CASE REPORT

Rare association of cyclopia with craniospinal rachischisis

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ABSTRACT

Cyclopia is a severe form of holoprosencephaly which results in children being born with just one eye, absence of nose and presence of a proboscis above the median eye. Incidence of cyclopia is around 1.05 in 1, 00,000 births, including stillbirths. The association of anencephaly with spinal rachichisis varies from 17-50%. However, the existence of cyclopia with anencephaly and spinal rachischisis has been reported only in 9 cases till date. We report one more case of cyclopia with anencephaly and spinal rachischisis. Awareness of this spectrum of association with cyclopia, albeit rare, will help in early antenatal diagnosis by fetal ultrasonography. Public education and strict adherence to folic acid supplementation can prevent this unfortunate anomaly.

KEY WORDS: Anencephaly, cyclopia, holoprosencephaly, spinal rachischisis.

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INTRODUCTION

Cyclopia is a rare anomaly resulting from an anomalous development of midline mesodermal structures. In cyclopia there is a gross deformity of the orbital region, resulting in the formation of a central cavity called the pseudo-orbit, absent nasal cavity and its replacement by a rudimentary proboscis which is situated above the pseudo-orbit.[1] Incidence of cyclopia is around 1.05 in 1,00,000 births, including stillbirths.[2]

Neural tube defects are categorised under birth defects of the brain, spine, or spinal cord. They occur in the first trimester of pregnancy. The two most common neural tube defects are spina bifida and anencephaly.[3]

Anencephaly occurs as a result of failure of neurulation with an incidence of almost 1:1000-1:20000.[3]

A rare and most severe form of neural tube defects is craniospinalrachischisis which is characterized by anencephaly associated with a bony defect of the spine and exposure of neural tissue. This lesion lacks skin over the spinal cord.[4]

An extensive review of literature search revealed 9 such reported cases in which anencephaly with spinal rachischisis was accompanied by cyclopia, proboscis, microphthalmia, a single nostril and other features of holoprosencephaly.[5] We report a case of a similar rare combination of true cyclopia with craniospinal rachischisis.

CASE REPORT

A 30 year old female with 5 months of amenorrhoea came to our hospital for an antenatal check-up. She had not visited our hospital earlier and this was her first antenatal check-up. She was 3rd gravida with two previous normal deliveries and both the children (elder female child 3 yrs old and younger male child 1 and half year old) are healthy and living. Hers was a third degree consanguineous marriage. She was immunized with 2 doses of T.T. and was taking regular iron and calcium tablets, but no folic acid supplementation. There was no history of hypertension, diabetes mellitus, renal disease or any other major illness. There was no history of any alcohol consumption. TORCH screening for antenatal infections had not been carried out. On examination she appeared moderately nourished. She had not undergone any first trimester ultrasound scan.

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Fetal ultrasonography in current antenatal check-up demonstrated a single live foetus of 19 weeks and 6 days gestational age. The calvarium was absent and there appeared to be no parenchymal tissue above the orbit. In the coronal plane a frog like appearance of the foetus was noted denoting a diagnosis of anencephaly. No other abnormality with respect to other organs was identified. Craniospinal rachischisis was not picked up on ultrasonography. The family was informed regarding the non-viability of this developmental disorder and counseled for termination of pregnancy. Dilation and curettage was performed and termination of pregnancy was performed following written informed consent of both the parents. The foetus was sent for post-mortem examination.

A female foetus weighing 160 gm with attached umbilical cord measuring 3.5 cm in length was received for examination. On external examination, single aperture for the eye measuring 10 × 10 mm was noted in the midline of the face which showed presence of two fused eye globes, and two separate pupils each measuring 2 × 2 mm. The nose was absent and was replaced by a proboscis above the median eye measuring 10 mm in length and 5 mm in diameter (Cyclopia). No cleft lip or cleft palate was noted. The cranial vault was absent and the brain was replaced by a protruding blackish vascular soft tissue mass (Anencephaly). Also noted a spinal cord defect (spinal rachischisis) limited to the cervical region. This area was devoid of overlying skin, and the cervical segment of the spinal cord was directly exposed to the exterior as the vertebral arches were deficient. Skull base was present but rest of the vertebral column below the level of rachischisis appeared normal. Scoliosis or retroflection of the spinal cord was absent. All four limbs were well developed with normal number of digits. No skeletal anomalies such as club feet were noted [Figure 1].

