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Clinical cases

Congenital anophthalmia. Report of a family series

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Abstract

Anophthalmia is the absence of an eye. This may be unilateral or bilateral and its prevalence is low. It results from developmental arrest of the globe during organogenesis. Three patients aged 22, 23 and 25, sisters, have congenital unilateral right-sided, bilateral and unilateral left-sided anophthalmia respectively. The only family history element is that their paternal great-grandfather also suffered from congenital unilateral right-sided anophthalmia. They were sent from the Regional Clinical Hospital to the Clinic of Trauma and Maxillofacial Prosthetics at Universidad de Concepción to be treated from their first months of life. The treatment included the use of sequential conformers to expand the eye sockets, and then individual ocular prostheses were prepared and installed. The rehabilitation of congenital anophthalmia is a major challenge. Early intervention, as was the case with these patients, makes a significant difference on the overall development of the patient and on the emotional well-being of the family.

Keywords: anophthalmia, ocular prosthesis, prosthetic eye.

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Introduction

Anophthalmia and microphthalmia are described as the absence of an eye and the presence of an atrophic eye in the eye socket; it may be unilateral or bilateral[1,2]. Congenital anophthalmia applies to all cases where there are no visible ocular remnants, and there is complete absence of ocular structures and neuroectodermal tissues inside the sockets. Therefore, to detect the difference between congenital anophthalmos and extreme cases of microphthalmos it is necessary to perform histological examinations[3].

Anophthalmia results from developmental arrest of the globe during organogenesis. Facial development begins in the fourth week of gestation and, by the fifth week, the eyes appear as an elevation of the lateral face. Congenital anophthalmia starts between the fourth and seventh week of development and is defined as the failure of outgrowth of the primary optic vesicle[13]. Congenital anophthalmia is much more severe when the arrest occurs early in the fourth week of gestation and there is no volume replacement in the rest of the development process[3].

The exact pathogenesis of anophthalmia remains unknown. It is believed that its genesis occurs in early gestation, and is classified into three type: primary anophthalmia is the absence in the closure of optic vesicles; secondary anophthalmia is caused by the arrest in eye development and is usually associated to failure of the neural tube formation; tertiary or degenerative anophthalmia is when there is regression or reversal of a previously formed optic vesicle[2,3]. A fourth type of anophthalmia would be the result of direct trauma to the globe.

Epidemiological studies have predicted two main factors causing anophthalmia and/or microphthalmia: heritable factors and environmental factors. High-resolution cranial imaging, post-mortem examination and genetic studies suggest that these conditions represent a phenotypic continuum, where we can identify different causes[2].

Heritable factors:

1. Chromosomal: Chromosomal duplications, deletions and translocations.

2. Monogenic: only SOX2 has been identified as a major causative gene, but scientists are studying other genes whose mutations might be linked to this pathology: PAX6, OTX2, CHX10, FOXE3 and RAX.

3. As part of a syndrome: Matthew-Wood syndrome, De Morsier's syndrome, among others.

Environmental factors also play an important role during pregnancy, including[2]:

1. Gestational infections such as rubella, toxoplasmosis, varicella and cytomegalovirus. Other viruses that have also been linked to this condition are herpes-zoster, parvovirus B19, the influenza virus, and Coxsackie A9, but there is no strong evidence in this regard.

2. Maternal vitamin A deficiency

3. Fever

4. Hyperthermia

5. Exposure to x-rays

6. Misuse of solvents and pesticides

7. Exposure to drugs such as thalidomide and warfarin

8. Exposure to alcohol

In addition, there are factors that could increase the risk of anophthalmia, such as[2]:

1. Maternal age over 40

2. Multiple births

3. Low birth weight

4. Premature birth

Birth prevalence for anophthalmia and microphthalmia has been estimated as 3 to 14 per 100,000 inhabitants respectively, although other evidence sets the combined birth prevalence of these malformations at 30 per 100,000 inhabitants[1,2]. This evidence suggests that one third of anophthalmia cases appear as part of a syndrome. Both anophthalmia and microphthalmia are more commonly bilateral[2].

