

## Case report

# NEPHROBLASTOMA IN A NIGERIAN NEWBORN: A CASE OF A COMMON KIDNEY TUMOUR IN AN UNCOMMON AGE GROUP.

## ABSTRACT

Nephroblastoma (Wilm's Tumour) is the commonest paediatric renal cancer worldwide. ~~It affects children mostly between the ages of one and four years old.~~ It is uncommon in infants less than six months of age and very rarely seen in neonates. The uncommon presentation of nephroblastoma in the newborn period of this index child, depicts the possibility of its sporadic occurrence in this age group. This consequently, poses clinical possibilities of misdiagnosis or delayed diagnosis as it could be difficult to distinguish between malignant and non-malignant kidney lesions in newborns, especially in resource-poor settings. It is important to highlight this clinical scenario, to increase one's index of suspicion, when evaluating abdominal distension or masses in the newborn age group. **Kindly reduce this abstract to clearly indicate reason for reporting. Nephroblastoma is reported to be uncommon in the new born period; presence may suggest sporadic occurrence. The rarity of occurrence could lead to misdiagnosis and missed diagnosis hence we report this .... To create awareness of its occurrence.**

**Keywords:** Nephroblastoma (Wilm's Tumour), Newborn, Nigeria

## INTRODUCTION

Nephroblastoma or Wilm's Tumour (WT) is an embryonic renal tumour of childhood. It was first described by Max Wilms in 1899.<sup>1</sup> It is the most common childhood kidney cancer worldwide. As Wilms tumour is embryonal in origin, it occurs mostly in young children. About 60% of the patients are between 1 and 5 years of age at diagnosis, 15 % are infants.<sup>1-7</sup> The average age of occurrence is 3 years, with females being slightly more affected than males.<sup>7</sup> Nevertheless, older children and adolescents could be affected. Neonatal nephroblastoma has been very rarely reported.<sup>1-6,9-12</sup>

Several authors globally have reported highest incidences of Wilm's Tumour in children of sub-Saharan African descent and in African-Americans but a lower incidence in Asian children.<sup>2,3,7,13-16</sup> It demonstrates substantial inter-ethnic variation in clinical, pathological, and molecular characteristics.<sup>3,6,10,16</sup> There is dearth of information on childhood cancer incidences, demographics, tumour genetics and outcomes in many low and medium-income countries (LMICs). This is partly due to suboptimal reports of cases, ineffective cancer registries to elucidate, record and report these population-based data **could this**

also be due to lack of histologic diagnosis?.<sup>3,8,16</sup>

A high index of suspicion is needed when evaluating a newborn child with abdominal distension-mass with or without pain. Prompt diagnosis and treatment improves outcome. This index case, confirmed to be nephroblastoma presented to our facility, and being the youngest so far, necessitated this report. **More literature review is needed, how many have been reported in Nigeria, how was diagnosis made, outcome.....and some differential diagnosis. How do you recognize anaplastic and the blastem? What is the justification for reporting this case?**

## **PRESENTATION OF CASE**

A two-month old Nigerian female infant, referred from a secondary health facility presented to the children out-patient clinic of this referral hospital. She was brought by her parents with presenting symptoms of abdominal swelling and weight loss, each of two weeks duration. She also had fever, paleness of the body, and diarrhoea, each of a week's duration respectively. The child had been apparently well from birth till mother incidentally noticed abdominal swelling, more prominent to the right of child's abdomen. It was initially small and painless, but became progressively larger, with associated pain when touched. There was no history of other swelling in any part of the body. No history of prior trauma. There was failure to gain adequate weight, with obvious thinning of both arms and these seemed to progressively worsen over the days.

