Case study

ANENCEPHALY AND ITS ASSOCIATED CONGENITAL ANOMALIES: A CASE REPORT OF A DELIVERY IN A RURAL HOSPITAL, IN EASTERN UGANDA

Abstract

Introduction: Anencephaly also called **cranioschisis**is part of neural tube defects spectrum which occur when the neural tube fails to close during the 3rd and 4th weeks of development leading to fetal loss, still birth or neonatal death. Literature show that causation of anencephaly is multifactorial involving interaction of genetics and the environment though not well characterized.In this case report, we present the features of anencephaly and its different clinical associated malformations.

Methods: A case report study design was employed to explore the prenatal and antenatal events that resulted into an anencephaly delivery. The intra-natal and immediate postnatal fetal observations and outcome were documented. We also documented the care given to the mother throughout ANC, time of delivery and postnatallyuntil discharge.

Results: 29-year G2P1+0 at 29W2D, presented with 2 days' sudden progressive per vaginal bleeding and clear non-foul discharge on 2nd day of admission with no history of abdominal pain, fever or trauma. Two days later she was delivered by Caesarean section to a grossly neural malformed preterm baby boy with APGAR score 6 at 1 minute and 4 at 5 minutes. Birth weight and length were 1.5 kg and 48.6cm respectively. The baby life indicators deteriorated progressively and finally died at 36 minutes after time of delivery.

Conclusion: Although interaction between genetic and environmental factors that play a role in the causation of anencephaly can not clearly be evaluated, there is an understanding of prenatal and antenatal factors that predispose to this case such as lack of Folate and or interference with its bioavailability, use of teratogenic drugs during pregnancy and antenatal maternal conditions. We therefore recommend routine supply of folate to mothers intending to conceive 3 months before pregnancy through first trimester and health education about use of native drugs and any other conventional medicines during pregnancy.

Key words: anencephaly, neural tube defects, neuroschisis, congenital malformation

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INTRODUCTION:

Anencephaly is part of neural tube defects spectrum which occur when the neural tube fails to close during the 3rd and 4th weeks of development leading to fetal loss, still birth or neonatal death **(Best, 2016).**

In anencephalyalso known as *cranioschisis*, a major portion of the cranial vault fails to form and the anterior neural pore fails to close. Anencephaly is a condition present at during intrauterine development that affects the formation of the brain and skull bones that surround the head. It results in only minimal development of the brain. The brain is exposed to amniotic fluid and gradually degenerates. The condition is incompatible with life (***Vishram Singh 2012).***

The brain lacks part or the entire cerebrum (area of the brain responsible for thinking, vision, hearing, touch, and movement). There is no bony covering over the back of the head and there may also be missing bones around the front and sides of the head ***(CDC, 2015).***

According to Best**2016**in mediscape and Copp et al 2015, causation of Anencephaly is multifactoral involving interaction of genetics and the environment although neither genes nor environment are well characterized. Some cases may be due to chromosomal abnormality or part of the complex process involving single gene defects or disruption of the amniotic membrane. Although NTDs are multifactoral in modal, rare cases have been found to be autosomal dominant or autosomal recessive in some families. The source also adds that it may be detected prenatally with USS and may be suspected as a result of an elevated maternal serum alpha fetoprotein (MSAFP) considered as a screening test as well.

Folic Acid has been shown to be an efficacious preventive agent that reduces the potential risk of anencephaly and other neural tube defects by approximately two thirds. Reproductive health providers need to have a diverse understanding about causes, presentation and prevention of neurodevelopmental disorders so as to prevent the incidences of such cases. In this case report therefore, we present the features of anencephaly and its different clinical associated malformations.

Pathophysiology.

In a normal human embryo, the neural plate arises approximately18 days after fertilization a process called *neurulation*. During the fourth week of development, the neural plate invaginates along the embryonic midline to form a neural groove. The neural groove progresses from midline towards the end directions completing closure at twenty fourth day for cranial end and 26th day for caudal end (Fig. 1). Disruptions of normal closure gives rise toNTDs.

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•*They are numbered as per they came in manuscript text.*

CORRECT THIS ALONG THE WHOLE ARTICLE.

