Adverse Outcome in *FAM111A* : A Case Report

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Background:

The *FAM111A* gene (615292) is speculated to possess antiviral properties and regulate gene transcription; however, its function is largely unknown. Heterozygous pathogenic variants in this gene are associated with autosomal dominant Kenny-Caffey Syndrome (KCS) (127000) and osteocraniostenosis (OCS, also known as Gracile Bone dysplasia) (602361). Both syndromes are associated with impaired skeletal development with short dense bones, short stature, primary hypoparathyroidism, microphthalmia, triangular face, and frontal bossing. While patients with KCS can have a normal lifespan without cognitive abnormalities, OCS is believed to be lethal in utero or in the neonatal period. [1]

Figure 1. Note the frontal bossing, microphthalmia, sunken nasal bridge, and short limbs

Case presentation:

- We report a girl with c.1579 C>A pathogenic variant in the *FAM111A* gene who died of respiratory insufficiency at 4 months
- She was born at 37 and 1/7 weeks after a pregnancy complicated by IUGR with ultrasound discovery of short tubular bones
- NICU course was significant for respiratory distress requiring CPAP and high flow nasal cannula for 21 days, left radial fracture and right radial and ulnar fractures, and hypoparathyroidism
- She had a triangular face, low set ears, short tubular bones, frontal bossing, and a large anterior fontanel.
- She required G-tube feeds due to failure to thrive
- PICU admission occurred at 3 months of age with refractory tachypnea and poor gas exchange requiring prolonged ventilation and increased ventilator settings
- Pressure volume loops were suggestive of malacia, and therefore, a telescopic laryngoscopy and bronchoscopy was performed, which demonstrated posterior wall intrusion of the thoracic trachea during episodes of agitation
- Genetic testing for 21 genes associated with surfactant metabolism defects revealed no variants
- She underwent a G-tube to GJ microjet conversion in an attempt to reduce her risk of aspiration without any change in respiratory condition
- Unfortunately, death occurred at 4 months after progressive pulmonary support led to development of pneumothorax and pneumoperitoneum and parents wished for comfort care at this time

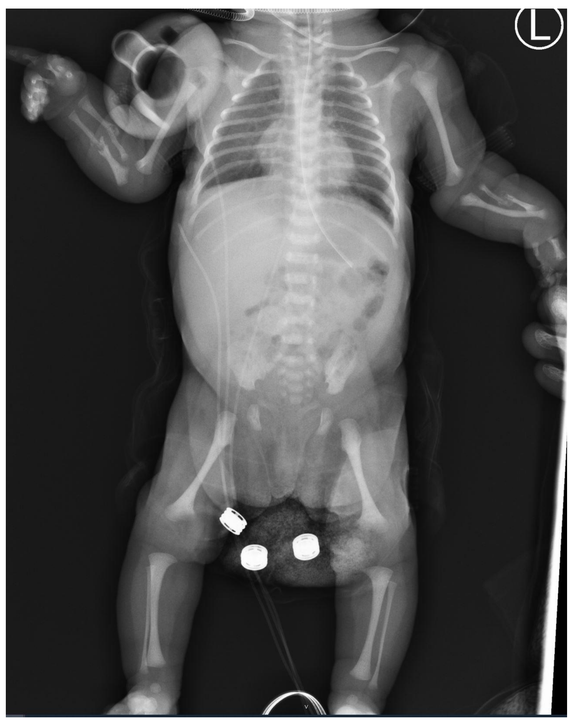

Fig. 2 Radiographs shows left radial fracture, right radial and ulnar fractures, and suspected medullary stenosis. Stenosis was not well appreciated in later radiographs

Conclusions:

- Our patient's lung disease was not restrictive, and did not appear to fit with typical KCS phenotype
- The c.1579 C>A variant seen here has been previously described in a patient diagnosed with osteocraniostenosis, who died at 8 months of age [1]
- Progressive respiratory failure was reported in one case of KCS; however, that patient developed symptoms at 8 years of age [2]
- This case highlights the clinical course of *FAM111A*-related conditions in the less-commonly described instances of infants who endure lethal complications of the disease
- Because our patient showed overlapping traits of both KCS and OCS, we suggest that her syndrome be referred to as a *FAM111A*-related disorder

References:

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