Bilateral Anophthalmia Plus Syndrome: A Case Report

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Abstract

The objective is to report a case of a 1-year old male who was born to non-consanguineous marriage with a history of varicella zoster (chickenpox) infection in the first trimester of pregnancy, having cleft lip and palate and bilateral microphthalmia with bilateral congenital cysts with malformed orbits, and ill-developed maxillary sinuses.

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Introduction

Anophthalmia plus syndrome (APS) is a rare multisystem congenital malformation syndrome, most commonly presenting as anophthalmia or severe microphthalmia with cleft lip and/or palate.[1] These can also be associated with facial clefts and/or sacral neural tube defects. Prevalence of anophthalmia is 3 per 1,00,000 live births while that of microphthalmia is 14 per 1,00,000 live births. A syndromic association like APS can be found in estimated one-third of such cases while the bilateral presentation is an even rarer finding. The congenital cystic eyeball has a frequent association with bilateral severe microphthalmia. Pathogenesis of anophthalmia/microphthalmia is a complex interplay of single gene mutation, chromosomal anomalies, and environmental factors.[2] The association with midline defects underlines a common genetic pathogenesis; but the paucity of literature regarding APS prevents any hypothesis to be proven. There are only a handful of such cases, the first series of which was described by Fryns et al in 1995.[1] Here we present a case of a 1-year old male child who presented with bilateral clinical anophthalmia, cleft lip, cleft palate and a bluish mass protruding from the lower eyelid since birth.

Case History

A 1-year old male who was born of a full-term, caesarean delivery (indicated for meconium-stained liquor) with an ante-natal history of varicella zoster infection in the mother in first trimester, to non-consanguineous parents (27 years & 20 years) and was their firstborn, was brought to ophthalmology OPD with chief complaints of absence of eyeballs in both sockets, and a bluish mass in the lower eyelids of both sides, more prominent on the right side. He had a history of unilateral cleft lip and palate with lip repair done 6 months back. No other deformities were noted by the parents.

Physical examination revealed weight in 25th percentile (9.5 kg), height in 95th percentile (79 cm), head circumference of 43.5 cm, bilateral empty orbits with remnants of conjunctiva and soft tissues, and a bilateral cystic bluish mass in the lower eyelids of both eyes (right being more prominent) (Figure 1), bilateral mid-facial hypoplasia and cleft palate with ill-formed dentures, and a healed scar on the upper lip (Figure 2). The remaining systemic examination was clinically normal.

B-scan ultrasonography over the mass in the lower eyelid showed cystic lesions suggestive of congenital cystic eyeballs. No evidence of rudimentary globe was found. MRI scan showed bilateral microphthalmia (axial length-OD: 8.33 mm, OS: 7.5 mm) lying approximately 13.9 mm behind the eyelids, with cysts in both the orbits (Figure 3,4). Both orbits were enlarged with dimensions of 29 mm × 27 mm. Maxillary sinus hypoplasia was also noted along with cleft palate. MRI Brain showed mild ventriculomegaly.

The parents were counseled for the prognosis, need of removal of cysts with orbital reconstruction to treat the mid-facial hypoplasia and cosmesis, and further follow-up was advised.

Figure 1: *Bilateral anophthalmos with bluish mass below the lower eyelids, more prominent on the right side (Depicted by arrow)*