Comment [HC2]: In Anencephaly

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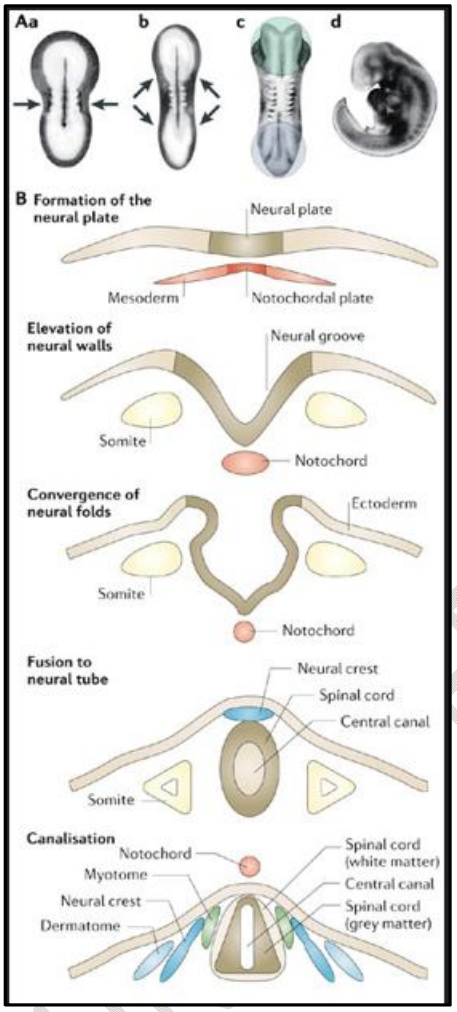

Figure 1: Phases of Neurulation in Neural Tube closure *(Source: Henk, 2006, P.724)*

Anencephaly result from failure of the neural tube closure at the cranial end of the developing embryo while the absence of the brain and calvaria may be partial or complete. Though not well understood, genes involved in folate metabolism are implicated in anencephaly (Fig. 2); methylenetetrahydrofolate reductase is associated with neural tube defects and VANGL1, a membrane associated protein is also implicated (Best, **2016).**

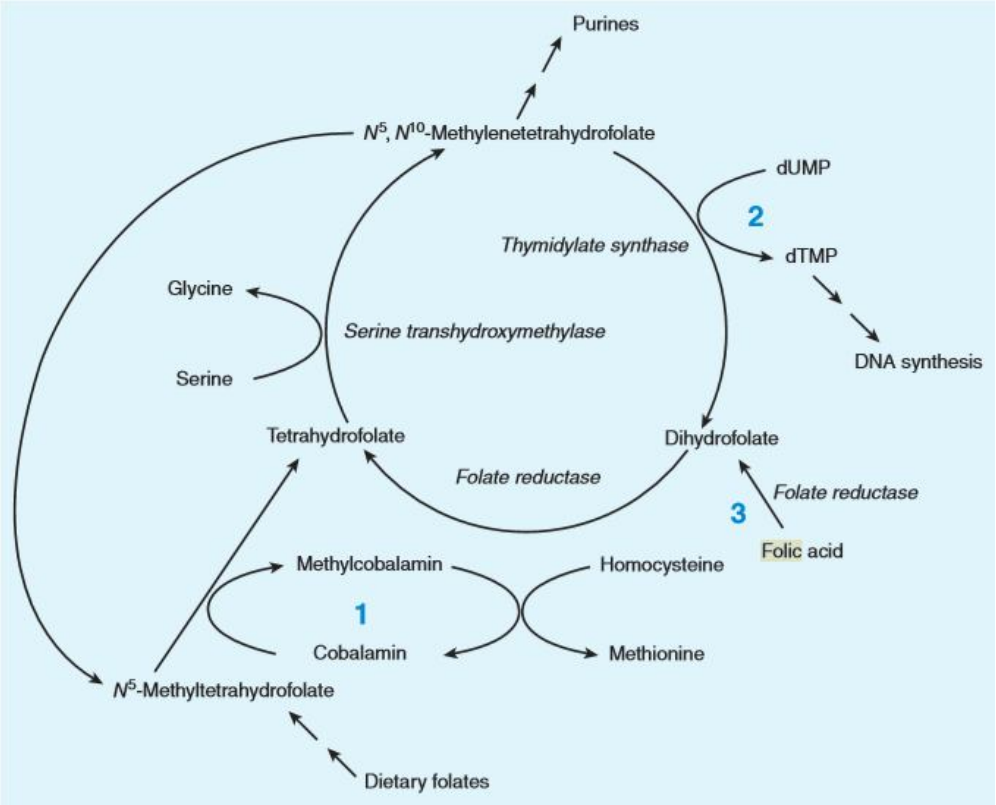

Figure 2: Folate Biometabolism in formation of DNA, *(Source: Katzung, 2012 p.587)*

During pregnancy, human brain and spine begin as a flat plate of cells, which rolls into a tube called neural tube. If all or part of neural tube fails to close, leaving an opening, this is known as an open neural tube defect. This opening may be left exposed or closed with bone or skin. Anencephaly and spina bifida are the two most common neural tube defects (***James Roland 2018, Laura Avagiliano et al*** 2015).An anencephalic infant presents a distinctive appearance with a large defect of the calvarium, meninges and scalp associated with a rudimentary brain, which results from failure of closure of the rostal neuropore, the opening of the anterior neural tube.

