



## Cyclopia of Goat: Micro and Macroscopic, Radiographic and Computed tomographic studies

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### Key words

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Cyclopia,  
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CT

### ABSTRACT:

Cyclopia is a rare unusual anomaly in which the anterior brain and the midline mesodermal structures develop anomalously. The orbital region is grossly deformed, resulting in the formation of a central cavity (pseudo orbit) with absence of nasal cavity. In the present study, a newly born male goat showing true cyclopia was examined grossly, radiographically, CT and histologically. The head was small and severely deformed with a hydrocephalus on the forehead. The upper and lower lip were present but small. The upper jaw was short due to the absence of the os incisivum and the deformity of the maxilla. A well marked malformed was present. The lower margin of the mandible was strongly curved and carries a prominent ventral peak. The maxilla was reduced. The frontal, lacrimal, nasal, premaxilla vomer bones, the orbit and nasal septum were absent. The dura mater was developed but the falx cerebri was absent. Only one eyeball was present and large with a thick optic nerve. There was only one optic nerve and there was no evidence of optic chiasma Cerebrum was poorly developed and there was no formation of cerebral hemispheres. The eye showed histologically some blood capillaries found in the substantia propria of the cornea. The retina showed areas of normal lamination, whereas in other areas, especially near the site of optic disk, it was replaced by numerous neuronal rosettes. These finding support the hypothesis that the craniofacial malformation in holoprosencephaly result from a developmental disturbance of the mesoderm at the rostral end of the notochord.

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### 1. INTRODUCTION

Congenital defects are structural or functional abnormalities that are present at birth, and may affect a single structure or function, parts of various systems or an entire system (Dennis and Leipold, 1979). Congenital defects of the central nervous system (CNS) can affect only the CNS or the CNS and the craniofacial skeleton (Leipold, 1986). Holoprosencephaly (HPE) is a developmental disturbance of the CNS, which is characterized by incomplete cleavage of the prosencephalon into two hemispheres (Wilson et al., 1989; Rossler and Mueake, 1998; Gripp et al., 2000;

Pasquier et al., 2000; Wolfgang and Veronica, 2009). Three forms of HPE are encountered; alobar HPE is the most severe form, with less severe forms including semilobar and lobar HPE (Bhig & Laurence, 1967; Cohen et al., 1971; Fitz, 1983). It is now assumed that teratogenic environmental factors during organogenesis have been regarded as the basis of holoprosencephaly (Benawra et al., 1980; Mollica et al., 1981). Therefore, the multifactorial etiology of holoprosencephaly is considered to be the cause of the heterogeneity of the clinical severity of the malformation (Ming & Muenke, 2002;

Arathi et al., 2003). Cyclopia is a severe form of the holoprosencephaly, involving the craniofacial skeleton (Dennis and Leipold, 1979) and is characterized by the presence of a median orbita containing a single eyeball (Noden & de Lahunta, 1985; Rüsse and Sinowatz, 1991). Varying degrees of cyclopic deformities, ranging from partially fused to completely separate eyeballs in a median orbita, with several craniofacial defects such as the absence of nasal bones and the upper incisor (Binns et al., 1959; Belloni et al., 1996). The proboscis has been referred to as a nose-like structure (Muller & Rahilly, 1989; kjaer et al., 1991; Hausmann et al., 1992; Belloni et al., 1996). The histological alterations of cyclopia appears to be more complex. The rosettes found in the dysplastic retina are fundamentally different than those of retinoblastoma, being composed of a variety of differentiated cell types. The dysplastic rosettes are essentially laminated retina failing to establish a polarized orientation, resulting in the formation of tubules (Chan et al., 2007). This malformation has been reported in the calf (Roberts, 1986; OZcan et al., 2006), buffalo calf (Thippeswamy et al., 1996), lamb (Binns et al., 1960), goat (Chakrabarti and Pal, 1991), deer (Bubenik, 1982), piglet (Bacon and Mathis, 1983; Evans, 1987) and man (Bacon and Mathis, 1983). The prevalence of holoprosencephaly in human is 1/16,000 live births with an incidence of 1/250 in first trimester embryos (Dubourg et al., 2007). Hereby, for a good understanding of craniofacial growth mechanisms, we present the radiography, computed tomography (CT), 3 D reconstruction CT as well as histological findings of a case of cyclopia encountered in a male goat kid with both facial and intracranial anomalies.

