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Short communication

Asymmetric optic tracts in a case of unilateral isolated clinical anophthalmia—A rare case report and review of literature☆

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ABSTRACT

Anophthalmia is a rare anomaly, the prevalence being around 3 in 100,000. It is defined as the absence of ocular tissue in the orbit. It can be seen in isolation or as part of a syndrome (in 1/3rd of cases) and can be unilateral or bilateral. Clinical anophthalmia is a term used to describe cases where the orbit seems to have no eyeball but histological studies may show evidence of ocular remnants. The present study reports the gross anatomical findings in a very rare case of unilateral and isolated anophthalmia of the right side. Despite the fact that the individual had only a rudimentary right optic nerve, an optic chiasm was developed and optic tracts were seen, but, interestingly, were asymmetric in the thickness, in such a manner that the right optic tract had increased thickness than the left optic tract. The details of the findings, with a brief review of anophthalmia and the mechanisms related to the morphogenesis of the chiasm and optic neural pathways are discussed. The exact embryogenesis of the pattern described in this case report is not clear, but this report will have implications in studies of axonal guidance and development of visual apparatus. A similar appearance has been reported in a follow up MRI study of early monocular enucleation in unilateral retinoblastoma cases, but the occurrence of asymmetric optic tracts in a case of unilateral anophthalmia is, to the best knowledge of the authors, a new finding in a very rare congenital anomaly.

1. Introduction

Anophthalmia is a rare anomaly, with birth prevalence 3 per 100,000.[1,2] Anophthalmia is defined as the absence of ocular tissue in the orbit. Some authors consider anophthalmia and microphthalmia (small eye) to encompass the same spectrum of anomalies and anophthalmia to be an extreme case of microphthalmia. This concept has been supported by histological evidence of residual ocular neurectodermal tissues in cases of clinical anophthalmia,[3] a term used to describe cases where the orbit seems to have no eyeball but histological studies may show evidence of ocular remnants. Anophthalmia can be found in isolation, termed isolated anophthalmia, or can be seen associated with other syndromes (in 1/3rd of cases). It can be unilateral or bilateral. The exact prevalence of these individual types has shown wide variations in different case series.[1] The present case report describes the gross anatomical findings of a case of unilateral and isolated clinical anophthalmia. The relevant embryological mechanisms are discussed further.

2. Case Report

We present a case of autopsy of a 52 year old male individual. He had pigmented skin and was not an albino. The length of the palpebral fissure (medial canthus to lateral canthus) was 3.5 cm on the left and 1.5 cm on the right. When the right eye lids were opened, from the facial aspect, complete absence of the right globe was noted and only amorphous soft tissues were seen in the orbit (see Fig. 1). The left eye was normal. On craniotomy and careful observation of the intracranial structures, the optic nerve on the right side was found to be nearly absent (see Fig. 2) with only

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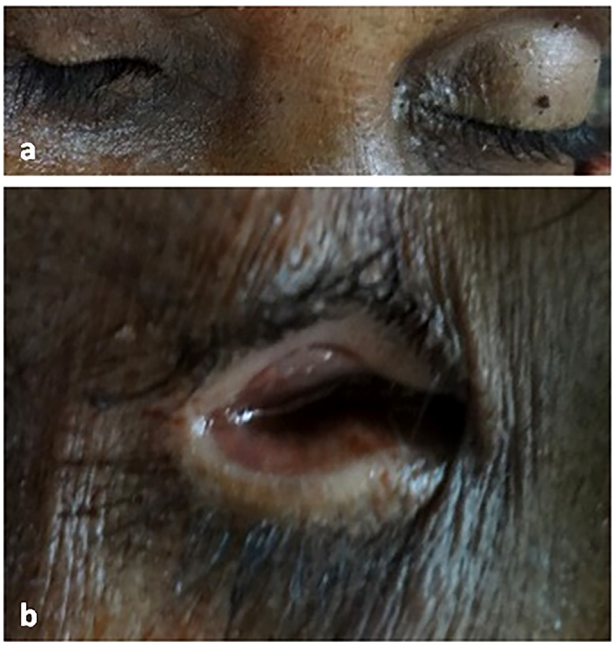

Fig. 1. Photographs of the eyes. **a.** Comparison of the right and left palpebral fissures. The fullness of the eye on the left and the small attenuated palpebral fissure on the right can be seen. **b.** Absence of eyeball within the right palpebral fissure. Soft tissues can be seen.

rudimentary nervous tissue seen along with the covering meninges. The right orbital roof was opened up, from the cranial aspect. No ocular structures were seen. Soft tissues and fat were seen but no definite extra ocular muscles were able to be identified. There were no other visceral anomalies detected during the autopsy.

