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 anophthalma, 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.

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 anophthalma, 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 arhinic 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 Arrhinia 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 abnormality 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).

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 cyclopecephaly.

**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.

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

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. Veratrum 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 cyclopyan 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

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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

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