## 2. MATERIAL AND METHODS

### The material:

A cyclopic male kid (billy) of balady goat delivered by normal route was obtained from a 2-year-old she-goat, brought to the department of anatomy and embryology, Faculty of Veterinary Medicine, University of Sadat city, by a local producer. According to the owner, the mother had a normal gestation period and had previously

delivered twins kid without any complications. After parturition, the kid survived for 10 hours then died.

### The methods:

The head of the kid was examined with CT and plain radiography. Afterwards, the kid was presented for necropsy. The eye ball of cyclopic kid was investigated histologically by normal H&E-staining technique. A Toshiba CT unit was used to scan the specimens with 3-mm-thick contiguous slices, the exposure values was KV = 130, and MAs/ref = 30/81. Three-dimensionally reconstructed technique was used. The radiographic examination was performed with high definition and mamofilms. The exposure values was KV = 42 – 50, MA = 100 and MAs = 30 according to skull dimensions. The examined specimens were photographed by digital camera, Olympus SZ-31MR 16 mega pixels.

## 3. RESULT

### External observation:

The head was small and severely deformed. There was only a single median orbita-like opening, which was about 3 cm in diameter, but the eyelids and eyelashes were absent. The nose was absent (Fig.1). Only one eyeball was present and large (Fig.5, 6), The upper and lower lips were present but small (Fig.1,4). The upper jaw was short due to the absence of the os incisivum and the deformity of the maxilla (Fig.1,4). A normally sized tongue protruded from the small oral cavity (Fig.1, 2). There was dorsal midline cyst in the forehead (Fig.2, 3). There was no dental pad or upper incisors (Fig.4) The cyclopic goat showed no abnormalities in the neck, thorax, abdomen, limbs and vertebral column (Fig.3).

### After opening of the cranium:

A protruding sac is seen on the fore-head region containing fluid, which results from the failure of the neural groove to close (Fig.2). After opening of this sac and cutting the dura mater, a part of the nervous tissue was exposed and protruded inside the sac of the fore head, and with investigation it appeared to be a single prosencephalic prominence (Fig.4, 6).

### Central nervous system:

**The dura mater** was developed but the falx cerebri was absent (Fig.4).

**Medulla oblongata:** no abnormal features were noticed except ill distinct pyramids and trapezoid body (Fig.5).

**Pons:** it was enlarged but no abnormal feature are detected (Fig.5).

**Cerebellum:** It was poorly developed. No abnormal feature was noticed in the cerebellum and it differentiated into the most primitive part; the flocculo-nodular lobe, and small median part; the vermis; and two small lateral cerebellar hemispheres (Fig.6, 7).

**Midbrain:** Macroscopically no abnormality was detected. The rostral and caudal colliculi were very large (Fig.6, 7). The cerebral crura were enlarged and the intercurl sulcus was replaced by faint intercrural fissure (Fig.5).

**Diencephalon:** thalami were fused rostrally but caudally a portion of third ventricle was seen in between the malformed thalami (Fig.7). Tuber cenerium and infundibulum of pituitary gland are absent (Fig.5).

**Optic nerves:** There was only one optic nerve and there was no evidence of optic chiasma (Fig.5). The entrance of the optic nerve to the eyeball was normal grossly (Fig.6).

**Cerebrum:** it was poorly developed and there was no formation of cerebral hemispheres (Fig.4). Both the lateral ventricles and the third ventricle were absent. Only, in the floor of the sac, the opening of the mesencephalic aqueduct was observed between the two thalami in front and the colliculi behind (Fig.7). The lower part of the third ventricle in between two thalami was recognizable and it opened widely above in the dilated sac (Fig.7).

**Hard palate:**

The palate was structurally abnormal, the rostral part showed an acute angle at the premaxilla region (Fig.8). The palatine ridge showed different manner of curvature and absent in the caudal third of the palate (Fig.8). The palatine raphae was faint rostrally, grooved in the middle part and elevated caudally (Fig.8).