Fever was high grade and continuous, temporarily relieved by use of acetaminophen syrup. Paleness of the body was noticed on the palms and soles of the feet. There was no haematuria, nor bleeding from any orifice.**any other adrenergic symptoms? no symptoms or signs suggestive of co-morbidities like WAGR syndrome, Beckwith-Wiedemann's syndrome such as hypoglycemia, enlarged tongue or organs.**

The mother commenced regular antenatal care at a gestational age of sixteen weeks at a secondary health facility, and had been compliant with prescribed routine medications, immunizations and investigations. There was no history of maternal tobacco smoking or alcohol ingestion. No intake of herbal concoctions, and no exposure to radiation. There was no maternal history of hypertension, gestational diabetes, antepartum haemorrhage nor pre-term rupture of membranes. Her pregnancy was uneventful. Child was delivered per vaginam spontaneously at term and weighed 3.6kg, with good APGAR scores at birth. Her due childhood immunizations were given. The index child was second of two children, and older female sibling was 18 months old, at time of index patient's presentation. There was no family history of similar illness and

~~A review of the systems revealed abdominal swelling, abdominal pain, diarrhea, vomiting, pallor and mild tachypnoea. There was no history of haematuria, bleeding from any orifice, jaundice, petechial spots or cough.~~

Examination at presentation revealed an ill-looking female infant, afebrile (37.2°C), moderately pale, anicteric, not cyanosed, no signs of dehydration, and no pedal oedema. She weighed 4.7kg, with an occipito-frontal circumference of 38cm which was normal for

age. There were no general physical or clinical features of syndromic Wilm's tumour.

Digestive system revealed a moist buccal mucosa, good oral hygiene with an asymmetrically distended abdomen more to the right. Bowel sounds were normoactive. There was a right-sided abdominal mass around the lumbar region, measuring about 10 x 10cm, firm, smooth and tender, with no differential warmth. It was difficult to get above the mass. No suprapubic fullness and female external genitalia were normal.

Child was mildly tachypnoeic with a respiratory rate of 48 cycles per minute. There was equal chest expansion, resonant percussion notes and vesicular breath sounds. Cardiovascular system showed a pulse rate of 124 beats per minute, full volume and regular. The apex beat was at the 4<sup>th</sup> left intercostal space, mid-clavicular line. The first and second heart sounds were normal. **Blood pressure?**

Central nervous system showed an alert child, with normal neonatal reflexes. A clinical diagnosis of Nephroblastoma (Wilm's tumour)?**stage** was made with neuroblastoma as a differential. A full blood count done at admission revealed moderate anaemia (haematocrit of 27%), normal total leukocyte count ( $9.1 \times 10^9/L$ ), Neutrophils-30%, Lymphocytes-64% and thrombocytosis (platelets count  $-802 \times 10^9/L$ ). **She was transfused with fresh whole blood in three aliquots. Post-transfusion haematocrit improved to 35%. Should come after results!!!!**

Serum Electrolytes Urea and Creatinine: showed normal biochemical values: Creatinine – 95mmol/L, Urea -2.0mmol/L, Sodium –133mmol/L, Potassium -3.3mmol/L, Chloride – 97mmol/L and bicarbonate –25mol/L, Phosphate -2.4mol/L, calcium -2.1mmol/L and Uric acid -0.38mmol/L respectively.

Screening tests for neuroblastoma–Vanillyl mandelic acid(VMA) and Homovanillyl acid (HVA) was done with normal results obtained:

VMA IN URINE -10.24 (Reference 5.9 -43.8 mcg/mg creat)

HVA IN URINE - 24.17 (Reference 3.4 -44.9 mcg/mg creat)

Chest radiograph showed normal findings.

The intravenous urographic studies following administration of non-ionic contrast, revealed a normal left kidney, with non-visualization of the right kidney and right ureter secondary to a renal mass.

Abdominal computed tomographic scan showed an enlarged right kidney measuring about 10.3 x 8.4cm with distortion of architecture. Right kidney harboured a huge heterogeneously enhancing soft tissue density mass with cystic areas measuring about 8.6cm x 10.2cm, extending from the right hypochondrium to the right iliac fossa. There was no demonstrable intra-tumoural calcification or bleed. The mass appeared well circumscribed without evidence of direct extension in adjacent organs/structures, with no convincing nodal enlargement. There was associated distortion of the calyces with no demonstrable excretion by the right kidney. The mass displaced the adjacent bowel loops to the left as well as the liver superiorly. There was demonstrable encasement of the left renal vessels, and no demonstrable abnormal filling defect (thrombus) seen in the inferior

vena cava. The left kidney measured 4.9 x 2.6 cm with good cortico-medullary differentiation and enhancement pattern. There was adequate uptake and excretion of contrast by the left kidney. No renal calculus or hydronephrosis was detected. The urinary bladder appeared normal. Other intra-abdominal organs were essentially normal and showed no features of metastases. A diagnosis of a huge right retroperitoneal mass likely nephroblastoma (Wilm's tumour) was made.

