Pierre Robin Syndrome and a Subglottic Mass in a Patient with Bruck Syndrome: An Unusual Presentation of an Extremely Rare Condition

ABSTRACT

The phenotypic spectrum of Bruck syndrome has broadened since its first description. Besides its orthopedic manifestations, other findings such as myopathy or cardiac disease have been reported in previous studies. A case is presented with Pierre Robin syndrome and subglottic mass. Because of the clinical picture of congenital high airway obstruction syndrome, emergency tracheotomy was performed upon delivery. An excisional biopsy under direct laryngoscopy was done later. The patient died of congestive heart failure when 8 months old. In conclusion, Bruck syndrome types 1 and 2 may not be phenotypically equivalent and there may be unexpected upper respiratory system findings.

Keywords: Bruck syndrome, Pierre Robin syndrome, tracheotomy, congestive heart failure, larynx

INTRODUCTION

Bruck syndrome differs from the classic osteogenesis imperfecta phenotype by the absence of blue sclerae and hearing loss, and the presence of congenital contractures and webbing (pterygia) of joints. The patients have normal intellect. There are 2 main types identified caused by different underlying mutations with similar phenotypic appearance: type 1 (FKBP10 gene, on chromosome 17q21) and type 2 (PLOD2 gene, on chromosome 3q24). The product of FKBP10 gene is a chaperone protein located in endoplasmic reticulum which ensures proper folding of collagen, and the patients who are homozygous for the mutated allele have decreased procollagen secretion and defective trimer formation of collagen type 1 and decreased cross-linking between collagen fibers. The protein encoded by the PLOD2 gene, on the other hand, is a telopeptide lysyl hydroxylase and the molecular defect causes aberrant cross-linking of bone collagen.

Here, a case is presented with Bruck syndrome with PLOD2 mutation who also had Pierre Robin syndrome (micrognathia, glossoptosis, and cleft palate) and a subglottic mass that necessitated an emergency tracheotomy procedure upon delivery.

CASE PRESENTATION

A 35-year-old female, gravida 3 and para 2, who was under prenatal obstetrical observation in another hospital, was applied to the department of obstetrics and gynecology in the authors’ secondary referral center. According to her last menstrual period, she was in the 28th week of her pregnancy. The patient and her husband had no history of consanguinity, and previous pregnancies and deliveries were uneventful. According to prenatal ultrasound examinations, the fetus had a short femur length according to the gestational age and findings consistent with fractures, so the family was offered whole exome sequencing (WES) due to the suspicion of osteogenesis imperfecta and non-invasive prenatal testing in the previous health care center. However, they refused both tests since they wanted the baby to be delivered, anyway. The family received genetic consultation. No other anomalies were reported in prenatal ultrasound examination. A cesarean section on the 32nd week 6th day was performed due to the early rupture of membranes and breech presentation.

A preterm, male baby (weight 1800 g, height 41 cm) was delivered in the operating room. After delivery, respiratory failure and cyanosis was observed despite application of face...
mask with oxygen supplementation, hence attending anesthesiologist attempted intubation and failed. The first author, who was available in the operating room for another case, was called on and emergency tracheotomy was performed. The patient’s airway was secured through a tracheotomy cannula with 3 mm of inner diameter. After the airway was stabilized, general head and neck examination revealed micrognathia, cleft palate involving both hard and soft palates, and glossoptosis, low set ears, and plagiocephaly. On musculoskeletal examination; the patient was hypoactive with short limbs and contractures. Grade 2 systolic murmur was audible on auscultation. The baby was needed to be transferred urgently to neonatal intensive care unit for close intervention and treatment; hence no detailed examination of the larynx other than direct structural evaluation with the help of the laryngeal blade of the anesthesiology team could be done. The examination revealed a soft tissue mass, obstructing the laryngeal inlet; however, due to the unanticipated involvement of the otolaryngologist, lack of imaging facilities in the operating room at the time, and urgency of the transfer, no photographic or video documentation of the examination could be obtained. The newborn’s lack of respiratory effort, breathing difficulty and decreased blood oxygen levels in pulse oximetry were attributed to prematurity by the neonatologist. Bilateral short femurs, bilateral bowing of tibia, right humerus fracture, flexion contracture of both lower limbs, and flexion of upper limbs were observed on X ray imaging (Figure 1). His echocardiogram showed patent foramen ovale.

Genetic analysis of COL1A1 and COL1A2 genes did not reveal any mutations for osteogenesis imperfecta; thus, WES analysis by next-generation sequencing was ordered and the PLOD2 gene was found to be mutated, leading to the diagnosis of Bruck Syndrome. A Velpeau bandage was applied for the right humerus fracture by the department of orthopedics. To rule out other possible coexisting airway anomalies, a computed tomography scan of the larynx was ordered, and detailed direct laryngoscopic examination under general anesthesia (DL) was planned after written informed consent was obtained.

Computed tomography scan showed laryngeal atresia with soft tissue density obliterating laryngeal lumen (Figure 2). Unfortunately, the timing of direct examination was delayed as the baby entered sepsis and his overall condition worsened. After his general status improved, a DL was done in the sixth month after delivery. On examination; the epiglottis, the false and true vocal folds, the arytenoids were intact and the vocal folds were mobile. However, there was a whitish subglottic mass moving with air ventilation through tracheostomy cannula which was in contact with but appeared to be separate from the vocal folds (Supplementary video). On palpation, it was hard in consistency and partially mobile with a peduncle attaching the cricoid cartilage lumen on the left side. An excisional biopsy was performed with the total excision of the mass. The pathologic examination revealed fibrosis with increased collagen deposition beneath a hyperkeratotic overlying epithelium resembling a hypertrophic scar (Figure 3).

During the period when a referral to a tertiary center was planned, the baby’s condition had deteriorated again with

Figure 1. Radiological imaging of findings: (A) Fracture in the right humerus. (B) Short femur and bowing of right tibia. (C) Healing of right humerus with callus formation.

Figure 2. Sagittal computed tomography slice showing laryngeal obstruction.

**MAIN POINTS**

- Bruck syndrome has underlying 2 main genotypic variants with variable phenotypic presentations.
- Clinicians should anticipate airway problems, especially in PLOD-2 mutations; and prenatal diagnosis and family counseling is important regarding prognosis and the emergency procedures that might have to be performed.
underlying sepsis, hence follow-up laryngoscopic examination could not be performed. Pulmonary arterial hypertension, moderate tricuspid valve regurgitation, and enlarged right atrium and ventricle were observed on echocardiography. He succumbed to death when he was 8 months old, due to congestive heart failure.

**DISCUSSION**

Despite being a very rare disease, the phenotypic spectrum of Bruck Syndrome has broadened since its first description in 1897. Besides its orthopedic manifestations; gastroschisis, myopathy, and congenital cardiac findings have been described which can be attributed to dystrophic collagen production. Congenital high airway obstruction syndrome (CHAOS) with concomitant tricuspid regurgitation and cardiac findings or micrognathia had PLOD-2 mutation. Although, it is currently believed that Bruck syndrome types 1 and 2 have similar phenotypic findings, with additional signs and symptoms in patients are going to be reported, it can be assumed that het-
erogeneity may appear in the future in these subtypes.

**Ethics Committee Approval:** N/A.

**Informed Consent:** Written informed consent was obtained from the patient who agreed to take part in the study.

**Peer-review:** Externally peer-reviewed.


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**Supplementary Video:** Subglottic mass in direct laryngoscopic examination.

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