The diagnosis can be made before and after birth through a combination of clinical features, imaging (ultrasound, computed tomography and magnetic resonance imaging) and genetic analysis[1,2]. Diagnosis is clinical, obtained by ophthalmological examination showing the complete absence of the globe or decreased ocular size relative to the contralateral eye[1]. Genetic counseling may be a challenge given the extensive range of genes responsible and the wide variation in phenotypic expression, which is indicated if the mode of inheritance can be identified. To establish a specific cause, it is necessary to undertake a comprehensive medical history, physical examination, family history, karyotyping and molecular genetic testing, imaging, renal ultrasonography, and audiology tests. Differential diagnoses include cryptophthalmos (or ablephary), cyclopia (also cyclocephaly or synophthalmia) congenital cystic eye and extreme cases of microphthalmia[2].

Case report

Three female patients aged 22, 23 and 25, sisters, have congenital unilateral right-sided, bilateral and unilateral left-sided anophthalmia respectively. The pregnancies were normal; their births were term births (40 weeks), spontaneous and eutocic; they had young parents who were healthy, not inbred and had no drug addictions. The mother

had no breakthrough processes, nor reported taking medication, alcohol, tobacco, or drugs during pregnancy. Besides the congenital anophthalmia finding, the patients had no other physical manifestations of malformations, and systemic pathologies were discarded at birth.

The initial ophthalmic exam of the 23-year-old patient revealed small palpebral fissures with absence of both eyes and other eye structures, and absence of extrinsic eye muscles.

In the two other patients, the only pathological finding in the cranio-facial examination was the presence of a small and sunken palpebral fissure in the corresponding orbital cavity. The eyelids were well-formed, with normal eyelashes and edges. There were no other facial asymmetries.

The only family history element is that their paternal great-grandfather was also born with congenital unilateral right-sided anophthalmia.

They were sent from the Regional Clinical Hospital to the Clinic of Trauma and Maxillofacial Prosthetics at Universidad de Concepción to start a rehabilitation treatment from their first months of life. First, sequential conformers were used to expand the eye sockets. Then, ocular prostheses were specially made for each patient (Figures 1 and 3).

Periodic check-ups are performed to maintain their eye prostheses. The patient with congenital bilateral anophthalmia is now under treatment with sequential conformers, after which new prostheses will be prepared (Figures 2 and 4).