The Paediatric surgical team reviewed the child, and 16 days into admission, an exploratory laparotomy was done, with a radical right nephro-urectomy. Intra-operative findings included: Haemorrhagic peritoneal fluid about 150mls, and a right-sided mixed-consistency mass (solid + cystic) attached with fibrous bands to the Inferior Vena Cava (IVC), with the duodenum and pancreas plastered to the superior pole. The perihilar lymph nodes and other organs were intact. Post-operatively, intravenous antibiotics and rectal analgesics were given till child was stable. The freshly excised gross specimen (Figure 1) was sent for a histopathological report. Five days post-operatively, child was discharged for follow-up with the Paediatric Oncology and Surgical teams respectively. She was scheduled to commence chemotherapy using the (VAD REGIMEN) -Vincristine, Actinomycin D and Doxorubicin, but parents opted out of further treatment, despite counsel for follow-up. **Did you do a verbal follow up to know eventual outcome?**

Characterization of the tumour was done by histological exam, which confirmed the diagnosis of nephroblastoma. (Figures 2A-F)



**FIGURE 1: FRESHLY EXCISED GROSS SPECIMEN OF THE RIGHT KIDNEY MASS**

**SURGICAL PATHOLOGY REPORT:**

**MACROSCOPY**

Received in formalin fixative, labelled with patient's name and hospital number was a 500g, ovoid, grey-white, markedly distorted nephrectomy specimen measuring 12.0 x 11.5 x 9.0 cm. The cortical surface showed a dull capsule with an area of breach (4.0 x 3.0 cm) and multiple fibrous bands (**FIGURE 2A**). The cut sections showed a markedly distorted renal parenchyma containing a poorly circumscribed, grey-white to tan-pink, firm, solid to cystic mass. The pelvicalyceal system was unidentifiable. The remnant renal tissue was mostly displaced peripherally (**FIGURE 2B**). No adrenal tissue or lymph nodes seen.



**FIGURE 2A** this is not necessary or choose between 1 and 2A



**FIGURE 2B**

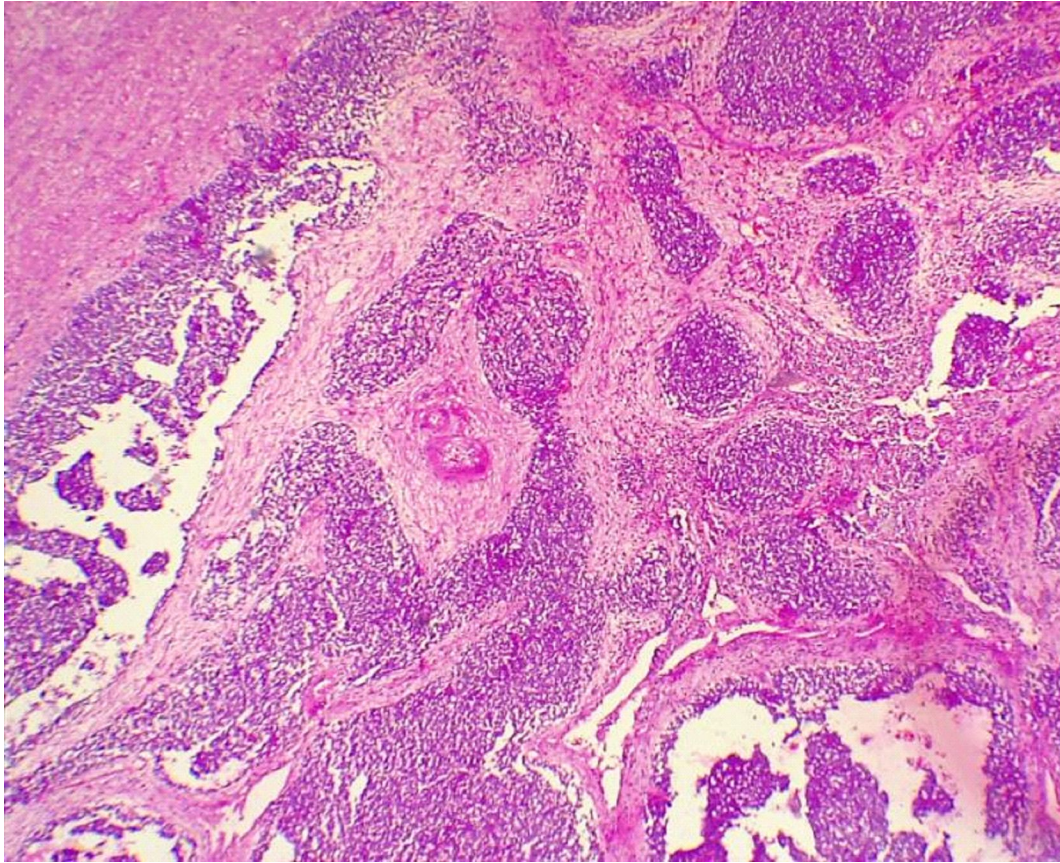
**FIGURE 2[A-B]:** Gross morphological features of the right nephrectomy specimen. [A] Shows the ovoid, grey-white, markedly distorted nephrectomy specimen with a dull capsule with and multiple fibrous bands. [B] The cut sections of the specimen showing a markedly distorted renal parenchyma containing a poorly circumscribed, grey-white to tan-pink, firm, solid to cystic mass (**red arrow**) with the remnant renal tissue being displaced peripherally (**green arrow**).