The additional anormalies include; folding of ears, cleft palate, and congenital heart defects in 10% to 20% of the cases. Most anencephalic infants die with several days of birth. Approximately 50% of cases of anencephaly have associated polyhydraminous (Kliegman R.M 2016).

In Uganda cases of neural tube defects are rarely reported, and there is no intentional formal recording of such cases most of which are go un-noticed.

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Epidemiology of anencephaly.

Geographical variation of NTDs exists with hot spots in Guatemala, Northern china, mexico, parts of UK. Hispanics and non-Hispanic whites are more affected than women of African origin females more affected than males(Best **2016, Williams LJ 2005 cited in CDC 2015).**

Anencephaly and spina bifida comprise 95% of neural defects and the remaining 5% is encephalocele. It is common in lower socioeconomic group. Recurrence risk after one affected child is 4% and about 70% of anencephalic fetuses are females mainly prevalent in 1st birth, young and elderly mothers (*Konar Hiralal, 2014***)**.

Uganda lacks recent accurate data on prevalence of birth defects and a national birth defects registry. 2006 march of demise global reports birth defects estimated prevalence of 60.9/1000 in Uganda, neural tube defects at 1.3/1000. Overall prevalence of birth defects 66.2/10,000, Hypospadias; 23.4/10,000, talipes equinovarus 140/10000, NTDs at 10.3/10000, microcephaly 1.6/10000, microtia and anotia 1.6/10000, imperforate anus 2.0/10000. 94% of all birth defects in resource limited settings (***Mumpe-Mwanja 2019).***

Linda WXu and colleagues in their study; Neural tube defects in Uganda: A follow up out comes from national referral hospital (Linda WXu 2018), revealed that out of a sample size of 230 participants; myelomeningocele accounted to 92%, hydrocephalus and club foot (18%). Anencephaly was not mentioned in the findings.

Frequency during pregnancy is higher than at birth prevalence because such pregnancies end early by spontaneous abortions, fetal death and pregnancy termination (Best, **2016).**

Recurrence risk is approximately 4% and increases to 10% if a couple has had 2 previously affected pregnancies.Kliegman R.M, 2016recommends that families with previously affected child of anencephaly use folic acid dose 10 times higher than what is generally advised for general population (4mg/day Vs 400 mcg/day)

Risks of Neural Tube Defects

Mai CT 2019, enlist that women with high risk include; women ≥35 years of age, previous pregnancy affected by birth defect, women with chronic diseases (such as; Lupus, high blood pressure, diabetes, epilepsy, and women on certain medications).

Many factors in addition to genetics are implicated as a cause of anencephaly including low socioeconomic status, nutritional and vitamin deficiencies and a large number of environmental and toxic factorsKliegman R.M (2016).

Investigation of congenital abnormalities prenatally.

The investigation done in this case was ultra sound scan.

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Ultra sound scan has been shown to be most commonly used and accurate in detecting neural tube defects as early as first trimester as supported by some earlier aricles (Goldstein and Filly 1988, Avagliano et al 2020). However, according to Shimony 2018, MRI is the mainstay imaging study test for neural tube malformation defects.

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Ultra Sound Scan done at 12th week of gestation is diagnostic. It also helps evaluate polyhydrominous which is a common feature (Shimony **2018).** This evidence adds that extra fluid behind baby's neck and increased fluid indicates chromosomal disorder or heart defect.

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Nancy and mennuti 2022, listed other investigations that could be of benefit though not routinely performed due to limited access that include;

1. MSAFP; effective in 2nd trimester for vast majority of cases with or without history.
2. Amniotic alpha fetoprotein in late 1st and 2nd trimester is diagnostic biochemical test for anencephaly. False positive is excluded by ACHE which is positive for open anencephaly. Cytogenic testing excludes trisomy 13. Abnormal levels of alpha fetoprotein may also indicate; multiple fetuses, miscalculated due date, chromosomal disorders, brain or spinal cord defects.
3. Chorionic villi sampling, for detection of chromosomal and genetic abnormalities.
4. Amniocentesis. For protein levels: ALF, AChE (produced by unborn baby).
5. Cell free fetal DNA (cff-DNA) done at 10 weeks of amenorhhea.
6. First trimester screening 11 to 13 weeks of pregnancy,
    a. Looking for defects related to baby's heart or chromosomal disorders like Down syndrome.
    b. Maternal blood screen to measure two proteins; human chorionic gonadotrophin and pregnancy associated plasma protein A (PAPP-A). Abnormally high or low protein levels indicates chromosomal defect or heart defect in the baby.