**Cranial bones:**

A well marked malformed mandible was present. The lower margin was strongly curved and carries a prominent ventral peak (Fig.9). Resulted from this curvature, the incisive teeth were positioned near to the coronoid process (Fig. 9). The mandible was massive and it's right and left halves diverge at relatively large angle as illustrated by X ray and C.T (Figs. 11, 13). There were four incisive, three premolars teeth and one molar tooth in each mandible (Fig. 10).

**The maxilla** was reduced and appeared as irregular bony mass and was malformed and 4 teeth analog were found in each mass (Fig. 10, 12). The frontal, lacrimal, nasal, premaxilla vomer bones, the orbit and nasal septum were absent (Fig.10, 11, 12, 13, 14, 15, 16). The base of skull formed by body of occipital and sphenoid bones appeared normal (Fig.13). The two ethmoidal fossa and etmoidal crest were observed (Fig.15, 18). As a result of absence of the above mentioned bones, the cranial cavity was small and malformed (Fig.16, 17).

**CT and X-ray findings;**

It showed a malformed maxilla with four teeth analog. There are four incisive teeth, three premolar teeth and one molar tooth on each mandible, the mandible was curved, with wide deep temporal fossa. The right and left halves of the mandible diverge at relatively large angle. The orbit was absent. The frontal, nasal, vomer and incisive bones were absent. Volume 3D dimension CT showed the large opening of the cranium due to the absence of orbit and the frontal bone. Sagittal and coronal CT scan showed one lens in on eyeball.

**Histological findings: Ocular findings**

**The cornea**

Except for some blood capillaries found in the substantia propria (Fig.19a), the cornea appeared to have the normal histological organization. Cornea consisted of anterior epithelium (stratified squamous epithelium), substantia propria and corneal endothelium (simple squamous epithelium).

**The retina**

It showed areas of normally laminated neural retina (Fig.19b), whereas in other areas, especially near the site of optic disk, it was replaced by numerous neuronal rosettes (Figs.20a, b; 21b).

**The optic nerve**

It was thick and spaced by the central artery of the retina (Fig. 21a)

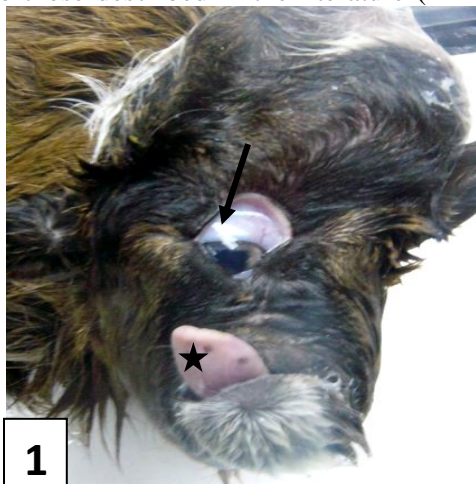
**4. Discussion**

Many reports on cyclopia describe the presence of a single median orbita that contains either a single eyeball (true cyclopia) (Binns et al., 1960; Binns et al., 1963; Bacon and Mathis, 1983; Camon et al., 1990; Chakrabarti and Pal, 1991) or incompletely fused eyeballs (synophthalmia) (Evans, 1987; Jie and Shi, 1991). Apart from the

classical description of cyclopia, several authors (Roberts, 1986; Van Allen et al., 1993; Cannistra et al., 2001) describe that anophthalmia may also be encountered in cases of cyclopia. In general, cyclopia is considered to result from defects at the neural plate stage of development and involves more specifically the rostral portion of the notochord and the mesoderm surrounding it (Jubb and Huxtable, 1993). Depending on the severity of the inhibiting agent that causes this congenital defect, various forms of craniofacial deformations ranging from a true cyclopia to synophthalmia can occur. However, if the inhibiting agent is severe enough, anophthalmia may be formed. In this respect, our study matches the classical description of cyclopia. In addition, in many cases of cyclopia, the presence of a proboscis dorsal to the median orbita has been described (Binns et al., 1963; Bacon and Mathis, 1983; Evans, 1987; Camon et al., 1990; Cannistra et al., 2001). However, such a structure was not present in this cyclop. In this male goat, deformations and deficiencies in the craniofacial bones such as arrhinia and brachygnathia superior and defects of the CNS such as prosencephalic aplasia were similar to those described in the literature (Binns

et al., 1960; Bubenik, 1982; Evans, 1987; Thippeswamy et al., 1996). In the light of these similarities and differences, we assumed that the current case is a typical cyclopia.

