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Alive without a brain: Acrania/anencephaly, anhydraminios, abdominal-ascites, amelia and agenesis of the kidneys

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ABSTRACT

A gravid middle-aged woman viewed on ultrasound demonstrated a viable anencephalic fetus at 25 weeks gestational age. The absence of the bilateral cerebral hemisphere, cranial vault, anhydramnios, abdominal ascites, and phaco-rhizomelia was discovered. We discuss evidence-based quadra –amelia in a non-consanguineous (negroid) couple of a 25-week prenatal scan. Apart from amelia on all four limbs, the fetus had abdominal ascites with other dysmorphic features. Tetramelia is known to be caused by mutation of the WNTB gene; in close relative inter-marriages. A diagnosis of ascites, amelia, anencephaly/acrania, and anhydramnios was made, and the prognosis was documented in this report.

Keywords: Gestational age, Consanguineous, Anencephaly, Acrania

INTRODUCTION

Anencephaly is documented in two types; holonencephaly (when there is a lack of closure posterior part of calvaric bones and brain) and mero-anencephaly (partially preserved vegetative function with the compromised anterior part of cerebrum and skull) [1]. The extreme rarity of this quadra-amelic congenital anomaly has stimulated us to document this fetal case report in our hospital. Very little data exists on etiology of amelia with compounding factors like thalidomide, diabetic pregnancy, drug abuse, chorionic-band-syndrome and some autosomal recessive mutations repeatedly fingered. The incidence of Amelia is about 8 per 10,000 stillbirths and 1.5 per 100,000 live births [1]. Anencephaly is a diseased condition resulting from the failure of closure rostral neuropore between the 24th and 26th day of the embryo (i.e., 3rd and 4th week of pregnancy, resulting in the partial absence of the calvarium (scalp and skull) and cerebrum [2–4].

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The majority of anencephalic neonates die within days after parturition [5]; like this case in question, demise was 7 days after birth. However, there are extremely rare cases [6] of survival beyond 6 months. As little as 10ml of ascitic fluid can be detected via ultrasound [4,7]; the causes of ascites are congestive heart failure, occlusion of the hepatic-veinous-shunt, pericarditis, malignant tumors, tuberculosis, pancreatitis, renal damage, and other causes [8].

Ascites formation in anomalies of the trunk (thorax and abdomen) has been linked to increased intraperitoneal fluid production and reduced rates of removal [9]. Early signs (anencephaly) could indicate a fetal pole below the 5th percentile and polyhydramnios [10,11]. Incomplete amelia / or rare forms of phocomelia variants are eponymically termed: Al-Awadi/ Raas – Rothschild Syndrome (AARR) Syndrome, Zimmer phocomelia, Schinzel phocomelia and Robert's SC phocomelia [12,13]. In men, the most common neural tube defects (NTD) are anencephaly due to a lack of closure of the neural tube (anteriorly) [2]. Machado et al. [14] showed a correlation of other malformations (e.g renal, skeletal, and facial) in addition to anencephaly in over >38% fetuses and newborns. In a study by Obeidi et al. [11] of 26 anencephalic gravidaes; 4 (15%) live deliveries were complicated by shoulder dystocia, while 27% (7) had complications of hydramnios and polyhydramnios. According to a report by Stoll et al. [15] anencephaly related to pulmonary and cardiac anomalies are rare. Limb bud development starts from 25th day in-utero to early 15th week [16] when fully formed.
Disruption in growth pattern results in shortened appendages, (complete) amelia, (partly) meromelia of the fore or hind limbs [16].

CASE PRESENTATION

A 30-year-old woman came for a routine ultrasound assessment in the antenatal clinic of Crystal Specialist Hospital (CSH), Dopemu - Akowonjo, Lagos, Nigeria. The patient was Gravida-2: Para-1 and came for the first time for antenatal care. To our surprise, normal fetal heart sound was present (Figure 1 and 3) at 132 bpm = FHR. There was no history of cannabis intake or high- fever presenting with rashes. Fetal ultrasound revealed bilateral humerii stumps, agenesis of forearm bones, and total compromised osteology of the hind limbs. Referral (to an external health facility) was made for DNA analysis of maternal blood and amniotic fluid; WNT3 – gene and ESCO2- gene mutations were suspected. On sonographic observation, she was in her 2nd trimester in Breech LOA (left occipito-anterior) presentation/lie: with astounding normo-cardia at 132 bpm. The fetus was grossly underweight, <5% (percentile) at an estimated 927g. In the present case, we analyzed motor behavior in an otherwise stringent fetal homeostatic environment; kinesis evaluation in combination with other anomalies.