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Some of the possible complications of congenital abnormalities;

1. Hydraminios 70%
2. Malpresentation (face or breech).
3. Premature labour.
4. Tendency of post maturity.
5. Shoulder dystocia
6. Obstructed labour if head and shoulders try to engage together because of short neck.

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Management

Medscape suggested termination of pregnancy when confirmed in which the couple is counseled.

The uterus is often refractory to oxytocin because of the low levels of estradiol as a result of insufficient production of precursor cortisol from the fetal adrenals. Use of prostaglandin vaginal gel (PGE2) has been proved to be effective in resistant cases.

During labor, there is a tendency to delay and shoulder dystocia may be managed by cleidotomy.

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Prevention

Pregnancy counseling on causes, prevention, preexisting medical conditions, ongoing medications, drug abuse (smoking, alcohol, among others) and time of conception.

Method

Study design

A case report study design was used to retrospectively document the circumstances and conditions of a mother before and during pregnancy, at time of labour and after delivery. Observational findings were recorded and presented in form of a clinical case according to guidelines for making a clerkship writeup or an obstetric case.

Study setting

This case report was a mother delivered in Amuria district General Hospital Operation theatre located in the heart of Amuria Town, Amuria District in the Teso sub-region, in far Eastern part of Uganda (Fig.3). The hospital is located about 400km by road on eastern route from Kampala capital of Uganda. Amuria hospital is a rural 100-bed capacity hospital serving apopulation of approximately 518,492people 92.2% of which are rural (UBOS 2020). The facility offers among others reproductive health services including operative obstetric services. There is a team of multi-disciplinary health workers including general practitioner doctors, nurses, midwives, allied health staff and administrative and support staff among others.

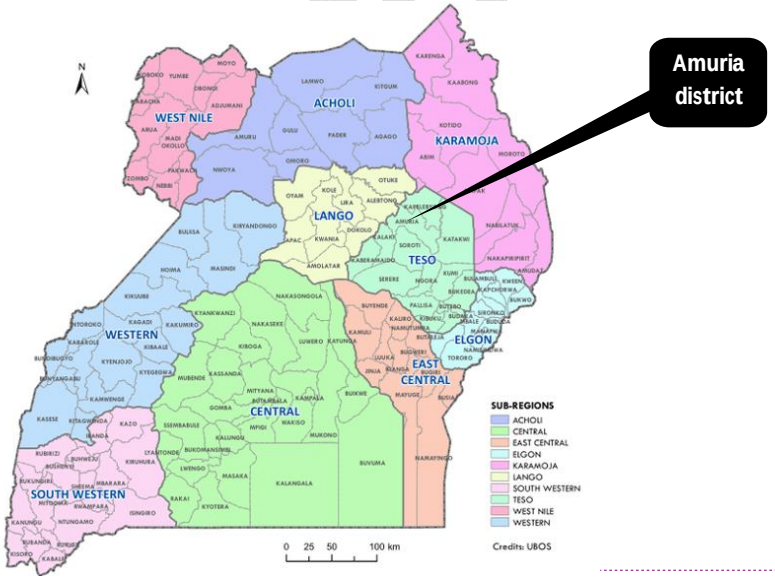

Figure 3: Map of Uganda showing districts and regions of Uganda (source: UBOS, 2020)

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Methods and procedures of data collection

Data was collected through clinical care-based observation and case notes recordings. Retrospective in-depth interviews were conducted with the mother and other care providers to enrich and substantiate delivery findings.

Case presentation

Maternal biodata

A patient was a 29-year old Gravida 2 Para 1 + 0 at 29 Weeks 2 Days of amenorrhea was admitted on June 7, 2020. She was anAtesot Catholic married in Komolo village Werasub-countyAmuria district. Her highest level of education was Tertiary institution and working as a secretaryat a local police station.

Presenting complaint.

Bleeding per vagina for 2 days.

History of presenting complaint.

The patient was well till 2 days prior to admission when she developed sudden bleeding per vagina which happened while in the garden digging. It was initially mild during the first day occurring in intervals of about every 2 hours and progressively intensified on the second day which prompted her to seek medical attention in nearest health center. The bleed was fresh and bright red with no clots only filling two pads on day 1 and 4 on day 2.This washer index episode of bleeding per vagina since conception, she reported no history of; trauma, abdominal pain, fever andwith no history suggestive of significant haemodynamic compromise.. While in the hospital she developed per vagina discharge of non-foul-smelling clear fluid on 2nd day of admission. She reported normal bowel and normal micturition habits.