In the present case we the neural retina was laminated, except near the site of optic disk, it was replaced by numerous neuronal rosettes. The neural rosettes are fundamentally laminated retina failing to set up a polarized orientation, resulting in the formation of tubules (Chan et al., 2007). Cyclopic malformation was reported in newborn lambs from ewes fed with *Veratrum californicum* on the 14th day of gestation (Binns et al., 1965). Three steroidal alkaloids, i.e. jervine, cycloamine and cycloposine, were suggested to be capable of inhibiting the neural development in lambs (Keeler, 1984). A detailed botanical investigation might be necessary for further information about the aetiology of this malformation. Several other teratogens, such as radiation, viral infections and hypovitaminosis are in the scope of possible other factors that may cause this congenital defect. Since there was no recorded history about the mother of the goat kid and due to the inability to detect a causative agent it wasn't possible to ascertain the cause of this malformation.

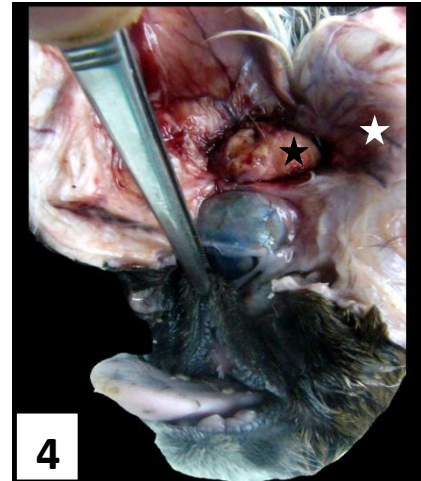


**FIG. 1:** Rostral view of the cyclopean goat head shows a single median orbita-like opening (black arrow) with one eyeball. The tongue (black star) protrudes from the small oral orifice. The eyelids, eyelashes and nose are absent.

**FIG. 2:** Lateral view of the cyclopean goat head shows dorsal midline cyst (black star) in the forehead, small upper jaw (white arrow), and large protruded lower jaw (black arrow).



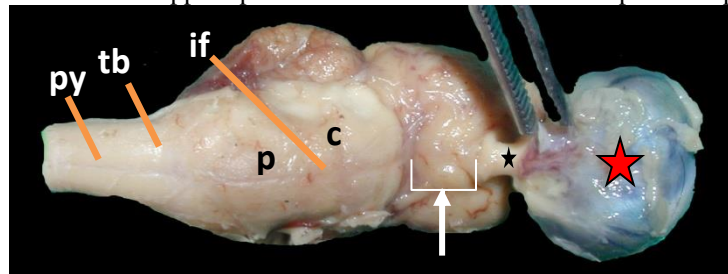
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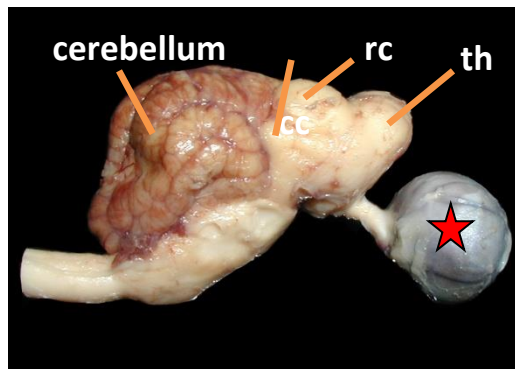
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**FIG. 3:** Lateral view of the cyclopean goat shows no abnormalities in the neck, thorax, abdomen, limbs and vertebral column.

