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Case Report

Severe Microphthalmia/ Anophthalmia in a Newborn with an Interstitial Duplication of 15q11.2-Q11.2

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- Severe microphthalmia
- Duplication of 15q11.2

CASE PRESENTATION

Our patient was a one-day old male who was born at 36 weeks and six days by repeat cesarean without any complications. The mom was a 30 year-old Gravida 6, Parity 3 female with history of three miscarriages all around three months of gestation. She received normal prenatal care and reports all normal ultrasounds during pregnancy. She had influenza during the pregnancy. She was treated with Tamiflu. She also took prenatal vitamins but denied any other medication, illicit drug, alcohol, or tobacco exposure. She had an elevated one hour diabetes screening with a normal three hour testing. Maternal Toxoplasma, Rubella, Cytomegalovirus, and Herpes Simplex Virus titers were all negative. Family history showed a 1 year old sibling who recently had a febrile seizure, and a 7 year-old brother with benign Rolandic epilepsy, ADHD, and stuttering. A maternal aunt had a retinal detachment around 17 years of age and a paternal uncle required eye surgery although the reason is unclear.

Physical exam (Figure 1) showed a healthy-appearing male newborn with a weight adequate for gestational age and a length and head circumference just above the 90thpercentile for gestational age. His anterior fontanel was open and soft. The left side of face showed a slightly shorter palpebral fissure, and slightly less full appearing left lower lip. The palate was intact, the nares were patent, and the ears were normal. The left orbit had a sunken appearance and fused appearance of lids. Slight separation of lid demonstrates some eyelashes protruding medially but we were unable to separate the lids beyond 1mm. Neither the Pediatric nor the Ophthalmology teams were able to visualize the remnants of the left, thus we were not able to measure the axial length by visual examination. The right eye appeared normal. It opened spontaneously. The right pupil was reactive, and the red reflex was present. The remainder of the examinationwas normal.

Hospital Course:

The following imaging studies were performed:

Head ultrasound: Negative.

Orbital ultrasound: (Figure 2) Normal appearing right globe, a probable lens is seen in the expected location of the left globe measuring 2x4 mm.

MRI brain without contrast: (Figure 3) In the expected location of the left globe there is an irregular shaped area measuring less than 10 mm. Findings suggestive of severe left microphthalmia with an atrophic optic nerve. The right globe was normal appearing.

Echocardiogram: showed a patent foramen ovale

Renal ultrasound: mild pelvic fullness in the left kidney

Newborn Hearing screen: passed bilaterally

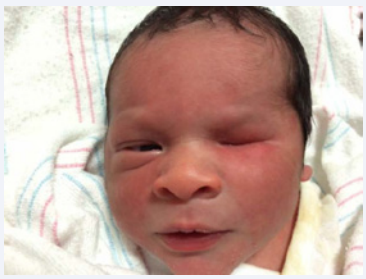

Figure 1 External examination of the patient with severe microphthalmia.

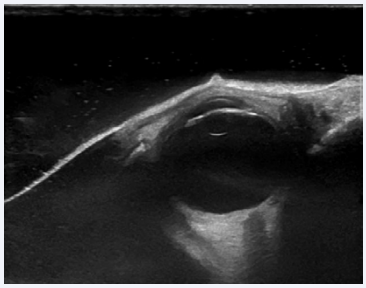

Figure 2 A probable lens showed, but no globe was visualized in the orbital sonogram.

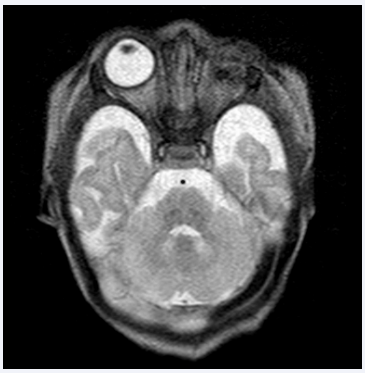

Figure 3 Head MRI showing a normal right globe and anirregular shaped area of decreased T2 signal measuring less than 10 mm in greatest diameter, most likely representing the abnormal left globe with severe microphthalmia.

Chromosome Microarray Analysis: 439 KB Interstitial duplication of 15q11.2 – q11.2

The ophthalmologic consultant interpreted the imaging studies as anophthalmia of the left eye and recommended outpatient follow-up to discuss cosmetic options and monitoring/protection of the right eye.

The genetics consultant assessed the patient as having severe microphthalmia vs. anophthalmia and that even though these cases have a 50% genetic cause, the patient did not have any findings of a genetic syndrome associated with that finding. They considered the family history significant for ophthalmologic problems, which could point towards a genetic component contributing to this finding.

DISCUSSION

Anophthalmia is a very rare condition which refers to the "complete absence of the globe in the presence of ocular adnexa" [1]. The finding can be associated with a number of syndromes or isolated and causes range from environmental, inheritable, to unknown. In this case, the patient did not exhibit any other abnormal physical characteristics that would point in the direction of CHARGE syndrome, Goetz Syndrome, Branchio-oculo-facial syndrome, Fraser Syndrome, or Goldenhar Syndrome. The patient's mother did have influenza during pregnancy and this is certainly a possible contributing factor as gestationally acquired infections are considered another possible cause [1].

The chromosomal microarray on our patient showed a 439 KB interstitial duplication of 15q11.2-q11.2. To date, the *deletion* of this area has been associated with variable expressions of delayed motor and speech development [2], developmental disorders and epilepsy [3], and Angelman and Prader-Willi syndromes [4]. *Duplication* has been associated with neuropsychiatric disorders [5], autism [6], and one patient with exomphalos, micrognathia, and Tetralogy of Fallot [7].

From the ophthalmologic standpoint, we found one study [8] that showed a duplication of the 15q11.2-q13.1 in one patient with right microphthalmia and left anophthalmia. Another study [9] mapped the autosomal dominant colobomatous microphthalmia locus to 15q12-q15, the region just distal to our patient's duplication.The clinical significance for our patient's duplication is unknown, but these reports plus the patient's family history may suggest a genetic component for severe microphthalmia/anophthalmia linked to the 15q region. Eye anomalies had not been previously reported in a patient with the 15q11.2-q11.2 duplication.

We suggest that a chromosomal microarray be performed in cases of severe microphthalmia/anophthalmia. Confirmation of changes in the 15q region may alert the provider to the early detection of other clinical problems, such as genetic syndromes and neurodevelopmental disorders.

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