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Germ Cell Tumour in a 10-Month-Old-Baby: A Case Study of University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State, Nigeria

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***Abstract*—** *This study investigated the outcome of treatment for ovarian germ cell tumours in a pediatrics' population at the University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State of Nigeria. To accomplish our goal, a ten-month-old baby on admission was monitored. The baby (KAD), a female from Cameroun, on admission presented with fever, intra-abdominal malignant swelling, cough, scaly skin lesions and leg swelling. She received nutritional support and was placed on medications including: artesunate; ceftriaxone; gentamycin; albendazole; and fluconazole. She experienced worsening symptoms and was certified dead while on treatment. Findings revealed that complications were as a result of patient reporting late for treatment.*

***Keywords*—** *Intra-abdominal malignant swelling, Germ cell tumour, Kwashiokor, Sepsis*.

I. INTRODUCTION

Cancer is a genuine term for a large group of diseases that can affect any part of the body. Terms like malignant tumours and neoplasms are equally used. A defining feature is the rapid creation of abnormal cells that grow beyond their usual boundaries, which can then invade adjourning parts of the body and spread to other organs through the process of metastases. Metastases are a major cause of death from Cancer (Ferlay *et al*., 2013). Cancer together with cardiovascular disease, diabetes, chronic kidney disease and respiratory disease account for 83% of all deaths arising from chronic diseases. Other less fatal but common chronic diseases are among leading cause of disability that severely affect quality of life (Raghupathi *et al.*, 2018). Of the 57 million global deaths in 2008, 36 million, or 63%, were due to non - communicable diseases, principally cardiovascular diseases, diabetes, cancers and chronic respiratory diseases. As the impact of non - communicable diseases increases, and as population's age, annual non - communicable disease deaths are projected to continue to rise worldwide, and the greatest increase is expected to be in low - and middle-income regions (Raghupathi *et al.*, 2018). Though, 80% of non-communicable disease deaths occur in low and middle - income countries and they are the most frequent causes of death in most countries, except in Africa. It is projected that even in Africa, deaths resulting from non-communicable diseases are rising rapidly to exceed communicable, maternal, perinatal, and nutritional diseases as the most common causes of death by 2030. Mortality and morbidity data reveal the growing and disproportionate impact of the epidemic in lower-resource settings. More than two thirds of all cancer deaths occur in low- and middle-income countries. Estimated percentage increase in cancer incidence by 2030, compared with 2008, will be greater in low-(82%) and lower-middle-income countries (70%) compared with the upper-middle-(58%) and high-income countries (40%) (WHO Global status report on noncommunicable diseases, 2010). Cancer is the second leading cause of death globally and responsible for an estimated 9.6 million deaths in 2018. Globally, about 1 in 6 deaths is due to cancer (Stewart *et al.*, 2014).

Measurement of incidence rates of childhood cancer in Africa is difficult. However, for several childhood cancers, incidence rates in Africa are higher than those in high - income countries. This applies to infection related cancers such as Kaposi Sarcoma, Burkett's lymphoma, Hodgkin lymphoma and hepatocellular carcinoma and two common embryonal cancers- retinoblastoma and nephroblastoma. 4.6% of cancers occur at ages 0 – 14, compared with 0.5% in high-income countries. The incidence of childhood cancer is on the increase averaging 0.6% increase per year, since mid1970s through 2009 and 0.8% per year during 2010 - 2014, resulting in an overall increase of 24% over the last four years. Estimates are 1 in 285 children were diagnosed with cancer in 2014 (Childhood cancer fact library, 2018). Cancers in the paediatric population are still a relatively uncommon cause of morbidity on the average, only 33 cases will occur each year in a population of 1 million. Information concerning ovarian tumours occurring in African children still remains limited (Parkin *et al.*, 2017).

Survival chances improve as the child gets older, thus plays significant role in the incidence and types of tumour seen in the children; each developmental stage is associated with different disorders and diseases. There is also remarkable geographic difference in the incidence and pattern of malignant tumour distribution, and death rate associated with specific tumours (Kupfer *et al.*, 2006). Many factors such as abnormal development, tumour induction and prevalence of underlying familial or genetic aberrations are implicated in tumorigenesis in children (Schofield *et al.*, 1999). Increased

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prevalence of previously uncommon tumours in children in our geographical setting, with male preponderance have been observed; ratio male: female being 1.2: 1, for age ranges from 5 days to 15 years. Tumours of mesenchymal origin have also been reported among paediatric population in Zaria, Nigeria (115: 60.8%) while epithelial tumours including germ cell tumours accounted for 74 (39.2%) cases. The age group from 1 – 5 years had highest cases of epithelial tumours while ages 6 – 15 years had the most tumours with 102 (54%) cases. The five common tumours over- all were; rhabdomyosarcoma, burkitt lymphoma, retinoblastoma, non-hodgkin's lymphoma and nephrobastoma (Samaila, *et al*., 2009). Malignant tumours in children are biologically and histologically distinct from adult tumours. They are leading cause of disease related death in children under 15 years (Jones *et al.,* 2017, WHO, 2018). 80% of children with cancer in high-income countries are cured but about 20% are cured in low- and middle-income countries (Gupta *et al.*, 2018; Howard, 2018).

