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Case Report

Congenital Cyclocephalic Holoprocencephalic Anophthalmic, Arhinic Cleft Palate Cyclopia in a Sahelian Twin Kid Goat from the Middle Belt Region of Nigeria

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Abstract

Here we present an extremely rare case of congenital anophthalmic arhinic cyclopia in a female twin kid goat from a multiparous two and half year-old Sahel doe goat from Makurdi, Benue State (middle belt region of Nigeria). The abnormal fetus was delivered at-term with a single eye ball found protruding midline sagittal plane. Cerebral hypoplasia with a single optic nerve was noticed. Cranio-facial dysmorphologies include brachycephaly, bilateral anophthalmia, pseudo orbit, palpebral fissures, eyelids absence and midfacial hypoplasia; musculature asymmetry, distortion, vestigial sinuses and bilateral nasal agenesia (arrhinia). The optic chiasma was absent. Oral cavity presented a malformed tongue, cleft palate and hypoplastic dental pads. Radiographic examinations of the head revealed a cranio-synostosis, rudimentary pseudo-orbit, hypoplastic maxilla, and prognathous mandible. Dissections of the head and skull showed an imperforate choana (achoana) as facial musculo-skeletal and respiratory anomalies, a single cerebral hemisphere without delineations as the nervous system abnormalities. The mixed conditions are extremely rare in Sahel goats and is to the best of our knowledge a first documented evidence in this breed. This developmental error is in congruence with standard characteristics of Bosma Arrhinia Microphthalmic Syndrome (BAMS). The current case is not compatible with life due to complications in other organs and tissues.

Keywords: *Developmental Abnormalities; Teratology; Cyclopia; Embryology; Environmental Toxicity; Sahel Goat*

Introduction

Embryonic malformations in humans and animals often appear as syndromes in which several organs demonstrate morphological abnormalities concurrently and may or not be compatible with life [1]. Congenital anomalies are attributed to genetic or chromosomal mutations, aneuploidies and translocations or developmental process impeding environmental factors [2] culminating in phenotypic dysmorphologies [2,3]. Cyclocephalic and arrhinic anomalies are characterized by failure of the embryonic prosencephalon to properly divide orbits of the eye into two cavities [4], whereas aberrant morphogenetic movements in mammalian eyes have been associated with up and down regulations of certain proteins critical for embryonic development at different growth stages as observed in Bosma Arhinia microphthalmia syndrome (BAMS) cases in humans [5].

Derangements in cell induction through paracrine factors (BMP4 and Fgf8) deficiencies in optic vesicle cells for induction of Sox2 and L-Maf transcription factors respectively needed for activation of lens-specific genes [6] with Lim1, Forkhead, Pax1, 2,3 and 6 transcription factors are involved in coordinated gene expression for eye development [7]. The Sonic Hedgehog (Shh) pathway is also extremely important for vertebrate facial morphogenesis, and is involved in a severe facial midline reduction with a single eye formed at the center

of forehead (cyclopia) [8] and a developmental disturbance of mesodermal structures at the rostral end of the notochord characterized by a poorly developed anterior brain [9]. Craniosynostosis; a premature fusion of sutures confirmed by the radiographic evidence is a common component of the abnormity and occurs roughly 1 in 2,000 live births [10]. It is attributed to the absence of dura mater necessary in maintenance of suture patency resulting in an overtly dysmorphic skull profile [11]. Trisomy 21, a live-born aneuploidy is the result of dosage imbalance of genes on chromosome 21 (Hsa21) and affects complex gene-regulatory interactions thereby altering development to produce varying phenotypes, including characteristic craniofacial complex dysmorphology [12] similar to the current case (Figure 1).