Review of other systems.

Central nervous system

She reported no history of; headache, loss of consciousness, convulsions, impaired vision and hearing.

Cardiovascular and respiratory systems

She reported no history of; cough chest pain, facial and limb oedema, difficulty breathing while lying on flat surface, dizziness, fatigability and breathlessness on exertion.

There was no remarkable history in ear nose and throat and musculoskeletal systems.

Current obstetric history.

The patient was a 29-year G2P1+0, LNMP at 29W2D of amenorrhea who attended first ANC at 20 weeks of gestation in Amuria General Hospital.She had the following tests done; RCT (negative), Hb

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estimation (10.2g/dl), BP (120/85 mmHg), weight (62 Kg), and height (1500cm).Medications given include; IPT, iron sulfate and folic acid..

On 5 different occasions, she had a history of LAP, burning pain on micturition, per vagina discharge of white foul-smelling fluid with associated genital itching and abdominal discomfort in suprapubic area. She was managed forurinary tract infections with standard protocol management according to Uganda MOH guidelines with temporal relief following full dose treatment.She then used unknown herbal medicines in 2nd trimester for 3 months,and noticed temporary relief after 1 month of use. She also reports being treated with unspecified medication from a local peripheral health facility for genital candidiasis.There was no history of exposure to X-ray and she had never done abdominal USS. She had no history of trauma to the abdomen, febrile illness and no known history of use of neurotoxic agents, folate antimetabolites and no previous history of prior per vagina bleeding during this pregnancy. She reportedinfrequent episodes of mild vomiting of food eaten in first trimester and resolved without treatment. She fed on her usual food throughout pregnancysimilar to previous pregnancynamely; silver fish, greens vegetables, cabbages, beans, red meat, millet bread and cassava, among others.

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There was no history of hypertensive disorders like preeclampsia during previous and present pregnancy.

The father of the current pregnancy was a new sexual partner and had 3 normal children with another sexual Partner.

Past obstetric history

She delivered 1st baby by SVD at term when she was twenty-four years old, birth weight 2.8kg, male, APGAR score not known but baby didn't cry immediately and was resuscitated. She had four ANC visits, no Abdominal USS done. She reports no other complications like PPH. The child is now 5 years, schooling.

Gynecological history.

She had menarche at 15years (primary 5), coitarche at 21 years and could not recall exact period of thelarche. She has had 3 sexual partners. No history of sexually transmitted illnesses likesyphilis, HIV. She had family planning 1 year after delivering first baby and she received 3 months injections four times. She changed to pills because of excessive bleeding during menses which was not comfortable with; she would only take pills when the husband is around. She also reports use of IUD but didn't specify the time although she agrees it was after stopping injectable family planning method.

She has never had any gynecological operations and she had never screened for ca cervix.

Past surgical history

She reported no history of surgical operation; no history of trauma/ accident and she has never been transfused.

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Past medical history

She reports no history chronic illnesses like diabetes, hypertension, asthma, cancer and no H/o drug and food allergies. No history of hospital admissions.

Family and social history

There is no known history of familial illnesses like sickle cell disease, asthma, epilepsy, diabetes, among others. She was the 4th borne to her mother and all siblings were alive with no congenital births among parents and sibling families.

The patient was in her 2nd marriage to a policeman who had another wife with 3 normal children (no congenital abnormalities). She had history of drinking a ½ glass and or little more of alcohol per day which she had stopped 3 years priorfollowing episodes of vomiting after eating mutton while taking alcohol. She had never smoked tobacco. The current husband smoked tobacco and took alcohol. She slept in a semi-permanent house under an insecticide treated mosquito net and used borehole water.

Examination Findings

General Examination

Mother was in a fair general condition, not in respiratory distress, afebrile with a temperature of 35.8C, no jaundice, no pallor, no cyanosis, no edema, and no dehydration.

Cardiovascular system

She had a normal BP of 123/85 mmHg, normal pulse of 90 beats per minute and $SpO_2$of 95%. Heart sounds 1 and 2 were normal with no added heart sounds and no murmurs, no cardiac rub.

Respiratory system

She was not in distress with respiratory rate of 14 breaths per minute. The chest was of normal shape, symmetrical, moving with respiration and no scars. Non-tender, no palpable masses, normal percussion note in all lung fields. Vesicular breath sounds heard in all lung fields with no added sounds like crepitations.

Urinary system.

There was no renal angle tenderness and the urinary bladder was not palpable, no urethral discharge and lesions in the urethral orifice.