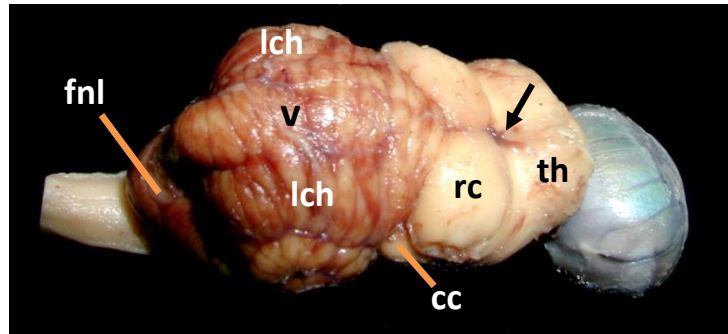
**FIG. 4:** Dorsal view of the cyclopean goat head after opening of the cyst of the forehead showing protrusion of the brain tissue (black star) into the cyst of the forehead. The dura mater (white star) is developed with absence of falx cerebri. The forceps elevate the small upper lip to illustrate the absence of dental pad and upper incisors.



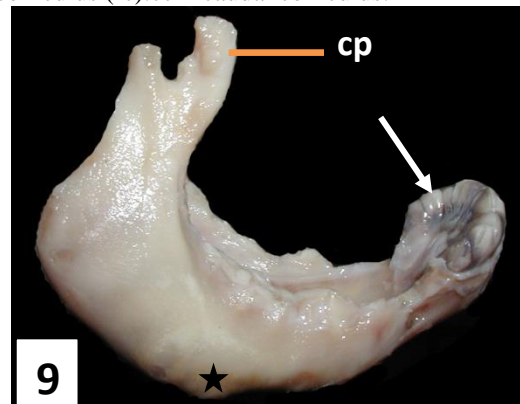
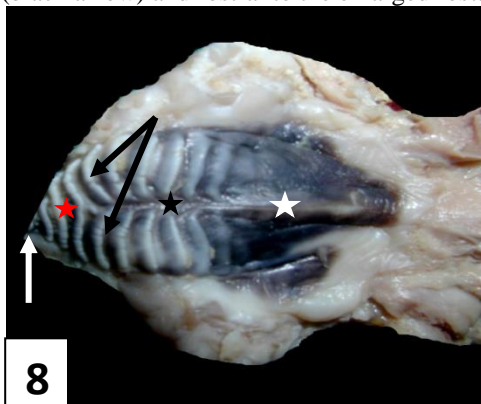
**FIG. 5:** Ventral view of the brain of the cyclopean goat shows absence of the telencephalon, large single eyeball (red star), very short single optic nerve which ends within the diencephalon by two divergent optic tract (black star), enlarged cerebral crura (c), narrow intercrural fissure (if), enlarged pons (p), ill distinct trapezoid body (tb) and ill distinct pyramid (py). The optic chiasm, tuber cenerium and infundibulum of pituitary gland are absent (white arrow). The optic nerve is single.



**FIG. 6:** Lateral view of the brain of the cyclopean goat shows absence of cerebral hemisphere, malformed thalami appear as a prosencephalic prominence (th), enlarged rostral colliculus (rc) and caudal colliculus (cc), large single eyeball (red star). The cerebellum is poorly developed with no abnormality.

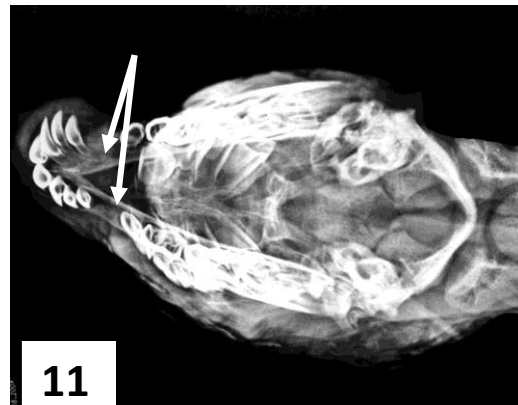
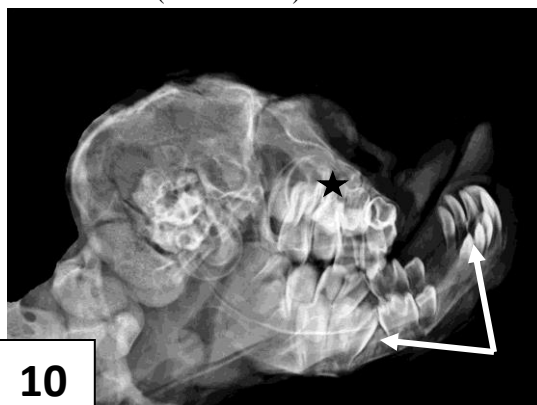


**FIG. 7:** Dorsal view of the brain of the cyclopean goat shows normal cerebeller component {Vermis (v), lateral cerebellar hemisphere (lch), flocculo-nodular lobe (fnl)}, malformed thalami (th), opening of the mesencephalic aqueduct (black arrow) and rostral to the enlarged rostral colliculus (rc).cc = caudal colliculus.