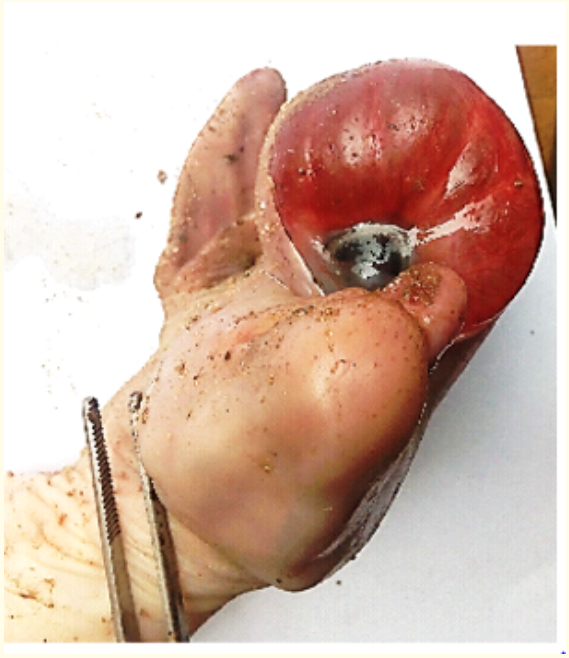

Figure 1: *A ventro-dorsal view of Sahel goat fetus with congenital cyclopia.*

Monstrous formations of several types in domestic animals have been reported in Veterinary literatures to a comparably wider extent than cyclopia in caprine species. Such malformations have been documented with a similar incidence in goats [9,13], sheep [14,15] in sheep, and also in Texel lambs [16]. The current case is unique due to the presence of a cleft palate, arrhinia, craniosynostosis, maxillary hypoplasia and prognathous mandible in addition to the cyclocephaly.

Case Report and Radiologic Findings

Necropsy observations

Facial musculoskeletal development

The cranium was globular with no discernible ethmoid, pterygoids, *Hamulus pterygoideus*, zygomatic arch, frontal and nasal bones, but the sphenoid remain underdeveloped. Unilateral craniosynostosis was observed in radiograph (Figure 3a and 3b), which impacted on the brain morphology, a midline pseudo orbit and hydrocephalus was present (Figure 2a). Nostrils and nasal cavity development was abrogated (Figure 2b and 3). There were no sinuses (frontal, maxillary and ethmoidal). A facial separation at the naso-maxillary junction existed; while the palatine process of the maxilla was attenuated, undershot and disjoint from the contralateral side. Atretic alveolar sockets were noticeable in both the upper and lower jaws.

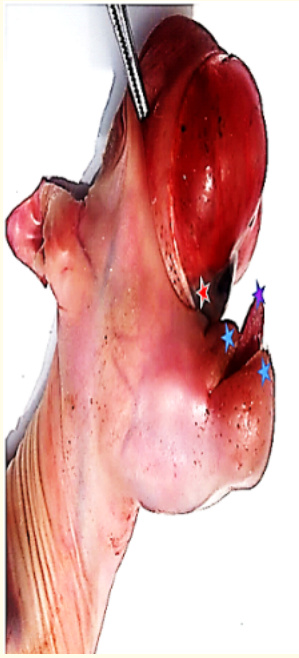

Figure 2a: *Right lateral showing the aberrant morphogenetic single eye, tongue and rudimentary maxillary and mandibular structures.*

