

Lazarovits G[1,2], Koplewitz BZ[2,3], Harel T[2,4] and Eventov-Friedman S[1,2]*

[1]Department of Neonatology, Hadassah Medical Center, Hebrew University of Jerusalem, Israel

[2]School of Medicine, Hebrew University of Jerusalem, Israel

[3]Department of Medical Imaging, Hadassah Medical Center, Israel

[4]Department of Genetics, Hadassah Medical Center, Israel

Abstract

Subgaleal Hemorrhage (SGH) is a serious complication of delivery that can be fatal. Most often, it occurs as a result of a difficult delivery. In this paper, we describe the case of a neonate with SGH and bone fractures. As a result of the hemorrhage, he suffered from hemodynamic instability and asphyxia. Additionally, the infant displayed dysmorphic features which raised suspicions of an underline disease. A thorough evaluation revealed that the infant was suffering from a rare fatal genetic disease rather than a birth injury.

Introduction

Subgaleal Hemorrhage (SGH) in neonates is a medical condition that occurs when blood accumulates between the scalp and the skull's periosteum. It occurs usually following an instrumental delivery (especially with a vacuum extractor [1]), a prolonged delivery, birth trauma, or a head injury. In severe cases it may result in significant morbidity including Disseminated Intravascular Coagulation (DIC), intracranial hemorrhage, hemorrhagic shock, seizures, and even death. Treatment of neonatal SGH depends on the severity of the condition. Mild cases may resolve spontaneously with supportive care, such as observation, analgesia, and close monitoring of the baby's neurological status. However, moderate to severe cases require urgent intervention, including blood transfusions, correction of any underlying coagulopathies and surgical drainage of the hematoma, when needed. The case report presented here discusses an unusual case, emphasizing the importance of investigating the underlying cause of severe SGH in depth.

Case Presentation

A 19-year-old woman was referred to cesarean section due to non-reassuring fetal heart monitoring following an unsuccessful internal version trial for breech presentation at 37 weeks and 4 days' gestation. This was the first uneventful pregnancy of an Arab Muslim healthy couple who were second degree cousins. Fetal ultrasound screenings were normal except for 10 mm right renal pelviectasis. The mother reported decreased fetal movements throughout the third trimester. Parents were offered late amniocentesis for genetic testing yet opted out. The infant was born after difficult head extraction and required intubation due to bradycardia and poor oxygenation. The Apgar scores were 1, 3 and 3 at 1, 5, and 10 minutes, respectively. Birth weight was 3,290 grams (69^{th} percentile [2]). There was no evidence of intrauterine asphyxia in the umbilical cord blood gases, which showed PH-7.19, PCO_2-85 mmHg, a base excess (-9) and HCO_3 19.7 mmol/L. Physical examination revealed head circumference of 35 cm (82^{nd} percentile [2]), SGH, micrognathia and a short thorax. Breath sounds were symmetric and aeration was fair. Heart sounds were normal. Multiple hematomas and swelling were detected in all extremities. Other abnormal findings included left hand deformation, a contracture of the left elbow and ulnar deviation of fingers on both hands; proximal interphalangeal contractures on several fingers, abnormal palmar creases (suspected single palmar crease, difficult to ascertain due to severe edema), and prominent heels. He had normal penis but underdeveloped/missing scrotal sac. Neurological examination also revealed quadriplegia, minimal and inefficient spontaneous breathing, and no response to pain. Upon admission to the NICU no spontaneous movements were detected. Blood pressure was low.

OPEN ACCESS

Correspondence:
Gilad Lazarovits, Department of Neonatology, Hadassah Medical Center, Hebrew University of Jerusalem, Israel, Tel: +972549374161; E-mail: gilad.lazarovits@mail.huji.ac.il

Received Date: *16 May 2023*
Accepted Date: *06 Jun 2023*
Published Date: *10 Jun 2023*

Citation:
Lazarovits G, Koplewitz BZ, Harel T, Eventov-Friedman S. An Infant with Subgaleal Hemorrhage, Hypoxic Ischemic Encephalopathy and Multiple Fractures – Iatrogenic or Genetic?. Ann Clin Case Rep. 2023; 8: 2426.
ISSN: 2474-1655.