Obstetric Abdomen and Pelvic exam:

The abdomen was grossly distended (Gravid), symmetrical withstriagravidarum and linear Alba. No visible masses, no scars. The abdomen was moving with respiration. Superficially, the abdomen was tensed and non-tender. On deep palpation, the liver, spleen and kidneys were not palpable and non-tender

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The obstetric pelvic examination showed:

- FH = 36/ 40.
- Lie = longitudinal
- Position = LOA
- Presentation = cephalic
- Absent uterine contractions
- Fetal heart = 120 beats per minute (by fetoscope).

Vaginal Examination

- Vulva and vagina were normal, soiled with blood, vagina was warm and moist.
- Cervix was thick and firm.
- Os was closed.

Other systemic examination findings were unremarkable.

Investigations done

Abdominal Ultra Sound Scan findings revealed a single live fetus with anencephaly at 28 WOA, in longitudinal lie, cephalic presentation. The scan also revealed polyhydramnioswith AFI of 35 cm and other neuronal fetal anomalies which included; spinal bifida, cleft lip and palate.

The uterine adnexa were normal. The ultra sound scan showed normal findings of; liver, spleen, urinary bladder and kidneys.

Hematological assessments revealed normal CBC parameters, Blood group O Rh D+, negative blood slide for malaria parasites and random blood sugar of 5.8 mmol/L

Urinalysis;

The urine was pale yellow clear in appearance.Negative findings of; proteins, glucose, ketones, bilirubin, urobilinogen, nitrites, blood, and a slightly acidic pH of 6.5.

Microscopic examination of urine revealed 5 epithelial cells per high power field, and no; pus cells, red blood cells, parasites among others.

Peri-natal Diagnosis

29 year old G2P1+0 at 29 W2D with multiplecongenital fetalabnormalities- anencephaly, spina bifida, cleft lip and palate, under lapping little right toe, short neck and low set ears.

Management plan

Maternal and partner counselling:

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1. Causes, management plan and the possible prognosis of this condition.The possible risk factors and prevention werehighlighted in the discussion, which included;
    a. minimizing exposure to; x-rays, radiations,
    b. Use of teratogenic drugs especially in first trimester like thalidomide, and there was need to consult a trained health worker before considering use of medications during pregnancy
    c. Infectious agents like viruses.
    d. Missing out ANC early interventions and health education among others.
    e. Inadequate intake of folic acid in first trimester.
    f. Chromosomalabnormalities.
2. Pre-conceptual care and ANCfor the next pregnancy to improve the outcome despite documented 4% chance of recurrence.
3. The need to terminate the current pregnancy as the abnormalities were severe and incompatible with life.The termination would be medical induction and cesarean section would be an option in case induction fails.
4. *Psychosocial Support.* The couple was referred to social worker for psychosocial support. The couple was advised not to blame one partner as cause but consider the occurrence of congenital abnormalities as accidental occurrence and may never occur though there's a possibility of recurrence and can be minimized with medical consultations before and during pregnancy.

Deliverynotes

Inductionwith Misoprostol was attempted according to Uganda MOH clinical guidelines (MOH, 2016). and there was no progress of labour after two days of monitoring. The decision for caesarean section was then made. The couple was counseled and consented for elective cesarean section. This was done on day 3 of admission under spinal anesthesiabypfanenstiel abdominal and crescentric lower segment uterine incision. A livesyndromicmale babywas born, weighing 1.5 Kg, length 48.6 cm and APGAR scores of 6/10 at 1 minute and 4/10 at 5 mutes. Newborn examination was done and revealed multiple physical abnormalities i.e. anencephaly, spine bifida, split face frog-like protruding eyes and cleft pallet (Fig.4), extra digits, plantarflexed under lapping right little toe (Fig. 5), short neck, low set ears and postero-hyperarched back (Fig.6).Excessive clear amniotic fluid was found. No resuscitation was tried due to gross congenital malformations. The baby died 32 minutes after delivery.

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Figure 4; Back of the baby showing spina bifida and exposed poorly developed brain tissue, absent calvarium and grossly malformed facial structures (Photo by Opolot I. and Emaru J. 2020).

Comment [HC25]: Is these photographs are from other study ???

Figure 5; Photo showing right foot with underoverlapping poorly formed little toe(Photo by Opolot I. and Emaru J. 2020).

Figure 6: Showing short neck and low set ears, cleft lip and palate (Photo by Opolot I. and Emaru J. 2020).