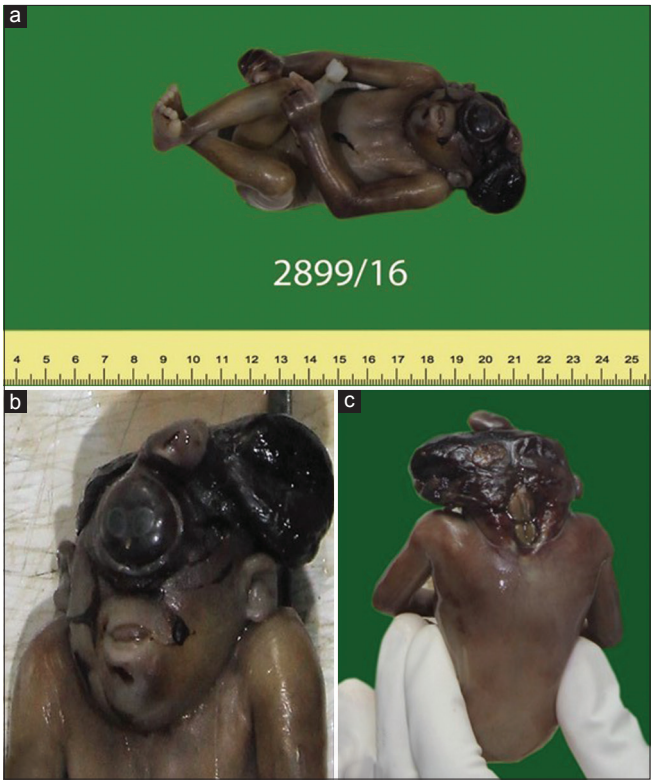

Figure 1: (a) Gross appearance of the fetus (Anterior View). (b) Gross appearance of the fetus (Close-up View) showing centrally fused eyeballs with two pupils, absence of nose and proboscis seen above the median eye. (c) Gross appearance of the fetus (Posterior View) showing spinal defect at the cervical region (spinal rachischisis) and absence of cranial vault (anencephaly) which is replaced by a blackish angiomatous sac like structure

Microscopic examination of the proboscis revealed, tissue lined by stratified squamous epithelium along with chondroid tissue, focal areas of calcification, cartilage and rudimentary neuro-epithelium [Figure 2]. Respiratory lining epithelium was not seen in the sections taken from the proboscis. No gross or microscopic anomalies were noted in thymus, heart, lungs, liver, spleen and bilateral kidneys examined. The adrenals could not be identified, probably indicating absence/marked hypoplasia. Sections studied from the protruding angiomatous mass and the cervical rachischisis segment revealed fairly well developed cord tissue with grey horns surrounding a central canal which contained clusters of large neurons with prominent nucleus and nucleolus. The exiting nerve roots were enveloped by a heavily vascularised leptomeninges with fetal blood vessels [Figure 3]. Based on the above findings a diagnosis of cyclopia with craniospinal rachischisis was rendered.

DISCUSSION

The prechordal mesoderm during embryogenesis forms the median facial bones and also induces rostral neuroectodermal differentiation. Defect in prechordal mesodermal development leads to the malformation of the facial bones and organogenetic cleavage of the prosencephalon.[2]

Three types of eye deformities have been seen in cyclopia: one eye (monophthalmia), two fused eyeballs (synophthalmia) or complete absence of eyeballs (anophthalmia). The foetus in this case report had synophthalmia.[2]

Environmental factors implicated in the development of cyclopia include maternal diabetes mellitus, maternal alcoholism, in utero infections with cytomegalovirus, rubella or toxoplasma and teratogenic drugs such as retinoic acid, cholesterol synthesis inhibitors as well as association of genetic factors such as chromosomal mutation, sonic hedgehog gene mutation or a part of syndrome.[6] The specific genes which cause the neural tube defects have not yet been identified. The methylene tetrahydrofolate reductase gene has been shown associated with development of neural tube defects.[3] Association of cyclopia with parental consanguinity has also been observed in various case reports.

In the index case history of consanguineous marriage and failure to take folic acid supplementation was present, however there was no significant history of past maternal diabetes, alcoholism or infections.

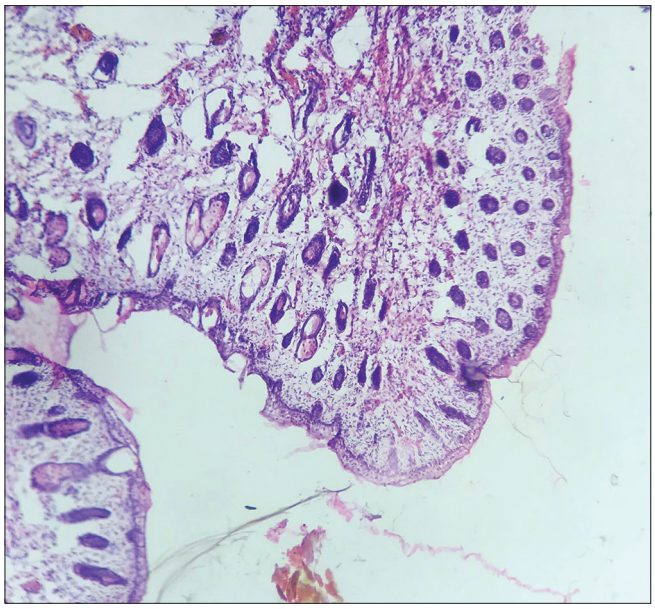

Figure 2: Photomicrograph from the proboscis showed tissue lined by stratified squamous epithelium and hair follicles (H and E, ×40)