## **MICROSCOPY**

Histologic sections show a triphasic malignant embryonal neoplasm composed of primitive blastemal, epithelial and mesenchymal components. The blastemal component consists of uniform round to oval cells with scant basophilic cytoplasm, hyperchromatic nuclei and frequent mitoses. The cells are disposed in diffuse sheets and nests separated by thin fibrous tissues. Some of the nests display comedo necrosis. The epithelial component consists of tubules, glomerular-like, rosette-like and papillary structures formed by dysplastic epithelial cells disposed within a loose fibromyxoid stroma. There is

involvement of the renal capsule with tumour cells. No area of anaplasia seen (**FIGURE 3 [A-D]**)

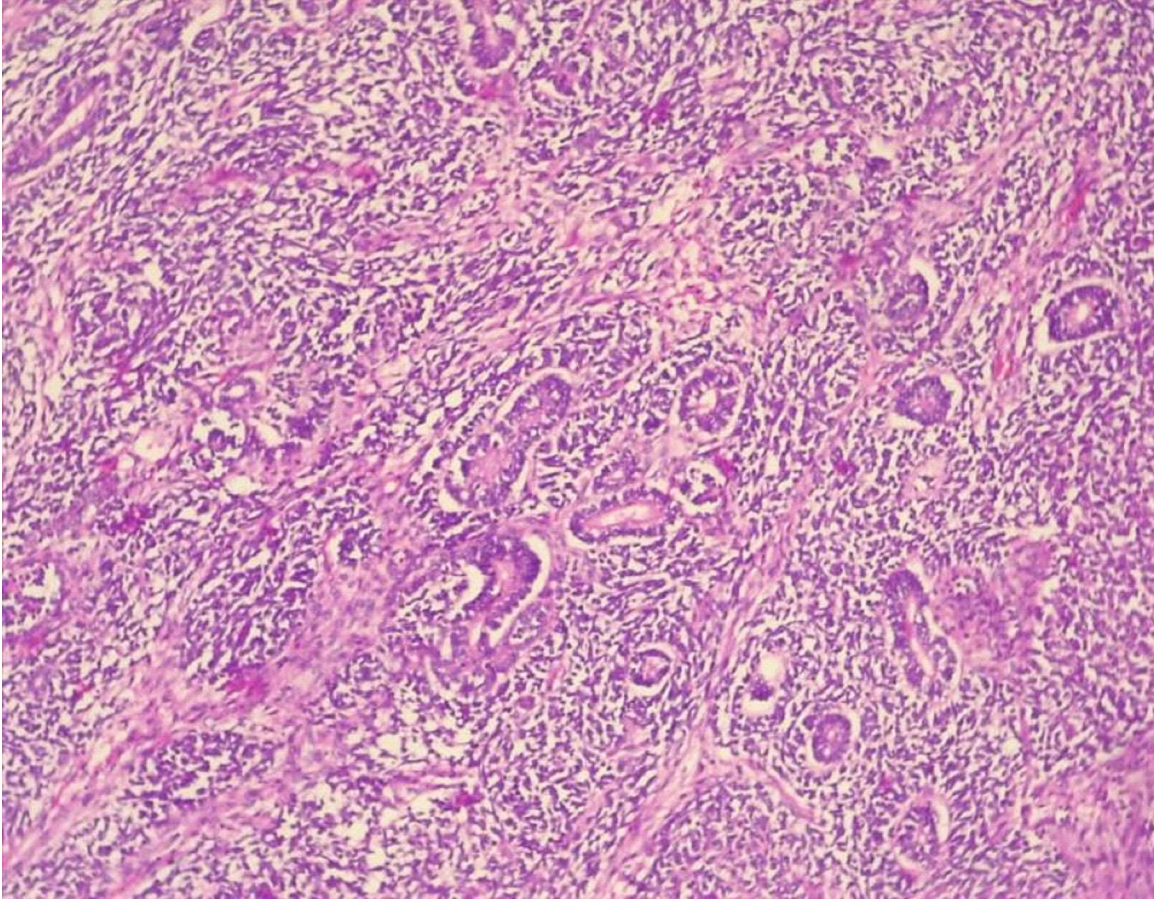
**FIGURE 3[A-D]:** Microscopic morphological features of the right renal mass.