The patient had no prior bleeding or complaints of abdominal pain. No past medical history of Poly Cystic Ovarian Disease (PCOD) or genitourinary symptoms. After inspection, a physical examination revealed a 'mean body habitus' of a female with normal abdominal and pelvic contours. The subject was advised and counseled on covering pregnancy options. Ultrasound imaging of the patient was not done in the first trimester. There was no history of acute radiation exposure, drug abuse or known family records of congenital anomalies. Selective feticide was not suggested due to ethical reasons. Bilateral fore limbs were poorly formed with a complete absence of pentadactyl manus. Our case is unique as the hypochondriac, and flank/lumbar region of the abdominal cavity completely lacked kidneys (agenesis) (Figure 2).

DISCUSSION

Tetra amelia combined with other defects indicates Roberts syndrome (not Roberts Sign), an antisocial recessive disease. Ultrasound is an effective diagnostic tool for prenatal identification of NTD [17]. Morphological records of defective brain structure in anencephalic pregnancies have been clearly understood. Keypur et al. [18] suggested (invasive) Chorionic Villous Sampling (CVS) as an indispensable tool for prenatal confirmation. Diagnosis of anencephaly with all non-existence anatomical structures is incompatible with life. Other malformations were also observed, such as urogenital defects and spinal compromise. Agenesis of limb buds during the 1st trimester may be due to exogenic, mechanical, vascular or teratogenic effects.

Psychological counseling is necessary for mothers

after a confirmed ultrasound diagnosis, as they exhibit general negative euphoria, including a state of loss, feeling of helplessness, and insomnia [19]. This lethal cocktail makes most fetuses die in-utero; what is unique and compelling about this case is its viability at scanning time despite (vital) viscera incompleteness. However, few of the live-born neonates survive beyond infancy and are severely physically disabled. Anencephaly is a potentially untreatable and lethal condition, with ultrasound diagnosis possible as early as the 11th week [20,21]. Alpha-fetoprotein (AFP) is useful as a neuro-anencephalic screening tool since elevated levels in liquor volume suggest neural tube defects (NTD). The accuracy of ultrasound cannot be overemphasized in this report. Phocomelic syndrome in-utero affects the normal growth projectile of the musulo-skeletal system, and it is sometimes with calvaric malformation [12]. The case tetra-amelia (not tetra-amelia syndrome) is different from partial 'Seal Limb Deformity' with the formation of irregular limbs (phocomelia), a form of meromelia (Figures 2 and 3). Pujari et al. gave phocomelia incidence as 0.62 in 1,000,000 births [12].

Oral declaration of fetal information to patients is expected in an atmosphere of neutrality in clarifying therapeutic and management procedures. A rare anencephalic report generates a need for training specialists' teams in psychology, medicine, and

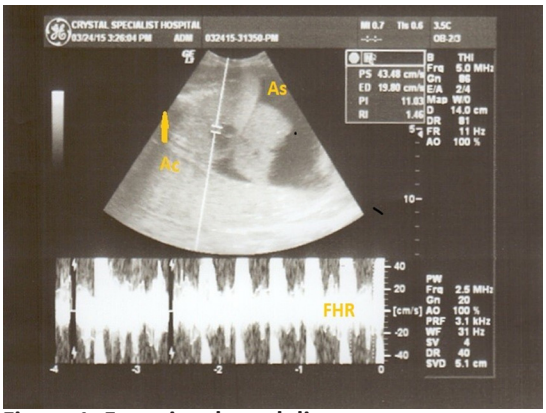

Figure 1: Fetus in a breech lie

Longitudinal presentation with the absence of any identifiable brain parenchyma and skull; anencephaly (acrania) ***(Ac)****. Observe the ascitic fluid* ***(As)*** *in-situ and echo, demonstrating fluffing of the tricuspid and pulmonary valves in diastolic and systolic phases, respectively.*

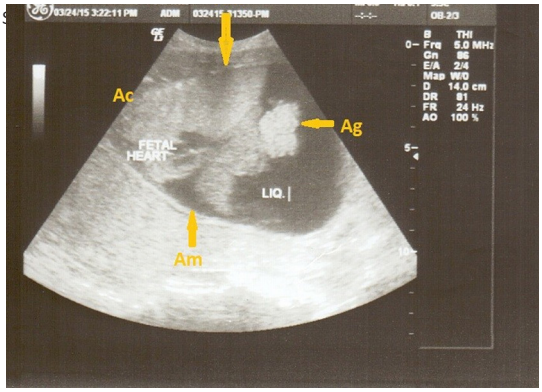

Figure 2: Fetal acrania (Ac) on early 2nd trimester ultrasound

Arrowed (in yellow color) is the lack of osteogenic structures of the forelimbs (amelia) ***(Am).*** *Note the hepatic lobes, absence of kidneys, and agenesis* ***(Ag)*** *of most abdominal viscera. Ethical protocols and permission of the hospital* ***(CSH)*** *were sought for publication, with informed consent obtained from the patient in line with the 1975 Helsinki Declaration on patient rights.*