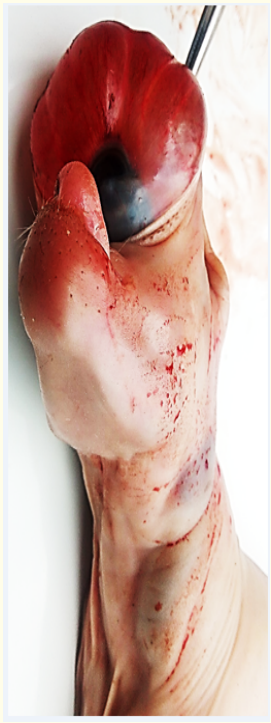

Figure 2b: *Left ventro-dorsal views of cyclopic fetus..*

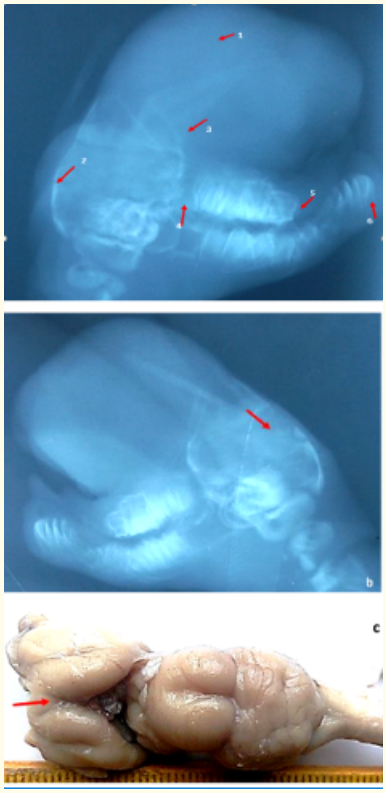

Figure 3a: *A right lateral radiographic view (64KV, 10 MAS) of the cyclocephalic skull of Sahel goat.*

Figure 3b: *A left lateral radiographic view (64KV, 10 MAS) of the cyclocephalic skull of Sahel goat showing; 1-hydrocephalus, 2. Unicoronal cranio-synostosis, 3. Arrhinencephaly (Nasal bone agenesia), 4. Palatoschisis, 5. Maxilla hypoplasia, 6. Prognathous mandible.*

Figure 3c: *A dorsal view of the attenuated cerebrum showing the falx cerebri.*

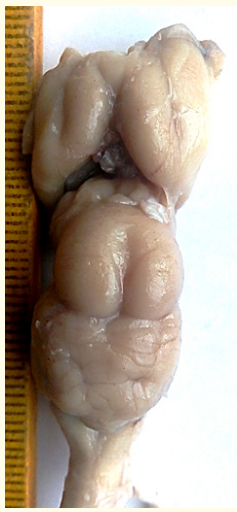

Figure 4

Day-old female twin kids Sahel ecotype goats with dam were presented to the Veterinary Teaching Hospital of Federal University of Agriculture Makurdi, Benue State, Nigeria. One of the kid goats was born dead whereas the other was apparently normal without phenotypic deformities. There was no history of abnormal kidding in the dam; the present twins were delivered normally. Integument covering remained primitive, and mostly hairless. Restricted to the lateral limits of the cleft is a thin membrane of tissue covering the facial region (Figure 2a-2c). There were no noticeable nostrils on the head, nasal passages and choana were atretic and separated. A pseudo-orbit was observed with an exaggerated size single eye dorsal and midline to a poorly differentiated maxilla. The frontal, premaxilla, lacrimal, vomer bones and nasal septum were absent. Ventrally, a cleft into right and left halves was observed in the atretic palatine process of the maxillary bone.

Nervous system

The endocranial dura mater was absent, cerebral cortex in the present case had no right and left hemispheres (arrested at the falx cerebri (Figure 3c)) and hypoplastic though cerebral rugae were noticeable, no olfactory bulbs I', the optic nerve II was singular back-tracked to the fore brain without a chiasm. A traceable oculomotor nerve III was seen, the maxillary component of the trigeminal nerve V' was thin consisting mostly of undifferentiated connective tissue.

Discussion

The necessity to understand the etiology of specific birth defects and its predispositions (breed, age, sex, climate) may reduce the risk of malformed offspring and in addition, tell us how the animal body is normally formed. Early defects are observed in the establishment or maintenance of midline structures, such as the notochord and the floorplate [8] and later cyclopia confirming the role of Shh proteins as an extracellular signal required for tissue-organizing properties of several vertebrate patterning centers [8]. Bosma arhinia microphthalmia syndrome (BAMS) is a rare condition characterized by abnormalities of the nose, eyes and pubertal challenges [17]. It is characterized by a high arch or opening in the roof of the mouth (high-arched or cleft palate) and reported to be caused by mutation of SMCHD1 gene protein responsible for a protein involved in regulating gene activity by altering the DNA structure and silencing of certain genes. Furthermore, it appears to be important in the development of nose, eyes, and other structures of the head and face [17,18]. Problems with nasal development may affect gonadotropin-releasing hormone (GnRH) neurons, which are nerve cells that control the release of reproductive hormones. GnRH neurons originate in the developing nose and then move to the brain. Impaired development of these neurons could explain hypogonadotropic hypogonadism in affected individuals.