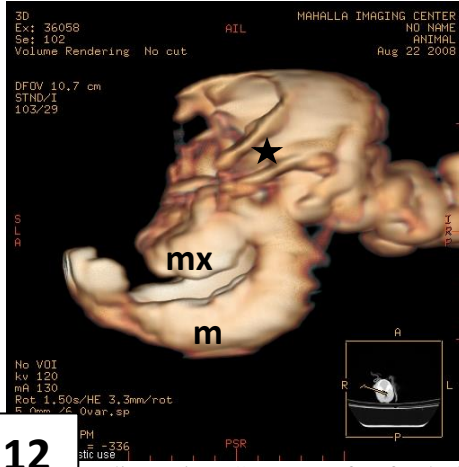
**FIG. 8:** Hard palate of cyclopean goat shows acute rostral angle (white arrow), curved palatine ridges (black arrows), palatine raphe is faint rostrally (red star), grooved in the middle part (black star), elevated in the caudal part (white star).

**FIG. 9:** Lateral view of the mandible of the cyclopean goat shows the strongly curved lower margin with central prominent peak (black star). The incisive teeth were positioned near to the coronoid process (cp). There are four pairs of incisive teeth (white arrow).

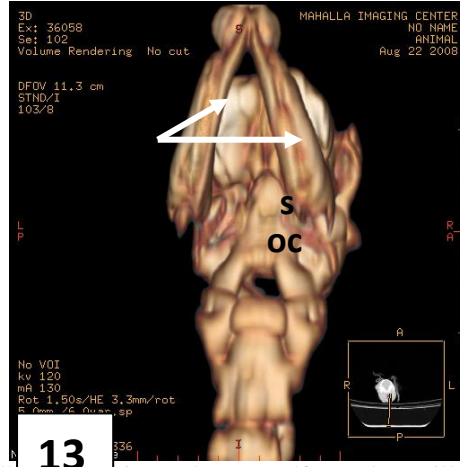


**FIG. 10:** Radiograph of head of cyclopean goat (lateral view) shows malformed maxilla (black star) with four teeth analog. There are four incisive teeth, three premolar teeth and one molar tooth on each mandible (white arrows). The frontal, nasal and incisive bones are absent.

**FIG. 11:** Radiograph of head of cyclopean goat (dorsal view) shows that the right and left halves of the mandible diverge at relatively large angle (white arrows).



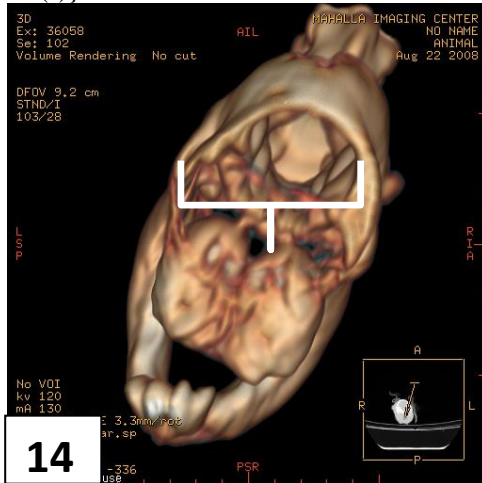
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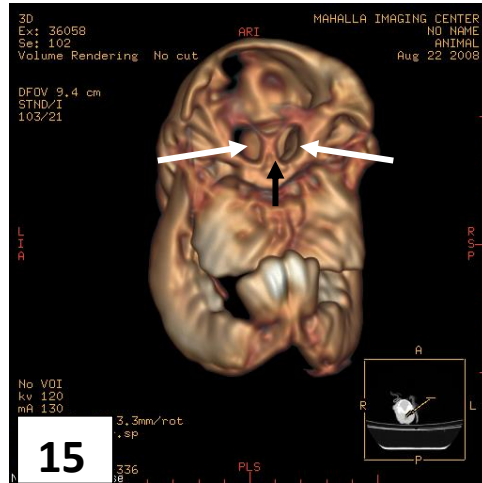
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**FIG. 12:** Volume 3D dimension CT scan of a fetal skull (lateral view) shows malformed maxilla (mx), curved malformed mandible (m), wide, deep temporal fossa (black star). The orbit is absent. The frontal, nasal and incisive bones are absent.