Fig. 1: Patient with congenital unilateral right-sided anophthalmia

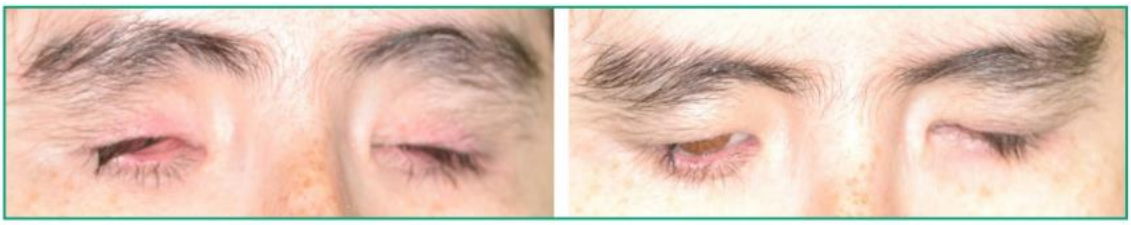

Fig. 2: Patient with congenital bilateral anophthalmia

Fig. 3: Patient with congenital unilateral left-sided anophthalmia

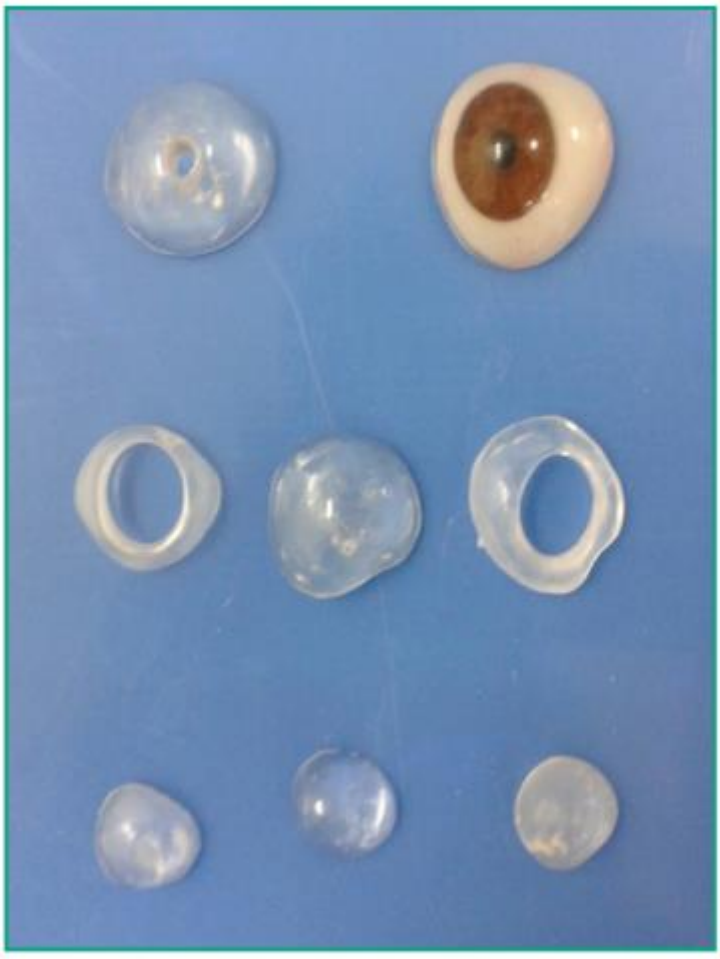

Fig. 4: Sequence of conformers used by patient with congenital bilateral anophthalmia

Discussion

When choosing a modality to treat an anophthalmic socket, the professional must consider the status of the affected eye, the contralateral eye, the severity of volume deficit, the patient's age, the patient's support system and the cause of the loss[4]. Each etiology leaves its own physical and psychological traits. Hence the importance of knowing if the eye loss or damage was a result of trauma, malignant tumors or congenital absence[5]. Patients with congenital anophthalmia or severe microphthalmia, without potential vision, must undergo early rehabilitation to "artificially" stimulate orbitofacial growth. Several techniques and materials (endogenous and exogenous) are used to expand orbital volume: serial acrylic conformers for conjunctival sac, inflatable balloon devices, conventional spherical orbital implants, mucous grafts, dermal fat, bone and muscle grafts[1].

However, although there are different types of treatment to replace the lost eye, individual ocular prostheses must be made whenever possible because they have better aesthetic and functional results, provide earlier rehabilitation than complex surgical options, and, in addition, are built considering the characteristics of the patient's eye socket[5,6].

Ocular prostheses are cosmetic facial prostheses which artificially replace the bulb or globe of the missing eye. It has the highest incidence in both adults and children, because the eye is a very sensitive or delicate organ compared to the rest of the facial organs, and as there are two eyes, they have more chances of being damaged[6].

Ocular prostheses restructure parts of the eyeball functions, compensate loss or deformity of the eye, and are responsible for integrating patients into society, free from the restrictions imposed by prejudice against the disability[7].

Ocular prostheses must:

1. Improve the natural appearance by preserving the anatomical shape of the cavity and its mobility. This last factor is the most important one to conceal the ocular prosthesis, as in conversations with prostheses

users, the appliances should not remain static but must have movement, even if it is minimal[6,7,8].

2. Have the maximum degree of adaptation to the tissues of the eye socket[6].

3. Keep the anophthalmic cavity filled, restore the lacrimal direction (it enables tear drainage) and prevent the accumulation of lacrimal fluid in the cavity[8].