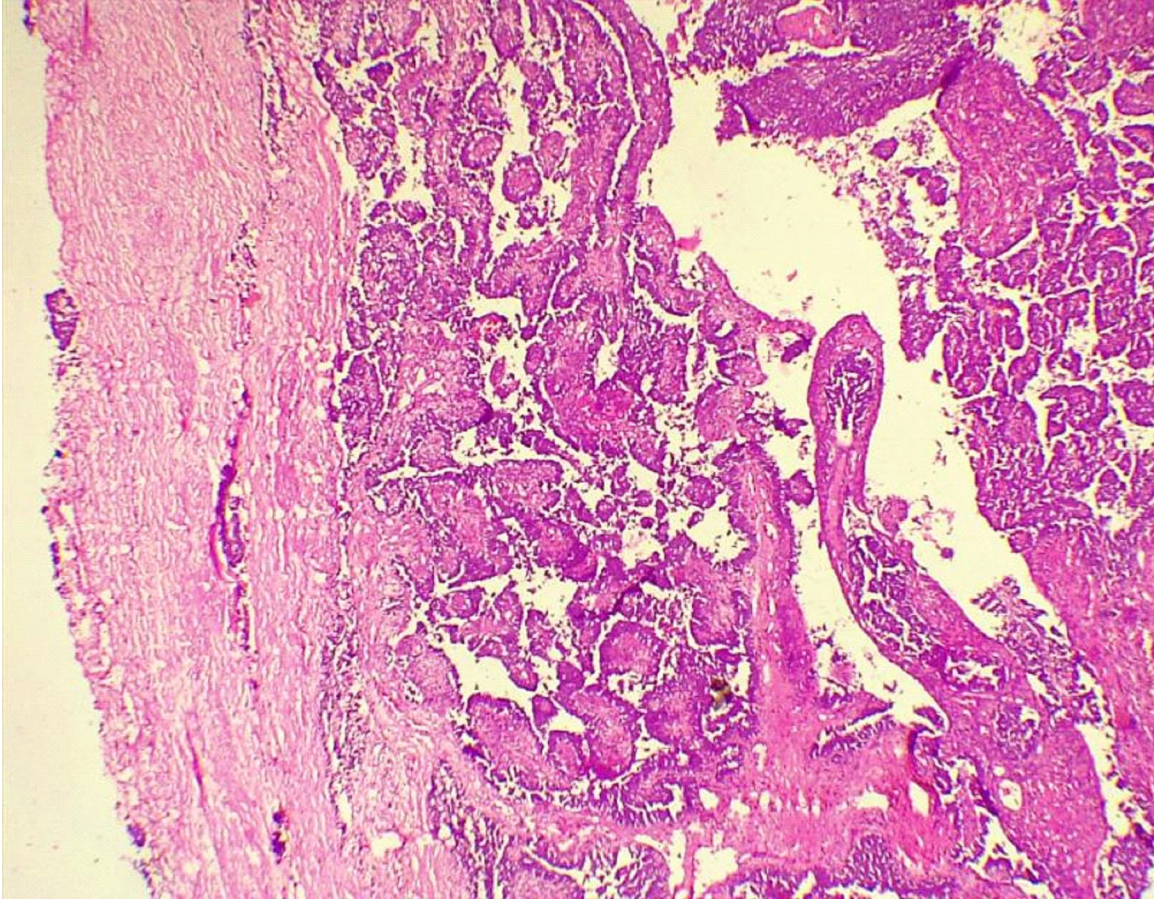
**FIGURE 3A:** Blastemal component composed of nests of undifferentiated cells (blue arrow) and stromal component composed of fibromyxoid stroma (green arrow) (H&E X 4)