Anencephaly is assumed to result due to failure of closure of the anterior (cephalic) end of the neural tube at 24-26 days after fertilization resulting in absence of the major portion of brain, skull and scalp. It results from the defective formation of neural tissue from the ectoderm (neurulation). The neural tissue is exposed and the cerebral hemispheres are absent. The neural tissue is rudimentary and enveloped by heavily vascularized mesenchymal tissue with large congested thin walled venous channels that may rupture to produce hemorrhage.[3]

The incidence of association of anencephaly with spinal rachischisis varies from 17-50%. It results from failure of closure of the anterior neural tube along with partial or complete exposure of the body of the neural tube. Depending on the site of involvement, the defect may be localised to the cervical region or may involve the whole length of the neural tube.[5]

Vertebral defects, pulmonary hypoplasia and club feet are more common in anencephaly with spinal rachischisis as compared to anencephaly alone. Vertebral defects include scoliosis and retroflexion of the spine. The association of anencephaly and spinal rachischisis is called cranio-spinal rachischisis.[5]

In the present case craniospinal rachischisis was limited to the cervical region and was not associated with any other spinal cord deformities. Associated lung hypoplasia was not identified.

In the largest series of 136 cases of anencephaly with spinal rachischisis, reported renal defects in 17%, cleft lip and/or palate in 10%, gastrointestinal defects in 9%, omphalocele in 5%, diaphragm abnormalities in 4% and spleen abnormalities in 2% of cases.[5] However, none of these above were identified in our case.

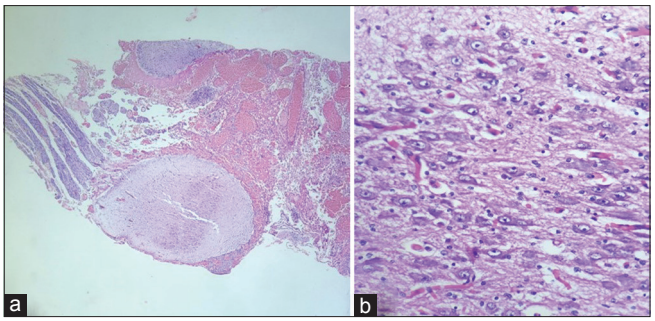

Figure 3: (a) Sections from spinal rachischisis shows cord tissue with central grey horns and surrounding white matter along with exiting nerve roots from one end enveloped by fetal congested leptomeninges (H and E, ×100). (b) Close up view of central grey horns show aggregates of large neurons with prominent nucleus and nucleolus surrounded by neuroglial tissue (H and E, ×400)

A PubMed search for craniospinalrachischisis with cyclopia revealed single case series study of 9 cases by Lemrie *et al*.[7] In their study they reported several coexistent visceral anomalies associated with neural tube defects. A large number of cases showed adrenal hypoplasia due to the lack of hypothalamus development. In the present case, the adrenals could not be identified which could reflect complete absence of adrenals.

Chromosomal abnormalities such as trisomy-D, monosomy-G mosaicism, translocation affecting chromosome 3 and group C chromosome, and chromosome 10 short arm deletions have also been recorded in cyclopia.[1] Karyotyping in our case could not be performed due to unavailability of fresh fetal blood sample or umbilical cord sample.

Cyclopia results from arrest of development of anterior end of the neural plate, hence it is always associated with abnormalities of the brain.[8] In the present case, cyclopia was associated with neural tube defect anomalies such as craniospinalrachischisis. This co-occurrence suggests probable arrest in prosencephalon development with involvement of precordal mesoderm leading to holoprocencephalic facial features which is uncommon finding in anencephaly. In the present case cyclopia and spinal rachichisis were missed on ultrasound examination.

CONCLUSION

Only few cases of association of Cyclopia with craniospinal rachischisis have been described in literature. The possible association between anencephaly and spinal rachischisis is unclear and also recurrence of these congenital anomalies in subsequent pregnancies is not known. In present case two identifiable risk factors - a history of consanguineous marriage and lack of folic acid supplementation were present. Hence we conclude that appropriate counseling in the antenatal period would help to prevent occurrence of neural tube defects and also awareness of spectrum of ultrasonographic findings of cyclopia can improve the accuracy of early prenatal diagnosis of cyclopia and will help in counseling the parents for termination of pregnancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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