Syndromic and Isolated Cryptophthalmos

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Cryptophthalmos is the congenital absence of eyelid with skin passing continuously from the head to the cheeks over a malformed eye. The term cryptophthalmos was coined by Zehender and Manz in 1872, when they first described a patient with bilateral cryptophthalmos and multiple congenital anomalies(l). In 1962 Fraser described 4 cases of cryptophthalmos and multiple malformations in two sibships(2). Cryptophthalmos is not an isolated malformation but part of a syndrome, characterized by four cardinal signs namely cryptophthalmos, anomalies of head, nose and ears, syndactyly and genital abnormalities(3). Identification of cases with anomalies other than cryptophthalmos in;-siblings of affected cases led to the use of the eponymic designation "Fraser syndrome". Only 27 cases of isolated cryptophthalmos, in the absence of other malformations have been reported(4-6).

In this report we describe 4 cases of cryptophthalmos. One patient had Fraser syndrome, one had bilateral isolated cryptophthalmos and the other two siblings had isolated unilateral cryptophthalmos. Autosomal recessive mode of inheritance is suggested in these two sibs with isolated unilateral cryptophthalmos who were born to consanguineous parents.

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Case Reports

Case 1: The patient was the second child born to a non consanguineously married 25 year old mother and 29 year old father, after 7 months of gestation. Pregnancy was uncomplicated. The first child of the couple was born preterm, at 7 months and was a macerated stillbirth, without any obvious congenital defects. The baby's birth weight was 900 g, height 42 cm, and head circumference 30 cm. The right upper eye lid was fused with the cornea while the left showed complete cryptophthalmos, the globe was palpable beneath the lids *(Fig. 1)*. TKe other anomalies noted included occipital encephalocele, malformed ears, depressed nasal bridge, small narrow nostrils, high arched palate, bilateral cutaneous syndactyly, hypoplastic nails, bilateral genu recurvatum, talipes valgus deformity and ambiguous genitalia. A postmortem examination showed laryngeal stenosis, bilateral renal agenesis and hypoplastic lungs.

Case 2: A 3 day old boy born after term to a consanguineously married couple weighed 2,250 g and his eyes were completely covered with skin with no eye brows. The rest of the general and systemic examination was normal, ultrasound abdomen did not reveal any abnormality, whereas ultrasound of eyes showed disorganized globes bilaterally.

Case 3: A7 year old was the first born to a consanguineously married couple. His right eye showed complete cryptophthalmos *(Fig. 2)*. the globe was felt beneath the skin. The left eye was normal and had normal vision and there were no other abnormalities.

Case 4: The younger sib seen at 10 months of age had similar features, *i.e.,* complete cryptophthalmos without any other anomaly. The parents were normal and no other family member was affected.

Discussion

The marked variability of expression described in patients with cryptopthalmos is exemplified by this paper. In Fraser syndrome, cryptophthalmos (93%) is associated with diverse abnormalities(7) like abnormalties of ear and nose (44%), abnormalities of genitals (49%), syndactyly (54%), renal agenesis (44%), urinary tract anomalies (37%), laryngeal stenosis (20%) and ovarian cysts (11%)(7). The diagnosis of Fraser syndrome is difficult when cryptophthalmos is absent. In such cases a history of sibling with cryptophthalmos will greatly help in diagnosis. Thomas *et al.* proposed 4 major and 8 minor criteria for diagnosis of Fraser syndrome and suggested that a diagnosis can be considered with at least two major and one minor criterion or one major and four minor criteria(6). Our first patient fulfilled these criteria. Isolated cryptophthalmos is a clearly distinct condition from Fraser syndrome(4,5). Thomas *et al.* in a review of 124 cases of cryptophthalmos, noted only 27 cases with isolated cryptophthalmos(6). Whether isolated or syndromic, cryptophthalmos occurs bilaterally more frequently(6).

Cryptcfphthalmos may exhibit a wide range of severity. Francois classified it

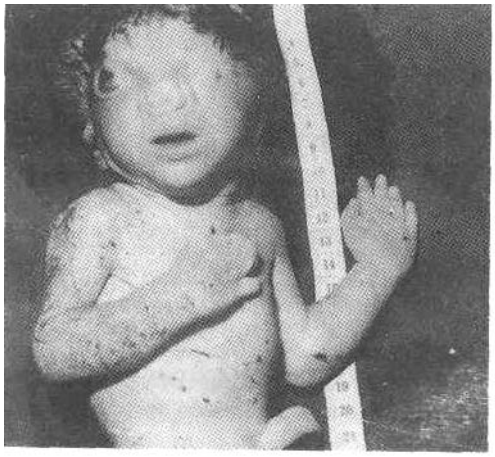

Fig. 1. Case 1 showing cryptophthalmos, occipital encephalocele, depressed nose and bilateral cutaneous syndactyly.