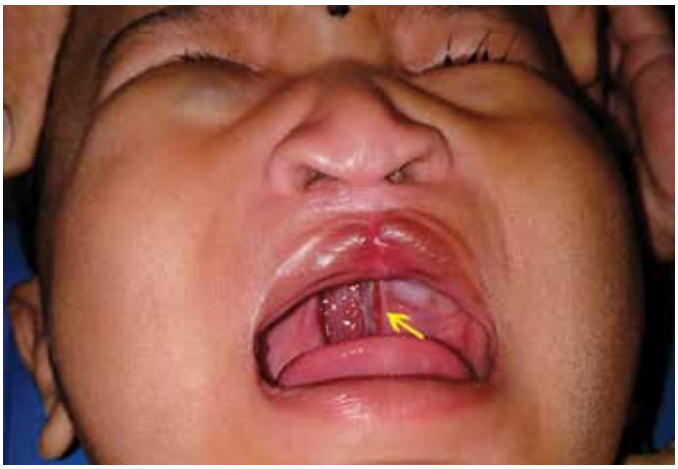

Figure 2: *Cleft palate (arrow) with repaired cleft lip*

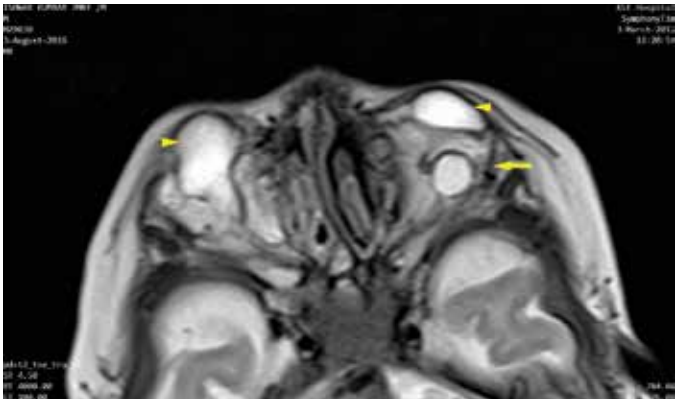

Figure 3: *Axial section of orbit on MRI showing bilateral cyst(arrow heads) and an anophthalmic eye in the right orbit (arrow)*

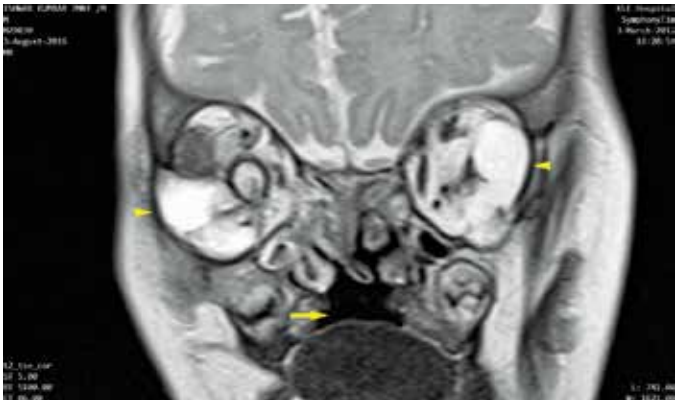

Figure 4: *Coronal MRI section showing bilateral cysts (arrowheads) and cleft palate (arrow)*

Discussion

Anophthalmia refers to complete absence of the globe in the presence of ocular adnexa (eyelids, conjunctiva, and lacrimal apparatus), while microphthalmia refers to a globe with a total axial length that is at least two standard deviations below the mean for age.[3] Without the radiological findings, severe microphthalmia (Axial length <10 mm at birth or <12 mm at age of 1 year) is often called as 'Clinical Anophthalmia'.

Congenital cystic eyeball is in itself an extremely rare manifestation which develops as a result of a partial or complete arrest in the invagination of the primary optic vesicle between the 2-7 mm stages of fetal development.[4] Arrested development occurring later in the 7–4 mm embryonic stage results in the more common microphthalmos with coloboma in addition to the cysts. Out of 46 cases that have been reported till date, the majority have a centrally placed large cyst while only Dash et al reported a case of a congenital ectopic en-cysted eyeball in the lower lid. Most of the cases reported till date are unilateral except for 2 cases. There is no proven or suspected chromosomal or genetic abnormality and only one case of Turner Syndrome and one with Orbeli Syndrome were found in the literature search. Histopathological studies of cysts suggest an inflammatory cause.[5,6]