**FIGURE 3B: Blastemal component composed of nests of undifferentiated cells with some of the nests displaying comedo necrosis (*yellow arrow*) (H & E X4).**



**FIGURE 3C: Epithelial component composed of small tubes and glomerular-like structures (red arrow) (H&E x10).**



**FIGURE 3D: Epithelial component composed of Papillary structures lined (brown arrow) (H&E x10).**

## **DISCUSSION**

Nephroblastoma is the most common renal malignancy of childhood. It is generally seen in children between 1 to 5 years of age, and rarely described in infants less than 6 months old.<sup>1-6,8-13</sup> Older children, adolescents and adults may also be seldomly affected.<sup>1-5</sup> Wilms' tumour (WT) occurring in the antenatal period accounts for between 2-3% of nephroblastoma cases and neonatal Wilms tumour, which has been scarcely reported, is said to have an incidence of 0.16%.<sup>1-6,9-13</sup> In this tertiary healthcare centre, nephroblastoma has remained the top-ranking childhood cancer presenting in the last decade.<sup>18-20</sup> The age range of children seen over the past several years has ranged between 9 months to eight years while the index case is the youngest presentation so far. Many reports have noted its occurrence more in females than males but others report otherwise. Generally, no significant gender predilection has been documented.<sup>17,21-24</sup>

This short presenting history of Wilm's tumour in the index child indicates the possibility of its onset, though undetected in the antenatal period. No family history of similar illness was elicited, which points to the possibility of a sporadic mutation. It has been documented, that the tumour develops sporadically, with no associated syndrome or hereditary predisposition in most of the children.<sup>3-6,9-17</sup> Facilities for genetic and molecular studies would have been beneficial, but is unavailable here, and likewise many other centres in low and medium-income settings.<sup>11,13,15,16,23</sup> Studies have shown that alterations in certain genes and chromosomes contribute to the development of Wilms tumour and notable, is the Wilms tumour gene 1 (WT1-gene) which plays a major role in normal kidney development. Thus, if mutated and dysfunctional results in development of the tumour and other disorders.<sup>3-7,9-13</sup> About 10-15% of all Wilms tumours are associated with cancer predisposing syndromes, but in patients with isolated disease, evidence for WT1 mutation exists in only about 5 -10% of the cases.<sup>3-7,9-13</sup> The index child had no suggestive physical syndromic features.

In about 80% of children, the clinical presentation of nephroblastoma is usually an asymptomatic abdominal mass noticed incidentally by a parent, caregiver, or primary care physician.<sup>2-6,8,12</sup> This was the case in our index patient, at six weeks post-natal age. Other non-specific clinical features include gross or microscopic haematuria, hypertension, abdominal pain, and fever.<sup>3-6,9-13</sup> Index child presented with some of these symptoms - abdominal pain and fever.

Besides physical examination, screening imaging tests such as an abdominal ultrasound scan, abdominal computed tomography (CT) scan and magnetic resonance imaging (MRI), can determine tumour size/extent, with a great certainty, and helps with preliminary staging of the tumour.<sup>6,9</sup> The index child had all these done, except an MRI, which were all in keeping with the diagnosis of a nephroblastoma. Apart from the moderate anaemia noted in the complete blood count, other ancillary biochemical and radiologic investigations were within normal range. **What are the similarities or differences in this case to earlier reports?**

The haemorrhagic peritoneal fluid noted intra-operatively may have contributed to the moderate anaemia at presentation while the weight loss noted can be attributed to the rapid growth of the tumour, with interference of optimal nutritional status in first few weeks of life. A similar observation to a case reported by authors from the Democratic Republic of Congo.<sup>13</sup>

