Abstract

Purpose of the Study: To evaluate morphologic data, risk factors, associated ocular as well as systemic abnormalities in cases of anophthalmia and microphthalmia.

Design: Retrospective, descriptive study.

Case Report: Four cases of anophthalmia were seen in Pediatric Clinic, Tripoli Eye Hospital in the first quarter of 2007. Two cases were boys and two were girls. Two cases had bilateral anophthalmos. The other two cases had one anophthalmic eye and the second eye was microphthalmic. So, we had 6 eyes with anophthalmia and 2 eyes of microphthalmia. Microphthalmic eyes showed chorioretinal colobomata and optic coloboma with no fixation. History of consanguinity was positive in one case. No other ocular or systemic abnormality were detected. All four cases came from western part of Libya, Aljabel Algarbi. One case gave history of folic acid intake by the mother during pregnancy, another case gave history of mother fever during pregnancy.

Recommendations: Proper antenatal care, avoid old age pregnancy, minimize multiple pregnancies, avoid environmental factors that may cause anophthalmia, microphthalmia. Proper genetic counseling is also needed. Antenatal diagnosis of these anomalies through chromosome analysis, US and MRI examinations. We also recommend proper management of these cases to improve vision, cosmetic appearance and avoid psychological disorders.

Keywords: Anophthalmia – Microphthalmia – Ultrasound (US) – Magnetic resonance imaging (MRI) – Genetic counseling – Prosthesis – Chromosomes.

Introduction

The eye begins to form at about 22 days of gestation and the globe structure is completed by 42 days. The first evidence of primitive eye formation occurs as the anterior portion of the neural tube is closing during the third week of gestation, a small depression (optic pit) is formed on either side of primitive forebrain, optic pit rapidly enlarge and form optic vesicle. Then the optic vesicles invaginate and form optic cup and the embryological development continue. Following the closure of embryonic fissure in the sixth week, most of the basic structures of the eye are present [1-3]. Rapid growth of the fetal eye occurs during gestational weeks 8-14 and eye growth parallel slower body growth after 30 weeks [4]. So, anophthalmia, microphthalmia can be diagnosed early in pregnancy by 7th week of gestation [5].

Definition and incidence:

The International Clearing House for Birth Defects Monitoring Systems defines anophthalmia and microphthalmia respectively as absence of an eye and the presence of a small eye within the orbit [6]. The combined birth prevalence of these conditions is up to 30 per 100,000 population, with microphthalmia reported in up to 11% of blind children. High-resolution cranial imaging, postmortem examination and genetic studies suggest that these conditions represent a phenotypic continuum. Both anophthalmia and microphthalmia may occur in isolation or as part of a syndrome, as in one-third of cases [7]. Anophthalmia / microphthalmia have complex etiology with chromosomal, monogenic and environmental causes identified. Chromosomal duplications, deletions and translocations are implicated. Of monogenic causes only SOX2 has been identified as a major causative gene. Other linked genes include PAX6, OTX2, CHX10 and RAX, SOX2 and PAX6 mutations may act through causing lens induction failure. FOXE3 mutations, associated with lens agenesis, have been observed in a few microphthalmic patients. OTX2, CHX10 and RAX have retinal expression and may result in anophthalmia / microphthalmia through failure of retinal differentiation [7-10]. Environmental factors also play a contributory role [9]. The strongest evidence appears to be with gestational-acquired infections, but may
also include maternal vitamin A deficiency, exposure to X-rays, solvent misuse and thalidomide exposure [10]. Diagnosis can be made pre- and post-natally using a combination of clinical features, imaging (ultrasonography and CT/MR scanning) and genetic analysis. Genetic counseling can be challenging due to the extensive range of genes responsible and wide variation in phenotypic expression. Appropriate counseling is indicated if the mode of inheritance can be identified [11,12]. Differential diagnosis include cryptophthalmos, cyclopia and synophthalmia, and congenital cystic eye. Patients are often managed within multidisciplinary teams consisting of ophthalmologists, pediatricians and/or clinical geneticists, especially for syndromic cases. Treatment is directed towards maximizing existing vision and improving cosmesis through simultaneous stimulation of both soft tissue and bony orbital growth. Mild to moderate microphthalmia is managed conservatively with conformers. Severe microphthalmia and anophthalmia rely upon additional remodeling strategies of endo-orbital volume replacement (with implants, expanders and dermis-fat grafts) and soft tissue reconstruction [13].

**Prognosis:**

The potential for visual development in microphthalmic patients is dependent upon retinal development and other ocular characteristics.