Post-operative management and outcomes

The mother was clinical stable after the procedure with;

Mild pain at incision site, no pallor, not in distress, BP130/85 mmHg, pulse 80beats per minute, RR 14 breath per minute, GCS 15/15 pale yellow urine out put 2500mls in 24 hours.

Treatment given to mother;

Antibiotics; IV ceftriaxone and IV metronidazole; Analgesics; IV paracetamol; IV fluids; normal saline 2 liters, dextrose 5% 1.5 liters in 24 hours; dressing of the incision site with povidone iodine and continuous bladder drainage for 24 hours.

Mother was counseled on family planning at discharge to prevent pregnancy for 2 years to allow scar healing.

Discussion

According to **DC Dutta*2013***anencephaly is common in lower socioeconomic group. Recurrence risk after one affected child is 4% and about 70% of anencephalic fetuses are females mainly prevalent in 1st birth, young and elderly mothers. The case in question is among the 30% with exceptional a male fetus, in 2nd birth as opposed to 1st birth but within the lower social economic similar to studies elsewhere.

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Anencephaly and some other NDTs rarely present as an isolation malformation as it was observed for this case.They are always associated with other syndromes and or malformations such as trisomies like down's syndrome, or rarely meckel Gruber syndrome (Yaqoubi and Fatema, 2018)and other isolated urogenital, gastrointestinal and or musculoskeletal malformations (Gole, Meshram and Hattangdi, 2014).

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Best cited in Medscape 2016points out the risks to anencephaly as;Folate antimetabolites, Maternal diabetes (insulin dependent DM), Maternal obesity, Mycotoxins in contaminated corn meal, Arsenic, Hyperthermia in early development. In this scenario, the mother had no history of diabetes, obesity. However, exposure to mycotoxins, arsenic, and folate antimetabolites could not be ruled out.

The mother reports no exposure to x-rays, no history of chronic medication no history of drug abuse during this pregnancy although the husband is a smoker and takes alcohol. She reports no history of syphilis infection. This is parallel to article A hospital based birth defects surveillance system in Kampala, Uganda by ; **Daniel Mumpe- Mwanja, Linda Barlow- Mosha,2019** which implicates High fertility rate, nutritional deficiencies, Exposure to teratogens, Weak regulation of medication, High prevalence of congenital infections to be risks for neural tube defects.

The mother was less than 35 years old and had no history of previous birth defect and chronic illness which are said to be among probable high risks to neural-tubal defects (**Mai CT et al 201)**

The mother attended first visit at 20 weeks indicating missing folic acid during first trimester when organogenesis occurs. She would have also benefited from other antenatal services including health education and counselling during the early development. Folic acid has been proved to help prevent neural tube defects. According to CDC 2015, folic acid supplementation beginning 1 month before conception to 12 weeks of pregnancy has shown reduced risk of neural tube defects by 85%. This might have been the main gap in the management of this patient.

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Management of neural tube defects with uterotonic agents using oxytocics to induce labour is less effective and so Medscape (Best 2016) recommends that since the uterus is often refractory to oxytocin because of the low levels of estradiol as a result of insufficient production of precursor cortisol from the fetal adrenals. Use of prostaglandin (PGE2) vaginal gel has been proved to be effective in resistant cases. It is not clear as to why Misoprostol given in this case was futile.

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Conclusion

Anencephaly and neural tube defects though not very common still do occur and cause a lot of psychological challenge to the parents and caregivers. Although interaction between genetic and environmental factors that play a role in the causation of anencephaly cannot clearly be evaluated, there is a clear understanding of prenatal and antenatal factors that predispose to this case such as lack of Folate and or interference with its bioavailability, use of teratogenic drugs during pregnancy and antenatal maternal conditions.

Recommendations

We therefore recommend routine supply of folate to mothers intending to conceive 3 months before pregnancy through first trimester and health education about use of native drugs and any other conventional medicines during pregnancy.

HMIS reports revealed that the rate of spontaneous abortions in Amuria General Hosptal in the preceding months was 58 in 1st trimester and 6 in 2nd trimester (Amuria Hospital HMIS 2020). This is presumably high for a target population of 518,492 with 25,924 calculated expected pregnancies per year and yet no studies have been done to rule out neural defect abnormalities which might be the contributing factors. Therefore, there is need to conduct a study to evaluate the frequency of neural defect abnormalities during early pregnancy because many pregnancies end early by spontaneous abortions, fetal death, pregnancy termination with no established causes.

Conflict of interest

The principal investigator was a staff at the facility where this case was delivered and managed and at time of management of the case the PI was a 5th year Medical student undertaking his pre-internship clinical placement at Amuria Hospital.