**FIG. 13:** Volume 3D dimension CT scan of a fetal skull (ventral view) shows that the right and left halves of the mandible diverge at relatively large angle (white arrows).The base of the skull appears normal {occipital bone (oc), sphenoid bone (s)}. The vomer bone is absent.



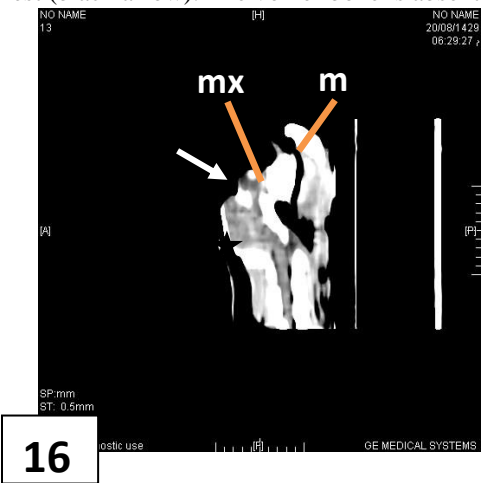
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**FIG. 14:** Volume 3D dimension CT scan of a fetal skull (rostro-dorsal view) shows the large opening of the cranium due to the absence of orbit and the frontal bone (white fork). The nasal and vomer bones and nasal septum were absent.

**FIG. 15:** Volume 3D dimension CT scan of a fetal skull (rostral view) shows etmoidal fossa (white arrows) and etmoidal crest (black arrow). The vomer bone is absent.



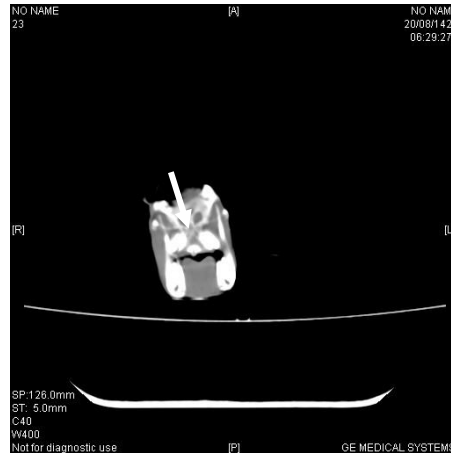
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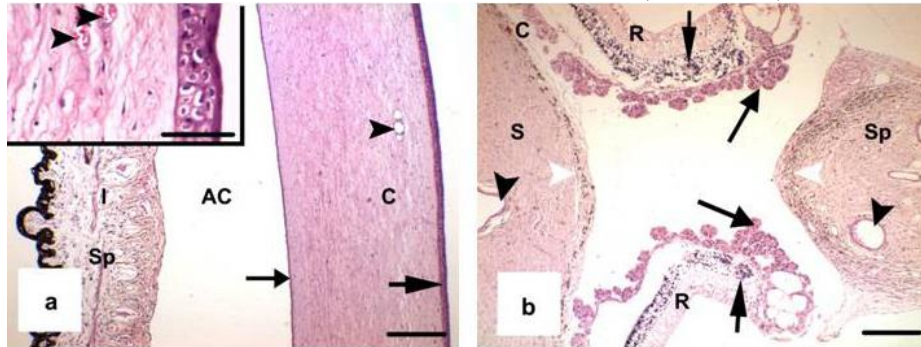
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**FIG. 16:** Sagittal CT scan of a cyclopean goat skull shows one lens in on eyeball (white arrow), malformed maxilla (mx), curved malformed mandible (m) and malformed small cranial cavity (black stat). The orbit is absent. The frontal, nasal and incisive bones are absent.