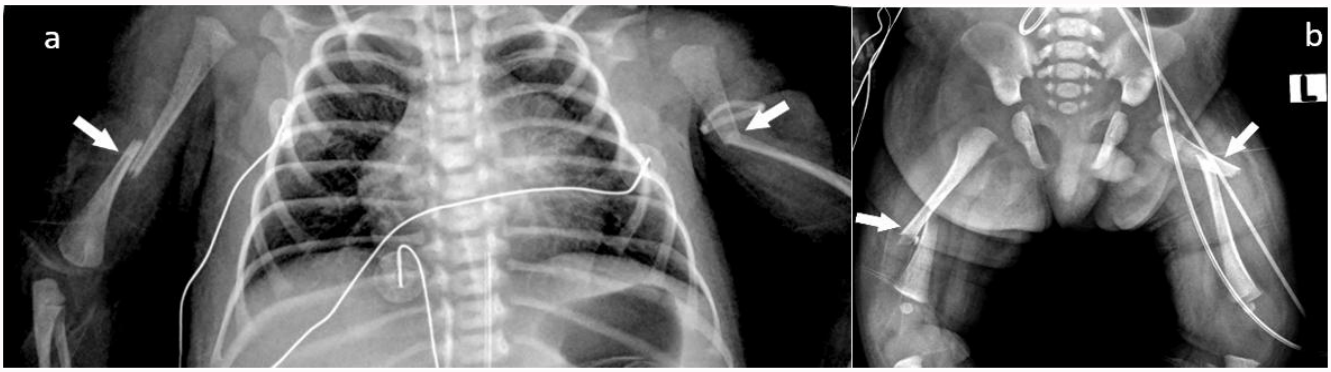

Figure 1: Radiographs of the chest (a) and the pelvis (b), showing bilateral fractures of the humeral and femoral bones (arrowheads). Note the gracile appearance of the ribs and the underdeveloped scapulae and pelvic bones, possibly related to intrauterine fetal hypokinesia.

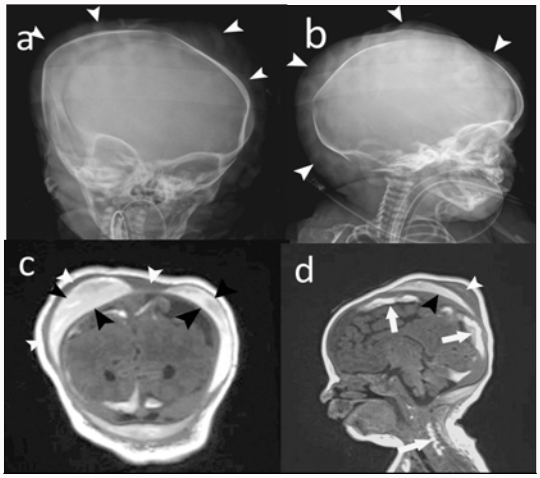

Figure 2: Anteroposterior (a) and lateral (b) skull radiographs and coronal (c) and sagittal (d) MR images, showing marked soft tissue swelling (arrowheads in a, b) due extensive SGH (white arrowheads in c, d) and bilateral cephalhematomas (black arrowheads), as well as parietal, occipital and cervical spine subdural hematomas (white arrows).

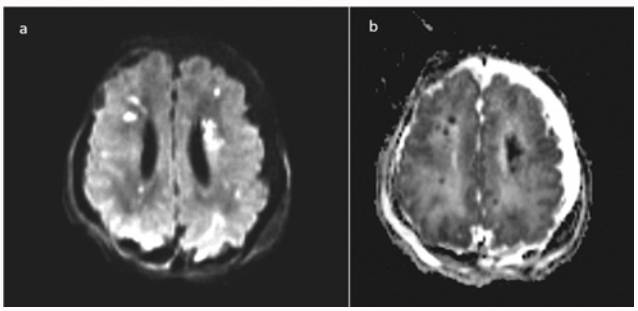

Figure 3: Axial MR images showing bilateral periventricular foci of increased signal intensity in Diffusion-Weighted Imaging (DWI, a) with decreased signal-intensity in the correlating ADC image (b), consistent with ischemic foci.

Arterial blood gases in the NICU revealed PH-6.97, PCO_2-55, base excess (-23). Lactate was elevated, at 11 mmol/L. Hematological blood profile showed hematocrit of 33%, thrombocytopenia (54 K/mL), and DIC with low fibrinogen of 44 mg/dL. Liver enzymes were elevated. Chest and pelvis radiographs showed fractures in bilateral femoral and humerus bones, as well as underdeveloped, gracile ribs, scapulae and pelvic bones (Figure 1). Initial cranial ultrasound demonstrated a large SGH with no brain parenchymal or intraventricular bleeding or midline shift. Due to signs of neonatal asphyxia a therapeutic hypothermia was initiated for 3 days. Cerebral function monitoring recording showed a burst suppression pattern typical to profound inactivation of the brain associated with severe Hypoxic Ischemic Encephalopathy (HIE). Brain MRI at the age of 8 days demonstrated bilateral cephalhematoma, bilateral subdural hematoma, and posterior fossa bleeding that exceeded to the spinal cord (Figure 2). Subcortical and periventricular foci of high signal intensity were seen in Diffusion-Weighted Sequence (DWI) with low signal intensity in the ADC map, consistent with foci of ischemia (Figure 3).