Nephroblastoma is usually unilateral and more commonly affects the right kidney as in the index patient.<sup>17</sup> However, about 5 -10% are bilateral and these are mostly familial. The index child had a right-sided and unilateral tumour which is in consonance with reports by other authors.<sup>17</sup> Grossly, the tumour is characteristically solitary, well-circumscribed and encapsulated. The size varies widely with an average of 10cm. In the index patient the tumour was solitary and large (11.0 x 10.0 x 8.5cm) replacing almost the entire renal parenchyma. The cut surface is usually soft, fleshy and tan-grey. Necrosis, haemorrhage and cystic changes are usually present as in the index case.

Tumour stage and histologic features/subtype have long been recognized as important

prognostic factors in the management of Wilm's tumour, and its staging is crucial in determining the treatment plan modality.<sup>6</sup> Accurate definition of the tumour stage at surgery and gross and microscopic histopathological examination is critical in proper staging of the patient.<sup>6</sup> Evidence of spread into the pelvicalyceal system and perirenal tissue was noted. In our index patient, intraoperative findings showed involvement of the peritoneal surface and haemoperitoneum, thereby placing the tumour at stage 3. Histology showed capsular and perirenal fat involvement.

Wilm's tumour grows fast and metastasizes early. About 15% of patients present with metastases at initial diagnosis, and this is mostly to the lungs.<sup>2,7</sup> Metastasis can also occur to other tissues/organs like lymph nodes close to the kidney and liver.<sup>7</sup> The surgical and histologic reports of our index case showed no feature of distant metastases, and child's chest radiograph was normal. Histologically, nephroblastoma classically shows a triphasic pattern with mixture of blastemal, epithelial and mesenchymal components although biphasic and monophasic patterns are not uncommon. The relative amount of each component has a prognostic significance and thus should be estimated by a pathologist. Our index case had a triphasic pattern with over 70% blastemal component making it a histological high-risk type/SIOP blastemal histology type and Children's Oncology Group (COG) unfavorable type.<sup>7</sup>

**Some of the information here should have been mentioned in the introduction!!!!**

With the advent of multimodal treatment regimens and specialized care, overall survival for children with nephroblastoma is now greater than 90% in developed countries.<sup>6,9,10</sup> On the contrary, poorer outcomes have been documented for children living in sub-Saharan African nations.<sup>3,12-16</sup> This has been attributed to various treatment challenges with strong pointers to socio-economic factors as reasons for this outcome.<sup>7,8,14-17,23-25</sup> Previous work has also shown evidence of a strong predisposition in people of sub-Saharan African ancestry to developing Wilm's tumour and also having molecular markers associated with poor prognosis and treatment-resistant disease.<sup>16</sup> Further studies and inclusion of African patients in molecular and genetic research is required to equitably advance treatment options for all patients with WT globally.<sup>16</sup> In neonatal WT, no effective treatment guideline has been established and chemotherapy is rarely indicated in neonates.<sup>9,13</sup> However, considering risk stratification with respect to the staging of index child -stage 3, chemotherapy with the VAD regimen (Vincristine, Actinomycin D and Doxorubicin) was scheduled to commence after surgery.<sup>11,16</sup> The parents however, declined further follow-up treatment despite strong counsel. This narrative has been a frequent bane in the treatment of childhood cancers in Nigeria and Africa as a whole, with widespread abandonment of complete treatment course and loss to follow-up.<sup>15,16,23-25</sup> This is especially so, when some slight relief in presenting symptoms is achieved like in the index case, being the significant post-surgical reduction in tumour bulk. Frequent follow-up with physical and imaging examinations is advocated in children not given adjuvant chemotherapy.<sup>12</sup> Unfortunately, the child's parents declined further treatment and follow-up.

## CONCLUSION

This report serves to alert every child healthcare provider and general physician, on the need for a high index of suspicion to the possibility of nephroblastoma in a newborn child presenting with abdominal ~~distension~~-**mass** with or without pain. It is also important to bear in mind that Wilms' tumour should be considered as a differential diagnosis of a neonatal renal mass, especially in resource-poor settings, where full diagnostic facilities may not be available, or parents too indigent to afford necessary screening tests.

**ETHICAL APPROVAL: Not required**

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