**Patients and Methods**

Four cases of anophthalmos seen in pediatric clinic in Tripoli Eye Hospital, in period from January 2007 to March 2007.

**History:**

1- Gestational-acquired infections such as rubella, toxoplasmosis, varicella, cytomegalovirus, herpes virus, influenza virus.
2- Any drug intake as thalidomide, warfarin and alcohol.
3- Consanguinity, family history of similar problem or other congenital anomalies as craniofacial disorders.
4- Exposure to X-rays.
5- Solvent misuse.
6- Maternal vitamin A deficiency.
7- Possible teratogens as herbicide, nicotinic acid, phenyl ketonuria, heavy metals.

**Diagnosis:**

Although diagnosis of anophthalmia, microphthalmia can be made pre and post-natally, yet in this study cases were only diagnosed after birth.

**Our diagnosis depended upon the following:**

1- Clinical features: We considered the eye microphthalmic when the axial length is two standard deviation below that of the population age-adjusted mean (axial length 21mm of an adult eye), corneal diameter 19mm.
2- Other associated ocular disorders such as: Sclerocornea, Peters anomaly, retinal dysplasia, papillo-macular fold hyperopia, squint.
3- Associated syndromes.
4- Imaging such as ultrasonography and CT/MRI-scanning.
5- Electrodiagnostic tests.
6- Genetic analysis: Chromosomal duplications, deletions and translocations have been implicated in both anophthalmos and microphthalmos selected genes with mutations linked to there conditions such as SOX2 gene. Cytogenic studies showed the locus to be at 3q26.3.
7- Examination for associated non-ocular abnormalities in our cases such as mental retardation, neurological abnormalities, facial dysmorphisms, post-natal growth failure, esophageal pathology and anomalies of male genitalia.
8- Genetic counseling when the mode of inheritance is identified.
9- Differential diagnosis from: Cryptophthalmos, cyclopia, synophthalmia and congenital cystic eye.
10- Affording any possible management according to the condition.
11- Laboratory investigation (TORCH).

**Results**

All 4 cases came from western part of Libya. In particular period of time 1st Quarter 2007, Aljabel Algharbi.

Maternal age less than 35 years in all 4 cases. Laboratory investigations negative for TORCH screen in all cases. Pediatric systemic examination: No other systemic abnormality detected.

The 2 cases with left microphthalmic eye have no fixation. Case of bilateral anophthalmia. History of Consanguinity (cousins). Two cases one eye right anophalmia, other eye left microphalmia. Two cases with left microphalmia: No fixation with microphthalmic eye, chorioretinal coloboma in microphthalmic eye.
Cases:

Case No. (1):
- 33 days male.
- Bilateral anophthalmos.
- History of other affected children in family (sister 3 years old other 2 normal, sister and brother).
- History of consanguinity.
- Folic acid tablets given during pregnancy.
- Baby has no other systemic abnormality (Picture 1 & Figs. 1,2).

Case No. (2):
- Sister of case 1.
- 3 years girl, bilateral anophthalmia.
- No other systemic abnormality (Picture 2 & Fig. 3) (CT scan orbit).

Case No. (3):
- 2 months male.
- Right eye anophthalmos.
- Left eye microphthalmos (with chorioretinal coloboma).
- No history of any abnormality during pregnancy.
- No history of consanguinity.
- No other systemic abnormality (Picture 3 & Fig. 4).

Case No. (4):
- 4 months female.
- Right anophthalmos.
- Left microphthalmos with chorioretinal coloboma and optic nerve coloboma.
- History of febrile illness during pregnancy (Picture 4).
Case 3 (Picture 3)

Case 3 (Fig. 4)

Case 4 (Picture 4)

Discussion

Recommendations:

1- *Antenatal care:*
   - Avoid pregnancy at very young or very old age (≤40 years), multiple births.
   - Avoid exposure to X-ray.
   - Avoid drug intake such as warfarin, alcohol, vitamin A deficiency.
   - Avoid viral infections such as rubella, herpes, CMV, influenza, ...

2- Avoid environmental factors such as heavy metals, solvent affording treatment misuse, thalidomide exposure, pesticide.

3- Genetic counseling.

4- Antenatal diagnosis:
   - Chromosome analysis by cytogenic studies upon amniotic fluid fetal cells (withdrawn after 14 weeks of gestation) or on chorioic villus sampling specimens.
   - Ultrasonography: Transvagal U/S at 12 weeks gestation in coronal, axial and coronoaxial planes.
   - MRI can supplement U/S findings.

References