The differential diagnosis for the hypotonia in this case included HIE, SGH with secondary DIC, and decreased movements due to cord compression from the spinal bleeding. The congenital contractures (arthrogryposis) and the history of decreased fetal movements raised suspicion of an underlying genetic diagnosis which included bone fragility. Parental consanguinity suggested the possibility of an autosomal recessive inheritance. Proband-only exome sequencing revealed a homozygous frameshift variant in ASCC1 (chr10:g.73972995AC>A [hg19]; NM_001198800.2; c.61delG; p.Val21SerfsTer43). The variant was not observed in public databases (gnomAD, TOPMed Bravo, GME variome). Two heterozygous carriers yet no homozygotes were found in the local database of approximately 15,000 exomes. It was classified as likely pathogenic according to ACMG guidelines [3]. Other variants in this gene have been implicated in autosomal recessive Spinal Muscular Atrophy (SMA) with congenital bone fractures 2 [SMABF2; MIM 616867]. Throughout his hospitalization, the infant's hemodynamic condition stabilized. However, no spontaneous movements or respiratory efforts were detected. Callus formation was not seen in the fractures' sites. At the age of one month, he had respiratory deterioration that led to his death.

Discussion

In this case report, we describe an unusual case of SGH. The common cause of SGH is difficult vaginal delivery especially with the use of vacuum extractor [1]. Other factors that increase the risk of SGH in neonates include a large head circumference, prolonged labor [4], and fetal distress during delivery. Rarely, cases are associated with coagulopathies such as hemophilia [5]. Cases of infants who are born hypotonic with other clinical and laboratory findings suggestive of HIE are numerous. The combination of SGH, HIE and multiple

fractures in this case, which were unproportioned and unexpected relatively to the maneuvers carried out during delivery, led us to perform a thorough genetic workup that resulted in the diagnosis of SMABF2. SMABF2 is a rare fatal autosomal recessive genetic disease in which neonates present with spinal muscular atrophy and congenital bone fractures. The disorder is characterized by fetal hypokinesia and severe hypotonia. These result in congenital contractures, consistent with arthrogryposis multiplex congenita, and increased incidence of prenatal fractures of long bones. Affected infants have difficulty breathing and feeding and often die in the first days or months of life [6-9]. The genetic mechanism is related to ASCC1 which encodes a protein of the ASC-1 cointegrator complex, which mediates the interaction of transcription factors with the basal transcription machinery to modulate gene expression. Knockdown of ASCC1 in a zebrafish model disrupted the highly patterned and coordinated process of motor-neuron outgrowth and formation of myotomes and neuromuscular junctions, and resulted in a swimming defect in the larvae [6]. Pathogenic variants cause a profound disturbance of neuromotor unit development. Accordingly, sural nerve biopsy of 2 patients showed signs of unmyelinated axon loss [6].

In summary, we present a case of an infant who suffered from pathological fractures and SGH that caused bleeding disorders, hemodynamic instability and asphyxia. After a thorough clinical investigation it was found that the cause for his problem was an infantile-lethal genetic syndrome, rather than an aggressive management in the delivery room. The genetic results led to appropriate counselling to the family for further pregnancies, including an explanation regarding autosomal recessive inheritance with 25% recurrence risk. Parents were advised to undergo preimplantation genetic diagnosis or prenatal testing in future pregnancies.

References

1. Colditz MJ, Lai MM, Cartwright DW, Colditz PB. Subgaleal haemorrhage in the newborn: A call for early diagnosis and aggressive management. J Paediatr Child Health. 2015;51(2):140-6.
2. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr. 2013;13:59.
3. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. Standards and guidelines for the interpretation of sequence variants: A joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015;17(5):405-24.
4. Levin G, Mankuta D, Eventov-Friedman S, Ezra Y, Koren A, Yagel S, et al. Factors associated with the severity of neonatal subgaleal haemorrhage following vacuum assisted delivery. Eur J Obstet Gynecol Reprod Biol. 2020;245:205-9.
5. Bayoumi MAA, Khider WM, Elmalik EE. Congenital haemophilia A presenting with subgaleal and intracranial haemorrhage following instrumental delivery. BMJ Case Re. 2022;15(4):e248030.
6. Knierim E, Hirata H, Wolf NI, Morales-Gonzalez S, Schottmann G, Tanaka Y, et al. Mutations in subunits of the activating signal cointegrator 1 complex are associated with prenatal spinal muscular atrophy and congenital bone fractures. Am J Hum Genet. 2016;98(3):473-89.
7. Giuffrida MG, Mastromoro G, Guida V, Truglio M, Fabbretti M, Torres B, et al. A new case of SMABF2 diagnosed in stillbirth expands the prenatal presentation and mutational spectrum of ASCC1. Am J Med Genet A. 2020;182(3):508-12.
8. Böhm J, Malfatti E, Oates E, Jones K, Brochier G, Boland A, et al. Novel ASCC1 mutations causing prenatal-onset muscle weakness with arthrogryposis and congenital bone fractures. J Med Genet. 2019;56(9):617-21.
9. Oliveira J, Martins M, Pinto Leite R, Sousa M, Santos R. The new neuromuscular disease related with defects in the ASC-1 complex: Report of a second case confirms ASCC1 involvement. Clin Genet. 2017;92(4):434-9.