A detailed history was taken from his elder sister and it was reliable. As per the history, the individual was born with right eye absent. No surgery was done in this person. His condition was not specifically investigated and no imaging studies of his skull or brain had been done. He had no history of any other significant illness. There is no history of any cancers in his family. His vision was normal in the other eye and he could do his daily activities. He had a twin sister, who had both eyes absent, but died soon after birth. There were no similar conditions of the eyes in any other members of his family. The findings and the history lead us to the diagnosis of an isolated and unilateral clinical anophthalmia.

The optic chiasm was developed and optic tracts were seen. Interestingly, the optic tracts were found to be asymmetric in their thickness, on both sides. The right optic tract (i.e. the optic tract on the ipsilateral side of anophthalmia) was seen to be of increased thickness when compared with the left optic tract (see Fig. 2). A histological examination could not be done.

3. Discussion

Anophthalmia is the congenital absence of the eye that results from interruptions in the normal sequence of embryologic events that occurs in the 4th to 8th week of intrauterine life resulting in maldevelopment of the ocular primordium.[4] Though the eyeball does not develop, eyelids are formed.[4] Mann[5] has classified anophthalmia into three – primary, secondary and consecutive or degenerative. Primary anophthalmia occurs when optic primordium does not develop. Secondary anophthalmia results when the entire anterior neural tube fails to develop. Degenerative or consecutive anophthalmia results when optic vesicles develop but eventually abort and degenerate.

Many cases of anophthalmia are associated with specific syndromes. If no syndrome is recognized clinically in a case of anophthalmia in the infancy period, a further clinical examination is recommended after three or four years as many syndromes may become apparent only later. The commonly associated syndromes are duplication 3q syndrome, Wolf-Hirschhorn syndrome, duplication 4p syndrome, trisomy 9 mosaic syndrome, duplication 10q syndrome, Patau syndrome and Edwards syndrome.[2]

Epidemiological investigations have shown genetic, heritable and environmental causes for anophthalmia. Certain drugs, maternal infections and pesticides (Benomyl) have been found as potential agents causing anophthalmia.[6,7]

The genetic mechanisms underlying the etiology of anophthalmia have been recently investigated. *SOX2* gene mutation (locus on 3q) is the most consistently demonstrated monogenic cause for anophthalmia[8] which has been shown to cause bilateral anophthalmia. Other genes implicated are *PAX6*, *OTX2*, *RAX*, *CHX10*, *FOXE3*, *CRYBA4*.[2]

In the present case, anophthalmia was non syndromic and isolated. The optic chiasm was developed, which was consistent with previous reports of unilateral anophthalmia.[2] There was rudimentary nervous tissue in the place of the optic nerve similar to previous cases.[9] In the literature, to the best knowledge of the