4. Inhibit the collapse of the eyelids[8]

5. Maintain muscle tone[8]

6. Protect the cavity[8]

The longer the time interval between enucleation and prosthesis installation, the harder it will be for the patient to adapt, due to the atrophy of eyelids and muscle hypofunction[8]. Therefore, besides focusing on volume asymmetry, the professional must address the condition of periocular structures by evaluating eyelids, eyebrows, forehead, midface and ears.

Unlike other maxillofacial prosthetics, such as nasal or orauricular prostheses, ocular prostheses must appear alive, as the eye is an expressive organ which is part of the person's character and expresses their mood. This adds a level of difficulty for the professional, who must try to capture the patient's mood in one session to be able to sculpt their gaze[5].

This poses a challenge for both the professional and the patient. Reproducing the patient's expression, character and personality present in the contralateral eye is almost impossible[5]. However, despite these difficulties and the fact that they do not restore vision, ocular prostheses remain a very good choice for the rehabilitation of anophthalmic patients, as they allow patients to recover their aesthetic appearance[7, 8].

Impact on quality of life

Besides restoring aesthetics and protecting tissues, the aim of globe reconstruction is to rehabilitate patients and to integrate them into society. Facial mutilation and the partial or total loss of vision caused by anophthalmia can be a stigma for both patients and their families. A change in the face usually entails many complications for the patient. It can influence their self-esteem and personal relationships as it is difficult to establish emotional ties, to face new challenges, and because it can cause insecurity and social rejection. The feelings most frequently reported by anophthalmic patients are shame, shyness, concern about concealing the condition, sadness and fear[5,9].

At present, rehabilitation efforts aim to address patients' psychological and emotional instabilities derived from the loss of eyes. This emotional instability is caused mainly by the negative effects of the use of ocular prostheses on their social relationships, rather than how the prosthesis looks compared to the natural eye. However, a significant degree of satisfaction depends on how the prosthetic eye resembles the contralateral eye, since the patient will continually compare the artificial prosthesis to the healthy eye[5,10].

We can analyze the anophthalmic patient's situation from two perspectives: psychosocial knowledge or self-perception, and psychological or psychiatric behavior.

The first is characterized by inferiority complexes, the fear of being socially marginalized, lack of confidence in themselves and problems to initiate and maintain social relationships. The help of family and friends is important for the patient's psychosocial recovery: studies reveal that support is essential to improve the patient's self-esteem[9,10].

In the clinical-psychiatric domain, anxiety and depression are the most commonly reported disorders. However, anxiety and depression are not easily detected by health professionals. Therefore, the mental health of anophthalmic patients should be assessed at the beginning of the treatment and then on a periodic basis, to ensure that patients have not developed these disorders[9,10].

However, despite self-perception and psychological problems, most patients reported an improvement after starting to use ocular prostheses. Aesthetic restoration and camouflaging the mutilation increase patients' confidence, which helps them resume their normal lives and routines[5,9,10].

Therefore, it is important to assess both the physical and emotional well-being of anophthalmic patients to identify those who need additional mental and physical support. Addressing psychosocial issues is key to the success of the treatment. The family's active cooperation

and participation is essential, as well as the work of an efficient multidisciplinary team. Comprehensive treatment includes technical and psychological approaches, which will improve the patients' ability to cope with their pathology and its consequences[4,9,10].

Conclusions

Orbital rehabilitation in congenital anophthalmia is a challenge that involves the ophthalmologist, the prosthetist, the patient and the family. Early intervention, as was the case with these patients, makes a significant difference on the overall development of the patient and on the emotional well-being of the family. Treating congenital anophthalmia is a long-term commitment between patients and their rehabilitation professionals. "Expansion treatment" with sequential conformers and subsequent rehabilitation with ocular prostheses is a simple and non-invasive approach for the enlargement of the socket, and so far it is the option that has had the best results according to the literature.

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