The most common categories of childhood cancers include leukemias, brain cancers, lymphomas and solid tumours such as neuroblastoma and wilms tumour (Steliarova-Foucher, 2017). Childhood cancer cannot generally be prevented or screened. Improving cancer outcomes for children requires early and accurate diagnosis with effective treatment. Most children cancers can be cured with generic medicines and other treatment methods like surgery and radiotherapy. Treat of childhood cancers can be cost-effective in all income settings (Gupta *et al.,* 2018). Avoidable deaths from childhood cancers in low - and middle-income settings arise from lack of diagnosis, misdiagnosis or delayed diagnosis, obstacles to accessing care, abandonment of treatment, or toxicity with higher relapse rates. Childhood cancer data systems are needed to drive continuous improvements in the quality of care, and to drive policy decisions.

As it has been said, ovarian germ cell tumours are a type of epithelial tumours which are associated with rapid growth unlike more common epithelial ovarian neoplasms, yet most patients present with stage a disease that is limited to one ovary. Germ cell cancers are ovarian germ cell tumours (OGCTs), which are derived from primordial germ cells of the ovary. They may be benign or malignant. The histologic types of OGCTs that arise from the ovary are similar to the ones that develop from the testis of men. OGCTs can be broadly divided into those that differentiate toward embryo like neoplasms (teratomas, their subtypes and dysgerminomas) and those that differentiate primarily toward extraembryonic fetal derived (placental-like) cell populations or a mixture of both. Categories of OGCTs include; Teratomas, Dysgerminomas, Yolk sac tumors, Mixed germ cell tumours and rare OGCTs (Gershenson, 2019).

Overview of clinical manifestations of OGCTs

OGCTs often produce hormones in the beta subunit of human chorionic gonadotropin (hCG) or alpha fetoprotein (AFP). Patients typically present with one or more of the following signs and symptoms:

- Abdominal enlargement,
- Abdominal pain
- Precocious puberty, abnormal vaginal bleeding presumably from hCG production
- Symptoms of pregnancy from hCG production. 85% of women with an OGCT have both abdominal pain and an abdominal mass; fever or vaginal bleeding, occurs in 10%. OGCTs tend to be large with median size 16cm.

Ascites, rupture (pre or intra- operative), and torsion are reported in 20, 20 and 5% of the cases respectively. Smith (2006), reported that distribution of OGCTs by histology was: pure dysgerminomas (33%), teratomas, immature plus mature with malignant transformation (39%), and non-dysgerminomas or mixed cell types (29%). Diagnosis is made by histology at time of surgical excision. The diagnosis is strongly suggested pre-operatively by the presence of an adnexal mass on pelvic imaging and an elevated level of an associated tumor marker (e.g. hCG AFP). For benign cystic mature teratomas, the diagnosis can be made with reasonable confidence using pelvic ultrasonography though removal of the cyst is advised.

OGCTs are often associated with hormonal or enzymatic activity. Some of these proteins can be measured in serum, producing a highly sensitive and variably specific marker to identify certain histologic components. Some tumour markers are present in some but not all tumours of a specific histology. Tumour markers produced by tumour types include: hCG present in embryonal cell carcinomas and ovarian choriocarcinomas, mixed germ cell tumours and some dysgerminomas, AFG present in yolk sac tumours, embryonal cell carcinomas and polyembryoma carcinomas, mixed germ cell tumours and some immature teratomas (most germ cell dysgerminomas are associated with a normal AFP), and Lactate dehydrogenase (LDH) present in dysgerminomas.

Malignant germ cell tumours are staged according to the International Federation of Gynaecology and Obstetrics (FIGO) staging system for epithelian ovarian cancer II; from stages I –IV. In virtually all stages, surgery is required for definitive histologic diagnosis, treatment and staging (if malignant) of OGCTs. Oophorectomy, ovarian cystectomy or resection of the ovarian mass can be performed, depending on clinical situation, and tissue sent for frozen section. Confirmation of the diagnosis should be obtained prior to definitive surgical treatment. Knowledge of herbal medicines and their potential toxicities are generally limited particularly in chronic conditions such as cancer.