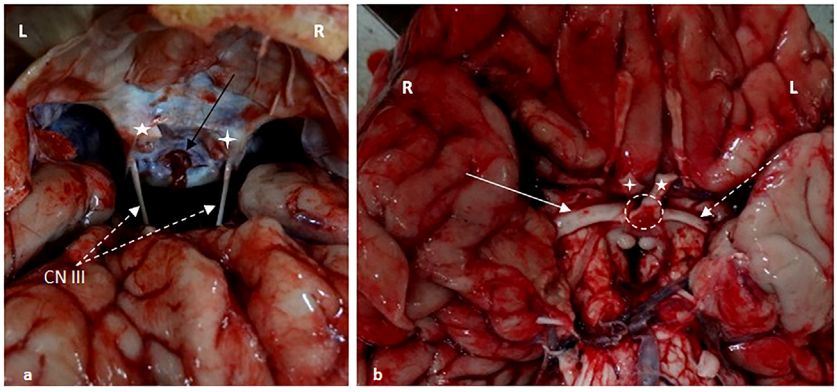

Fig. 2. Photographs of the brain during dissection. Right and left orientations are given on the top of the photos as L and R. **a. Cranial view**- The brain is being removed from the cranial fossa (viewed from the cranial aspect). The left optic nerve can be seen (cut, white 5 spoked star). The right optic nerve is rudimentary (white 4 spoked star). Both 3rd cranial nerves are seen in the background as tensed (white dashed arrows). Pituitary stalk (cut) and diaphragma sellae is also seen (black arrow). **b. Ventral view** of the brain with the optic nerve cut and the optic chiasm and the optic tracts visualized on the ventral brain surface. The right optic tract (white continuous arrow) is seen to be of increased thickness when compared with that of the left optic tract (white dashed arrow). The optic chiasma is illustrated using a dashed white circle. Note the left optic nerve (white 5 spoked star) and also the remnant of the right optic nerve (white 4 spoked star), which contained leptomeninges and rudimentary nerve tissue.

authors, the occurrence of asymmetric optic tracts in a case of unilateral anophthalmia is not reported before.

This report may have important implications especially in the understanding of axonal behavior in the chiasmal morphogenesis. Here in the absence of histology, the cause of the asymmetry can be speculated, at this point, as more fibres may have decussated the optic chiasm in the absence of contralateral eye fibres. The alternatives for this 'decussation hypothesis' can be that the axons in the tract may have undergone hypertrophy or the axons in the tract may have more myelin sheath synthesized, which would both imply compensatory mechanisms. Whatever be the reason, the gross anatomical findings in autopsy of this case, point to some central consequences, possibly neuronal plasticity, due to unilateral anophthalmia.

Previous radiological studies of unilateral anophthalmia cases have stressed on brain anomalies, craniofacial dysmorphism, globe and optic nerves, orbital tissues and comparison of CT and MR imaging, but have not specifically mentioned the morphological appearance of retrochiasmal optic pathways.[9,10]

In one recent MRI study, by Kelly et al.,[11] a similar finding of asymmetrical optic tracts was described. This was done as a follow up study in a series of cases which underwent early monocular enucleation of the globe, conducted in cases of unilateral retinoblastoma. Here also the contralateral optic tract was larger in size than the ipsilateral tract in early monocular enucleation. It has to be noted that in this case a late monocular enucleation had no effects on the optic tract morphology. Our gross anatomy findings clearly support the study results of Kelly et al. Moro et al. has also described medial geniculate body volume asymmetry in a group of cases which underwent early monocular enucleation, suggesting multisensory plasticity as the reason behind this.[12]

Optic chiasm is considered to be a very popular model for understanding guidance of axons. The chiasmal decussation is an integral part of the normal binocular vision in mammalian visual pathway. The phenomenon of segregation of retinal axons into retinotopic groups and the decision of crossing or not crossing the midline has attracted the minds of numerous developmental biologists. The formation of optic chiasm is considered to have a number of discrete steps, which together produce the final developmental sequence and the precise retinotopic projection into the corresponding hemispheres.[13]

Studies have determined genetic and molecular determinants that guide the retinal axons to their target. The expression and function of the *Robos* and *Slit* are well documented in studies on retinal axonal guidance. The binary decision as to cross the midline or not to cross the midline is controlled, to some extent by the *Roundabout (Robo)* receptor on the retinal axons and its ligand, *Slit*, an inhibitory extracellular matrix molecule secreted by the midline glia in the chiasm.[14] The other important determinants implicated are Ephrin B2 and EphB1.[15]

Neveu et al.,[16,17] in their study, on human unilateral anophthalmia cases, have demonstrated that the visual evoked potential (VEP) is symmetrical (no difference in amplitude or latency). They inferred from this phenomenon, that the anatomical chiasmatic decussation in human unilateral anophthalmia cases was also symmetrical. They state that in humans and marsupials, unlike those of mouse and albino chiasm, the development of the chiasm and posterior neural pathways remains unaffected, by the presence or absence of one eye, and there were no midline interactions. Our gross anatomical findings are in discordance with this VEP observation, the reason for which needs to be investigated further.

As this report shows a new finding in a very rare case, it will be of interest for neuroanatomists, developmental biologists and neuroradiologists and further studies may be necessary to get the clear picture behind this peculiar asymmetric pattern of optic tracts in unilateral isolated clinical anophthalmia.

Conflict of interest

The authors declare that they have no conflict of interest.

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