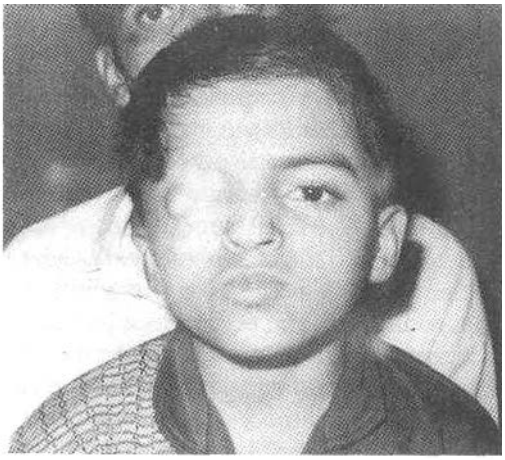

Fig. 2. Case 3 with unilateral cryptophthalmos.

into 3 clinical types(3). The first type is a complete and typical cryptophthalmos, second type is a typical partial cryptophthalmos and the third type is abortive, where the upper eye lid adheres to the superior aspect of the globe. Saal *et al*. proposed a fourth type in which eye lids were well formed but fused interiorly (4). Cryptophthalmos is associated with poor prognosis for vision except for the abortive type because of associated ocular anomalies(4).

The pathogenesis of this condition is unknown. The most characteristic malformation present in this condition occurs in areas which remain temporarily fused *in utero* like the eye lids, the digits and the vagina(6). The separation of eye lids occur by a process of controlled necrosis of palperbral tissue between 17-18 weeks of gestation(8). Some attribute cryptophthalmos to the defect in gene responsible for this programmed cell death(6). Schauer *et al.* found adhesions of lens to inner aspect of the layer of skin, and connective tissue covering the cryptophthalmic eye as a common feature^). So they argued that the lid anomalies are a sequelae to abnormal lens development(9). A role for vitamin A metabolism has also been suggested as pathogenic mechanism from the observation in animal models in which mothers had hypovitaminosis A(6). Other proposed theories include primary failure- of the ectodermal and mesodermal differentiation, intrauterine inflammation producing fusion of the eye lids to globe, amniochorionic bands with pressure on eye lids and defective differentiation of the conjunctiva(5).

The mode of inheritance in Fraser syndrome is autosomal recessive(6). Most of the cases of isolated cryptophthalmos are sporadic(6). The pattern of inheritance in our family with 2 sibs born to consanguineous parents is highly suggestive of autosomal recessive type. Prenatal diagnosis in severe Fraser syndrome is possible if two of the four features, *viz.,* microphthalmia, obstructive uropathy, syndactyly and oligohydramnios are present(10).

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Aplasia Cutis Congenita with Congenital Contracture of Knee

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Aplasia cutis congenita is a rare developmental anomaly that most commonly involves vertex of the scalp and may be associated with other congenital anomalies. Although isolated congenital absence of skin and congenital knee contracture is known,, association of these two conditions is not reported. We report on a child with absence of skin of left lower limb with contracture of left knee at birth.

Case Report

A two days old full term female child was admitted with complaints of absence of skin on left lower limb and inability to extend the left lower limb since birth. He was the first child of non-consanguineous parents without any significant antenatal or family history. General, systemic and neurological examinations were within normal limits. Local examination revealed circumferential absence of skin on lower two thirds of left thigh, knee, leg and foot. The granulation was healthy. Examination of the knee revealed fixed flexion contracture *(Fig. 1)*.

X-ray of left lower limb showed no bony abnormality. The patient was treated with dressing and antibiotics. Posterior plaster slab was applied in extension for knee contracture. The lesions were healing well. We advocated skin grafting but the patient did not turn up.

Discussion

Aplasia cutis congenita is a disorder in which localized or widespread areas of skin are absent at birth. The defect most commonly involves vertex of the scalp(l) and presents as solitary or multiple ulcers measuring upto several centimeters in diameter. Other parts of the body such as the trunk or limbs may be affected, often symmetrically, with or without accompanying scalp lesions(2). Association with other developmental abnormalities such as a cutaneous organoid nevi, cleft lip and palate, syndactyly, clubbing of hands and feet, congenital heart disease, vascular lesions and malformations of the brain are known(2,3).

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