Case Report

The Case of intra-abdominal malignancy (Germ cell tumour) with background severe acute malnutrition (Kwashiorkor) and severe anaemia in a ten-month old baby with weight 7.7kg, who hails from Yaounde, Camerounian, French by tribe, a Catholic Christian, with main complaints of:

Fever	X	2/12
Abdominal-swelling	X	6/52
Cough	X	6/52
Catarrh	X	6/52
Scaly-Skin-Lesions	X	1/52
Bilateral Leg Swelling	X	3/7

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History of present illness

Patient was in apparent good health until two months ago when she developed fever. Fever was initially low grade, intermittent, occurred at night and day, but became high grade intermittently, worse at night. For the above symptoms, mother gave water-based enema and alcohol-based herbs to drink. Abdominal swelling was noticed six weeks ago, which was insidious in onset and progressive, gradually increasing in size till present size. Associated history of generalized abdominal pain, moderate and intermittent. There was positive history of passage of watery stools 6 times a day, non-bloody mucoid. Positive history of vomiting and diarrhea. There is weight loss. Presence of scaly lesions on skin of a week duration, which was noticed after baby's mother, gave the baby an alcohol herbal concoction to drink and herbal enema. Hyperpigmented scaly lesions involving the upper left, lower left and trunk. Bilateral leg swelling was noticed three days ago, gradual in onset and progressed to present state, nil associated decrease in urine output. There was positive history of reduced appetite.

At onset of illness, patient was taken to General Hospital, Iquita, Oron, Akwa-Ibom State of Nigeria, where patient was treated on outpatient basis with oral medication for cough and catarrh, and requested to do laboratory investigations and ultrasound scan, which she did not do. Rather she patronized traditional healers, only to come back at General Hospital, Iquita, Oron later when the situation had worsened, and was referred to University of Uyo Teaching Hospital, Uyo, Akwa-Ibom State of Nigeria for treatment.

Past medical history

Patient had cough and catarrh six weeks ago, which had abated.

Past medication history

Positive history of herbal medicines use

Pregnancy history

Patient booked for Antenatal clinic at 3 months at General hospital, Iquita, Oron, Akwa-Ibom State of Nigeria. Mother was regular on antenatal visit, had two doses of tetanus toxoid injection and two doses of intermittent preventive treatment for malaria (IPT). Pregnancy was carried to term; she delivered through spontaneous vaginal delivery (SVD).

Neonatal history

Baby cried well at birth, no neonatal complications.

Immunization history: Adequately immunized baby except for measles.

Nutritional history

Baby took breast milk and water from birth. Was fed on demand, fed on both breasts for about 10 minutes/feed till 5 months. Nan and custard were added to feeds at 5 months, whilst still breast- feeding. Baby commenced irish potatoes/guinea corn, garri and soup at seven months. Feeds thrice a day. Baby stopped breast feeding at nine months of age.

Family history

Patient is the third of three siblings in a monogamous family. They live in two room apartment, poorly ventilated, nil use of insecticide treated nets, and use of water closet system. They drink satchet water.

Social history

Father is a business man, mother is a hairdresser.

Allergies

No known drug allergies.

Physical examination

On examination, an acute on chronically ill-looking child, irritable, moderately pale, febrile, anicteric, acyanosed, nil signs of dehydration, nil peripheral lymphadenopathy, pedal oedema up to the knees.

TABLE 1. Showing vital signs

Dates	Pr (b/min)	Rr (c/min)	Bp (mmhg)	Temp (°c)	Heart sounds
03 – 09	160	32	-	37.6	S1S2 only
04 – 09	144 - 152	60	-	-	S1S2 only
06 - -09	-	36 – 60	-	-	S1S2 only
07 – 09	140	30	-	-	S1S2 only
08 – 09	132		No Appropriate Cuff		S1S2 only
09 – 09	152 - 174	40 – 78	-	37.0	S1S2 only
10 – 09	140 - 148	48 – 52	-	36.5	-
12 – 09	140	58	-	37.8	S1S2 only
13 – 09	140	62 – 64	-	37.1	S1S2 only
15 – 09	122 - 140	28 – 60	-	Within range	S1S2 only
16 – 09	118 - 126	30 – 32	-	35.8 – 36.5	S1S2 only
17 – 09	110	40	-	35.3 – 35.5	S1S2 only