Developmental anomalies caused by environmental agents include congenital microphthalmia, aphakia, aniridia, and optic nerve hypoplasia [19], phocomelia [20], microphthalmia [16], diplopagies [21], non-syndromic unicoronal craniosynostosis in man [10] and several other hereditary disorders in small ruminants [3] attributable to toxic ingestion in early gestation. Exogenous agents such as certain xenobiotics, chemicals, viruses, radiation, and hyperthermia could serve as disruptors in development. The main sources of pesticide exposure to humans are through the food chain, air, water, soil, flora and fauna, teratogens may route via toxic ingested chemical agents such as herbicide-sprayed plants, Jervine alkaloids-containing toxic plants (e.g. *Verathrum californicum*) which inhibits cholesterol synthesis necessary for Hedgehog production and reception hence predisposing to occurrence of this form of congenital anomaly [22] during susceptible period (at determination; where there is irreversible commitment of eye cells in a non-neutral environment with respect to the developmental pathway) [7].

A similar report of cyclopian monster occurrence in twin lambs has been documented in sheep [14] affecting only one of the pair while the other is without apparent abnormalities. This suggests the cleavage stage of development (14th day of gestation) as a possible period of embryonic toxicity [23-26].

Presumptive emerging factors which may further predispose or contribute to monstrosities in pregnant animals (in the present case, Nigeria) is insurgence or terrorism, these impose constraints in feeding and watering routines due to displacements and compromising farm procedures, thereby increasing vulnerability of domestic species.

The integration of anatomical information about congenital malformations permits the discovery of genes responsible for inherited defects, period of occurrence and possible disrupted developmental steps [7,15] resulting in altered phenotypic expression of genes.

Conclusion

Prevention of monstrosities in small ruminants is warranted and should consist of restrictions in grazing, scrutiny of feeding protocols especially in early gestation as well as strict policy on intensive management. Demographic age and sex distribution per particular in particular time period in farm(s) has contributed in subtle ways to monstrous birth events [18,22]. Literary evidence showed the epidemiology of congenital malformations to be up to 25% in lamb flocks grazing pastures contaminated with skunk's cabbage (*V. californicum*), hence, Seleniferous pastures should be avoided [14,23] with strict feed and feeding protocol.

Declaration

Ethics Approval and Consent to Participate

Ethical approval was sought and given for this case report to the Veterinary Teaching Hospital FUAM (CVM/FUAM/ECA/18-12)

Consent for Publication

The co-authors agreed to publish and authorized me as the corresponding author

Availability of Data and Material

The data/datum relating to this investigation is available both as soft copies and archival specimen on request

Competing Interests

The authors declare no conflict of interests

Funding

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Authors' Contributions

Dr. Samuel, O.M was responsible for the design and writing of the manuscript whereas Drs. Anike, W. and Okachi, I. were concerned with dissections of the case specimen while Drs Samuel and Adamu, S.S. did the radiographic/radiological investigation

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Informed Consent

Consent of all concerned was duly taken before commencement of the study.

Bibliography

1. Noden DM And De Lahunta. "The Embryology of Domestic Animals". Development Mechanisms and Malformations. Baltimore, MD: Williams and Wilkins (1985): 49-57.
2. Winter RM. "Analyzing human developmental abnormalities". *BioEssays* 18.12 (1996): 965-971.
3. Saperstein G. "Congenital defects and hereditary disorders in ruminants". In: Large Animal Internal MEDICINE, 3rd edition (B. P Smithed.), St. Louis, MO: Mosby (2002): 1465-1555.
4. Shaw ND., *et al.* "SMCHD1 mutations associated with a rare muscular dystrophy can also cause isolated arhinia and Bosma arhinia microphthalmia syndrome". *Nature Genetics* 49.2 (2017): 238-248.
5. Brasseur B., *et al.* "Bosma arhinia microphthalmia syndrome: Clinical report and review of the literature". *American Journal of Medical Genetics Part A* 170A.5 (2016): 1302-1307.