Anophthalmia Plus Syndrome (APS) is also known as eponymous Fryns Anophthalmia/Microphthalmia Syndrome after the case series published in 1995.[1] The cases series reported 100% involvement of anophthalmia/severe microphthalmia, 89% incidence of oro-facial clefts, and 33% presence of ear anomalies, while coloboma was noted in microphthalmia cases. Few other case reports since Fryns have been reported, all of which were included in a brief review done by Makhoul et al in 2006.[6]

With a vertical transmission rate of 25%, the first-trimester infection with chickenpox doesn't result in spontaneous abortion, but congenital varicella syndrome is a known entity with the incidence rate of 2%. While skin lesions and limb hypoplasia are most common presentations, ocular anomalies like microphthalmia, chorioretinitis, and cataract have been reported in 44-52% of the cases.[7] Cleft lip and palate association with intrauterine varicella infection has not been widely reported or proven yet.

Leichtman et al in 1994 reviewed causes for microphthalmia/anophthalmia in association with multiple syndromes; and multiple syndromes also were found to be associated with cleft lip and palate in the same study.[8] Fryns had suggested an autosomal recessive inheritance pattern for the APS, though it has not been conclusively proven.[9] Verma & FtizPatrick in 2007 have described chromosomal abnormalities associated with Microphthalmia/Anophthalmia/Coloboma (MAC Syndrome) which accounts for about 30% of such cases while single gene mutations account for 1% of the disease spectrum.[2] Recent genetic studies done by Williamsons and FitzPatrick in 2014 demonstrated a genetic cause in 80% of the cases with bilateral severe microphthalmia/anophthalmia.[10]

Due to a small number of cases reported with the simultaneous presentation of microphthalmia/anophthalmia with oro-facial clefts, the genetic association and locus determination still remains elusive, and risk factors for such syndromes need to be evaluated , as consanguinity was found to be present in only 1 reported case till date.

The index case fits into the description of Anophthalmia Plus Syndrome, and associated presence of cystic eyeball may be one of its variation. Treatment of such cases are mainly for cosmetic reason as the cystic lesions rarely turn malignant, and therefore the treatment often gets delayed. Orbital exploration, removal of the cysts and placement of appropriate orbital implant to aid the normal mid facial development is important and needs to be emphasized to the parents to help them understand the need of treatment.

References

1. Fryns JP, Legius E, Moerman P, Vandenberghe K, Van den Berghe H. Apparently new 'anophthalmia-plus' syndrome in sibs. *Am J Med Genet* 1995, 58:113-114.
2. Verma AS, Fitzpatrick DR. Anophthalmia and microphthalmia. *Orphanet J Rare Dis* 2007; 2:47.
3. Bardakjian T, Weiss A, Schneider A. Microphthalmia/Anophthalmia/Coloboma Spectrum. 2004 Jan 29 [Updated 2015 Jul 9]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle.
4. Mann I. Development Abnormalities of the eye. *Philadelphia, JB Lippincott Co* 1957; 66-69.
5. Duke-Elder S. System of Ophthalmology, Congenital Deformities. Part II, Henry Kimpton London 1964; 111:451 & 481.

6. Makhoul IR, Soudack M, Kochavi O, Guilburd JN, Maimon S, Gershoni-Baruch R. Anophthalmia-plus syndrome: A clinical report and review of the literature. *Am J Med Genet Part A* 2007; 143A:64–68.
7. Andreou A, Basiakos H, Hatzikoumi I, Lazarides A. Fetal varicella syndrome with manifestations limited to the eye 1. *Am J Perinatol* 1995; 12:347–348.
8. Leichtman LG, Wood B, Rohn R. Anophthalmia, cleft lip/palate, facial anomalies and CNS anomalies and hypothalamic disorder in a newborn: A midline developmental field defect. *Am J Med Genet* 1994; 50:39-41.
9. www.oprha.net (ORPHA:1104)
10. Williamson KA, FitzPatrick DR. The genetic architecture of microphthalmia, anophthalmia and coloboma. *Eur J Med Genet* 2014; 57:369–80.

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