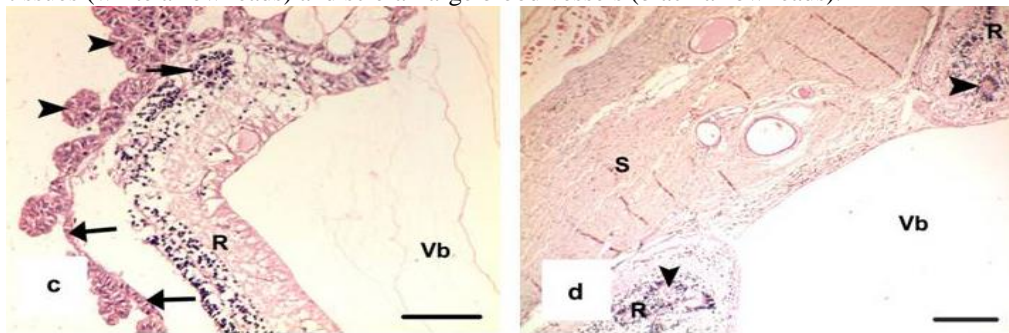
**FIG. 17:** coronal CT scan of a cyclopean goat skull shows one lens in on eyeball (white arrow) and malformed small cranial cavity (black star).



**FIG. 18:** Transverse CT scan shows Ethmoidal fossa and Ethmoidal crest (white arrow).

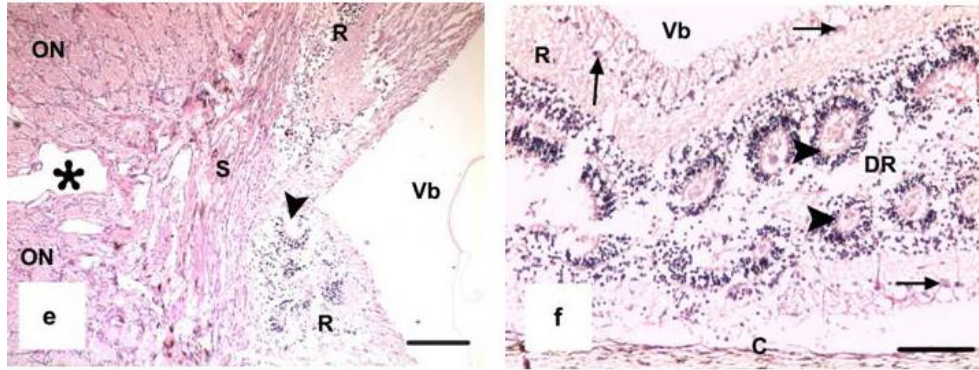


**Fig. 19:** H&E-stained Photomicrographs. ). Scale bars: 200  $\mu$ m  
a; cornea (C) anterior corneal epithelium (longhead arrow), corneal endothelium (arrow) unusual intra-corneal blood vessels (arrowhead), anterior chamber (AC), iris (I) and muscle sphenictor pupili (Sp).  
b; sclera (S), choroid (C) and retina (R) with rosettes (longhead arrow), corresponding acinoid choroidal structures (arrow), intra-ocular sclero-choroidal septum (Sp) extending into the globe cavity and showing the choroidal pigmented tissues (white arrowheads) and scleral large blood vessels (black arrowheads).



**Fig. 20:** H&E-stained Photomicrographs. ). Scale bars: 200  $\mu$ m  
c; higher magnification of retina and associated choroid displaying normal laminated retina (R) and choroid (arrows) and retinal rosettes (longhead arrow) and associated acinoid choroidal structures (arrowhead), vitreous body (Vb).  
d; region of optic disk displaying sclera (S), vitreous body (Vb) and folded dysplastic retina (R) with rosettes (arrowhead).





**Fig. 21:** H&E-stained Photomicrographs. Scale bars: 100  $\mu$ m  
**e;** higher magnification of optic disk region showing optic nerve (ON) spaced by a large cavity at its sagittal plane (asterisk) and folded retina (R) with rosettes (arrowhead), sclera (S) and vitreous body (Vb).  
**f;** higher magnification of dysplastic retina (DR) with rosettes (arrowhead) sandwiched between choroid (C) at one side and normal retina (R) with ganglionic cells (arrow) next to vitreous body (Vb)

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