6. Furuta Y and BL Hogan. "BMP4 is essential for lens induction in the mouse embryo". *Genes and Development* 12.23 (1998): 3764-7375.

7. Gilbert F. "Developmental biology 9th edition". Sinauer Associates Inc. Sunderland, Massachusetts USA (2010): 88.

8. Chiang C., *et al.* "Cyclopia and defective axial patterning in mice lacking Sonic Hedgehog gene function". *Nature* 383.6599 (1996): 407-413.

9. Rasheed R., *et al.* "Cyclopia of goat; Micro and macroscopic, Radiographic and computed tomographic studies". *Alexandria Journal of Veterinary Science* 42.1 (2014): 1-10.

10. Aldridge K., *et al.* "Brain morphology in non-syndromic unicoronal craniosynostosis". *The Anatomical Record* 285.2 (2005): 690-698.

11. Ogle R., *et al.* "Ogle Regulation of cranial suture morphogenesis". *Cells Tissues Organs* 176.1-3 (2004): 54-66.

12. Starbuck JM., *et al.* "Trisomy 21 and Facial Developmental Instability". *American Journal of Physiologic Anthropology* 151.1 (2013): 49-57.

13. Alhaji NB., *et al*. "Congenital Anophthalmia and Choanal Atresia in Two Months Old Kid: A Clinical Report". *Journal of Veterinary Anatomy* 6.1 (2013): 17-21.

14. Pugh GD and NBaird. Sheep and Goat Medicine (2nd edition), Saunders (2011): 343-401.

15. Van Der Linde-Sipman JS., *et al.* "Morphology and morphogenesis of hereditary Microphthalmia in Texel sheep". *Journal of comparative Pathology* 128.4 (2003): 269-275.

16. Goncalves MA., *et al.* "Hereditary microphthalmia in Texel lambs in Brazil". *Small Ruminant research* (2017).

17. Gordon CT., *et al.* "De novo mutations in SMCHD1 cause Bosma arhinia microphthalmia syndrome and abrogate nasal development". *Nature Genetics* 49.2 (2017): 249-255.

18. Jansz N., *et al.* "The Epigenetic Regulator SMCHD1 in Development and Disease". *Trends Genetics* 33.4 (2017): 233-243.

19. Wyman M. "Eyes diseases of Sheep and Goats". *The Veterinary Clinics of North America* 5.3 (1983): 657-675.

20. Smolec O., *et al.* "Congenital peromelia in Simental calf". *Veterinarska Stanica* 42.1 (2011): 302-304.

21. Samuel MO., *et al.* "A case of omphalo-ischiopagus (dicephalic dithoracic abdominopagus tetrascelus tetrabrachius) in lambs". *Anatomia Histologia Embryologia* 43.4 (2014): 320-323.

22. Coppock RW And MM Dziwenka. "Teratogenesis in livestock". In: Reproductive and Developmental Toxicology (R. C. Gupta, ed.), USA: Elsevier Press (1996): 1127.

23. Binns W., *et al*. "A congenital cyclopian type of malformation in lambs induced by maternal ingestion of a range plant Verathrum californicum". *American Journal of Veterinary Research* 24 (1963): 1164-1175.

24. Binns WO., *et al.* "Chronologic evaluations of teratogenicity in sheep fed Verathrum californicum". *Journal of. American Veterinary Medical Association* 147.8 (1965): 839-842.

25. Dorsky R., *et al.* "Xath5 Participates in a Network of bHLH Genes in the Developing Xenopus Retina". *Neuron* 19.5 (1997): 981-994.

26. Wang X., *et al.* "Molecular cloning, characterization, and potential roles of cytosolic and mitochondrial aldehyde dehydrogenases in ethanol metabolism in Saccharomyces cerevisiae". *Journal of Bacteriology* 180.4 (1998): 822-830.

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