REFERENCES

1. Avagliano L, Massa V, George TM, QUreshy S, Bulfamante G, and Finnel RH. Overview on Neural tube defects: from development to Physical Characteristics. Birth defects Res. 2019 Nov 15; 111(19) 1455-1467, https://dio.org/10.1002/bdr2.1380.PMC 2020.
2. Center for disease control and prevention 2015, Folic Acid: Birth defects count. (2020).
3. *Copp AJ, Adzick NS, Chitty LS, Fletcher JM, Holmbeck GN, and Shaw GM. Spinal Bifida. Nature Review Primers, 1, PubMed. 2015.*
4. *Konar Hiralal. DC Dutta Dc Dutta's textbook of obstetrics, 7thEditionJaypee Brothers Medical Pub ISBN-13: 9786222864, (2014)*

Comment [HC29]: ***In References instead of DOI you have mention DIO which leads to wrong link.***

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5. Henk JB, Shaw GM, Heijer M, and Finnell RH., Neural tubal defects and folate: case far from closed. Nature Reviews-Neural science Nov 2006(7). 724-730. PubMed (2006).
6. Roland J. What is anencephaly? Healthline. 2018.
7. Katzung, Masters and Trevor. Basic and clinical Pharmacology, 12th Edition McGraw-Hill Companies, Inc United States ISBN: 978-0-07-176402-5. (2012),
8. Kliegman R.M Bahrman RE jenson HB and Stanton BF., *Nelson's Textbook of paediatrics 11th edition***Saunders, an imprint of Elsevier Inc.**(2016)
9. *Avagiliano L, Valentino Massa and Richard H. Finnell* 2015 birth defects
10. Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ, Lupo PJ, RiehleColarusso T, Cho SJ, Aggarwal D, Kirby RS. National population-based estimates for major birth defects, 2010-2014.Birth defects Res. 2019 Nov 1.111(8): 1420-1435. https://dio.org/10.1002/bdr2.1589.Epub 2019 Oct3. PMID: 31580536; PMCID: PMC7203968. (2019).
11. Best RG., Gregg AR., Lorenzo N., and Nelson SL. Anencephaly. Medscape WemMD LLC. (2016)
12. Mumpe- Mwanja D., Barlow-Mosha L., Williamson D. et al.A hospital-based birth defects surveillance system in kampala, Uganda. BMC pregnancy and child birth 19, 372 (2019)https://dio.org/10.1186/s12884-019-2542-x
13. Nancy and Mennuti, Fetal Neural tube defects: Diagnosis, management and treatment. GLOWM 2022.
14. Sims – Williams HJ., Sims – Williams HP., Kabachelor EM., Fotheringham J. and Warf BC. Ten-year survival of Uganda infants with meningomyelocele closure. J Neurosurg Pediatr. 2017 Jan; 19(1): 70-76. https://dio.org/10.3171/2018.7PEDIS16296.Epub 2016 oct 21. PMID: 27767901 (2017)
15. Uganda Ministry of health. Uganda clinical guidelines, Kampala-Uganda.2016
16. *Vishram Singh.Text book of clinical embryology 2nd Edition. (2012)*
17. Wart BC. Chills Nervsyst. Hydrocephalus associated with neural tube defects, characteristics, management, and outcome in sub-Saharan Africa (2011).
18. Williams LJ, Rasmussen SA., Flores A., and Kirby RS. Decline in prevalence of spina bifida and anencephaly by race and ethnicity: 1995-2002. Pediatrics 2005 Sep; 116(3):580-6. https://dio.org/10.1542/peds.2005-0592.PMID: 16140696. PubMed(2005)
19. Ministry of health. Health management information system Volume 1, Health Unit Manual. Ministry of Health, Kampala-Uganda (2010).
20. Uganda bureau of statistics. Uganda National Population statistics. UBOS, Kampala-Uganda (2020).
21. Gole RA., Meshram PM., and Hattangdi SS. Anencephaly and its associated malformations. J Clin Diagn Res. 2014 Sep; 8(9): AC07-AC09. https://dio.org/10.7860/JCDR/2014/10402.4885.(2014).
22. Yaqoubi HNA and Fatema N. Meckel Gruber syndromeassociated with aencephaly – an unusual reported case. Oxford Medical Case Reports, 2018(2) Febuary 2018, omx. https://dio.org/10.1093/omcr/omx092.

Comment [HC30]: ***In References instead of DOI you have mention DIO which leads to wrong link.***

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Comment [HC36]: ***•All references are not as per Vancouver style. Some are incomplete some are not in Vancouver style, some have missing page numbers, some have wrong page link.REWRITE ALL THE REFERENCES AS PER VANCOUVER STYLE.***