TABLE 2: Showing review of systems

Date	Abdomen	Liver	Spleen	Respiratory	Cns	Mss	Digestive system	Rectal	Gus
07-04		Nil involvement	Nil involvement					No perianal swelling, normal anal tone	
08-09	Hard with irregular surfaces, mass is 16 x 24			Dyspnoei vesicular breath sounds	Concious, irritable, tone reduced in all limbs	Petechial haemorrhages on the left and upper limb			
09-							Bowel sounds		

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09							vesicular. Moist buccal mucosa		
12-09	Abdomen grossly distended with scarification marks			Vesicular breath sounds			Moist buccal mucosa		

Date	Abdomen	Liver	Spleen	Respiratory	Cns	Mss	Digestive system	Rectal	Gus
13-09	Full MWR, mass is 15.4 x 12.0 x 9.1 cm	Liver displaced superiorly	Spleen displaced superiorly			Hyperpigmented flaky skin lesions, shallow ulcers on buttocks and right knee			
16-09	Asymmetrically distended, MWR. Abdominal				Conscious with wisened old	Global hypotonia, lower limbs greater than upperlimbs	Moist oral mucosa, nil oral thrush, diarrhea x $^3/_7$		Excoriations on whole perinum
17-09	Distended				Conscious	Mildly pale, bedsore on right lower thigh	Vesicular bowel sounds, dry buccal mucosa, poor oral hygiene, passing loose stools x 6 at night		Pelvic mass firm, non-tender

TABLE 3: Feeding Chart

Date	F-75 morning	F-75 evening
06 -09 -2019	Irregular Feeding	Feed Changed from Pap to Milk
10- 09 – 2019	Inconsistency with Food Timing	Inconsistency with Food Timing
16 – 09 – 2019	Child Tolerating F-75 at 65 mL 2 hourly	

TABLE 4: Laboratory investigations: full blood count results (06/09/2019)

Test type	Values
Haemoglobin	8.4 g/dl ↓
Packed Cell Volume	27% ↓
Red Blood Cells	3.4 X 10^{12} /L ↓
Mean Corpuscular Volume	81 FL
Mean Corpuscular Haaemoglobin	24 PG ↓
Mean Corpuscular Haemoglobin Concentration	30 G/DL ↓
Total White Blood Cell Count	13.3 X 10^9 /L ↑
Platelets	158 X 10^9 /L
Neutrophils	51% ↑
Lymphocytes	32% ↓
Monocytes	17% ↑
Eosinophils	0% ↓
Erythrocyte Sedimentation Rate	200 MM In First Hour ↑

TABLE 5: Results of other laboratory investigations

Tests	Dates / Results						
Abdominal Ultrasound Scan	03-09	04– 09	06 – 09 Pelvic Mass Likely Ovarian Origin Seen	07– 09	09 – 09	12 - 09	13 – 09
Abdominal Ct Scan						Extensive Left Heterogenous Mass with Malignant Radiographic Features. Mass Measures About 15.4 X 12.0 X 9.1 Cm	
Random Blood Sugar				4.3 Mmol/L			
Retroviral Scan						Negative	
Liver Function Tests			Total Proteins 45g/L ↓(62-82) Albumin 23g/L↓(36-52)				
Electrolyte, Urea And Creatinine			Bicarbonate 20 Mmol/L↓(22-28)		Potassium 2.8mmol/L (3.2 – 5.0)		
Packed Cell Volume		28%↓(29-45%)					35%

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TABLE 6: Current medications

Dates	Medications
03 – 09	Iv Artesunate 23mg At 0 Hr, 12 Hrs, 24 Hrs, 48 Hrs, Iv Ceftriaxone 385mg 12 Hrly, Iv Gentamycin 12.8mg 8 Hrly, Tabs Albendazole 200mg Stat, Tab Zinc 20 Mg Daily, Tab Folic Acid 5mg Daily, Suspension Multivite 5mls Daily, Apply Topical Zinc Oxide 12 Hrly On Genital Area X 2/52, Oral Fluconazole 46mg Stat,Then 23mgdaily X 2/52
04 – 09	Ensure Iv Rocephin 385mg 12 Hrly, Improvised Resomal 39mls Every 30 Mins X 4 Doses Then Every 2 Hrs, 77mls X 5 Doses, To Reasssess, Oral Vit A 100,000iu Days 0, 1, 14, Continue Other Management
12 – 09	8.5mls of 15% Kcl to 70mls Of 4.3% Dextrose Saline Over 24 Hrs At 3dpm Via Soluset
16 – 09	Stop Gentamycin, Tab Zinc Gluconate 10mg Daily X 14/7, Caps Vit A 100,000 Iu On Day 1, 2, 14, Caps Vit E 400iu Daily X 2/52, Tabs Vit C 100mg Every 8 Hrs X 2/52
17 – 09	Commenced Resomal Via Nasogastric Tube 39mls Every 30 Mins X 4 Doses, As Prescribed (3mls/Kg). (Had 6 Doses)