It can be argued the Greek work word 'anencephaly' (i.e., without head) is actually misleading by anatomical standards. The 'encephalon' part of the central nervous system (CNS) in the calvaria (consisting of the diencephalon and telencephalon), brainstem (medulla, pons and midbrain) [14] might not be totally missing [22], as part of the cerebellum telencephalon and diencephalon are

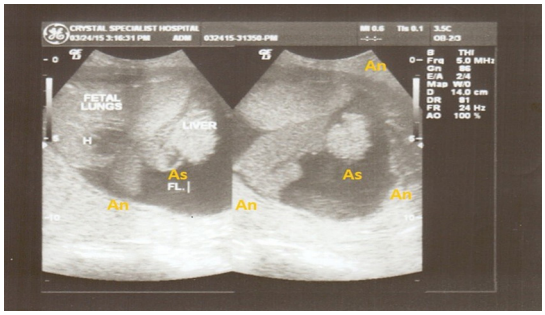

Figure 3: Ascites filled (free fluid) space between the peritoneal lining of the abdominal wall and incomplete bowel loops

Outside the fetal body habitus is the absence of liquor/ amniotic fluid, anhydramnios ***(An****). B-mode; Longitudinal axial view of the fetus demonstrating acrania* ***(An)*** *with no associated cranial vault. Neither the 'Frog Eye Sign'' or 'Mickey Mouse Sign' was demonstrated. Figure shows free fluid* ***As*** *(measuring approximately 562 mm2) in the epigastric, umbilical, hypochondriac and general abdominal cavity****.***

present. Sonological diagnosis can be reliable at 20 weeks of gestation. Bilateral amelia (Figure 5) is a rear defect that could be caused by autosomal recessive mutation and causal factors like amniotic band syndrome and maternal alcohol.

There might be a future history of recurrence in some families. In most hospitals, two options are presented: (a) expectant management or (b) selective feticide followed by surveillance ultrasound. This case could be a result of embryonic loss of mesenchymal migration in the 18th week of gestation, leading to calvaric loss and juxtaposition of cortical structure, similar to an observation by Cheng et al. [23]. Skull-bone formation goes through an initial precondesation [34] or mesenchymatous stage. Within the first 28days of gestation; the head region has mesenchyme generating from 2 regions, i.e., cranial neural crest and unsegmented paraxial mesoderm [24]. Bilateral mesodermal structures on either side of the notochord and neural tube disperse to form lateral columns of the paraxial mesoderm. Towards the end of 21days the paraxial mesoderm stratifies and forms somites which generate sclerotomes [25]. The viscerocranium is formed exclusively from neural crest mesenchyme, while the neurocranium generates from the paraxial mesenchyme derived from the head mesoderm and neural crest, i.e., first-five somites (rostrally) and endodermal cells. Contrary to our findings (Figure 1), the normal fetal head should be fairly large, with an oval cranium and centered orbits. These features can usually be observed above ten weeks' gestational age. An obvious important finding in fetal anencephaly diagnosis using POCUS is the absent calvaria. Other features (but not all-inclusive) are echogenic particles in the liquor/fluid consistent with a fragmented cortex that develops during the transition from acrania to anencephaly [26,27]. The medico-legal decision in respect of induced abortion and pregnancy is up to the couple; we referred them for constant psychological evaluation and monitoring. In agreement with the documentation of Johnson et al. [20,28], anencephaly is indeed a multi-factory fetal anomalic condition. As observed in Figure 1, anencephalic case, respiration of the fetus FHR = 132 bpm, which was normacardiac will have to be spontaneously coordinated by the brainstem spinal cord and cerebellum [29]. Though oral interaction with patient denied consanguinity, it is highly suspected as channels of inheritance are involved in its etiology such as the X-linked dominant and autosomal recessive genes.

CONCLUSION

There is a general perception by ultrasonologists to classify the anencephalous as a 'pseudo-animate-being'; incompatible with survival. However, this view is opined by the daunting physiologic challenges an anencephalous newborn will face, even though neonatologists and pediatricians agree to proceed to give standard care. Establishing national genetic laboratories connected with local clinics would greatly help reduce the occurrence of genetic diseases through appropriate counseling and prenatal diagnosis. Our anencephalous fetus is viable, with stack distinction from brain death being the functional activity of the 'brain stem remnant.

The presence of associated abnormalities like the incomplete genesis of the intestines, ascites, and amelia points to the fact that anencephaly consists of more than a single etiological entity. Studies are needed to establish these connections with other malformations. In agreement with Hall et al. [29], the Zika virus has been shown to cause head abnormalities, specifically microcephaly. The acronym 'PHEIC' (Public Health Emergency of International Concern) was proscribed in early 2016 by the WHO. Later medical officials in Brazil began to notice an increase in cases of fetal microcephaly by late 2015 and later declared a 20-fold-increased incidence (microcephaly) in the region with the Zika virus outbreak.

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