II. Assessment

There is a caution regarding the use of Cephalosporin's (Ceftriaxone) if gastro-intestinal disorder. Baby was receiving ceftriaxone despite history of recurrent diarrheal episodes (EPOCRATES). There is a caution for administration of aminoglycosides (gentamicin) if dehydration. Patient was accessed with moist buccal mucosa on admission which later progressed to marked dehydration on admission, however dosing at 7.5 mg/kg/day in sub-divided dosing was adequate (EPOCRATES). There is caution required for administration of fluconazole if electrolyte abnormalities. Patient was observed to be hypokalemic, k^+ values at 2.8 mmol/L (EPOCRATES). Caution with vitamin E dosing for 1 to 3 years, 200 units/ day (EPOCRATES). Refusal to carry out required abdominal CT scan due to financial concerns. Delay in carrying out required AFP,hCG, Lactate dehydrogenase tests. Baby had been having diarrhoea with severe weakness. Need for urgent electrolyte, urea and creatinine screening. Baby appears severely dehydrated.

Plan

- To investigate Prescriber on concerns regarding use of cephalosporins in view of recurrent diarrhoeal episodes.
- Gentamycin dosing was stopped for the patient before discharge.
- To intimate Patient relative to do required electrolyte, urea and creatinine tests.
- To intimate prescriber with dosing requirements for specified age.
- Patient relative was counseled on need to carry out abdominal CT scan for definitive diagnosis.
- Encourage patient relative to do required hormonal assay, to identify Germ cell tumour subtype.
- To consult with Prescribers, on the need for parenteral nutrition, to provide daily nutritional needs.
- To consult with Prescribers on the need for chemotherapy as, pelvic mass is rapidly increasing in size.

III. Discussion

Generally, there are increasing new cases of cancer seen in the Paediatric population in the wards. However, these are mostly referrals. Common symptoms associated with the conditions have been abdominal swelling and pain. Baby's mother received treatment from general hospital Iquita, Oron for cough and catarrh but defaulted on laboratory investigations and ultrasound scan. Her use of alcohol - based herbals and enemas appear to have complicated her baby's condition which rapidly deteriorated thereafter. Baby's mother reports appearance of skin lesions and skin scarification exactly one week after conclusion of herbal concoction. The bilateral leg swelling was also consistent with anaemia which was treated. Though she delayed in carrying out required investigations in teaching hospital, Uyo, the delay to presentation at UUTH, UYO has frustrated available time for effective interventions which could have been life saving for the baby. Regrettably, prevention and screening methods do not exist for Childhood cancers, but improving cancer outcomes for children require early and accurate diagnosis with effective treatment. Baby developed hypokalemia on admission was treated but no follow up test was carried out, to define her new status. Patients with malignancies commonly experience serum abnormalities including hyponatremia, hypokalemia, hyperkalemia, hypophosphatemia and hypercalcemia.

It also appears that inadequate feeds and timing of the feeds could have worsened her nutritional status. The inability to tolerate the quantity of fortified pap necessitated change of feeds from fortified pap to fortified milk which she tolerated. The diarrheal episodes worsened baby's nutritional status causing severe malnutrition and dehydration. The use of parenteral nutrition to ensure adequate baby nutritional needs would have been helpful. Increasing abdominal size of pelvic tumour could be associated with metastasis which has been associated with fatality. Diagnosis of Germ cell sub type may

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have been delayed from unavailable hormonal tests results which were not done. Malnutrition, dehydration, metastasis, respiratory distress and sepsis could have been responsible for the death of the ten- month old baby diagnosed of Germ cancer.

IV. CONCLUSIONS

Deaths from childhood cancers in Africa are increasingly becoming a cause of concern. There is need to mobilize care, funds and advances in technology to curb this trend. The deaths from childhood cancers in low- and middle-income settings can be attributed to lack of diagnosis, misdiagnosis or delayed diagnosis, obstacles to accessing care, abandonment of treatment or drug toxicity with higher relapse rates.

List of abbreviations

CT……Computed tomography

AFP….Alpha-fetoprotein

hCG….Human chorionic gonadotropin

SVD… Spontaneous vaginal delivery

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