

Congenital mesoblastic nephroma in a premature neonate: A case report and review of literature

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Abstract

Congenital mesoblastic nephroma (CMN) is a renal stromal neoplasm of infancy. It comprises 3-10% of all pediatric renal tumors. We report a case of CMN in a 30 week old premature female neonate seen at autopsy who was born to a 26-year-old woman by emergency cesarean section on account of polyhydramnios.

Key words: Congenital, mesoblastic nephroma, polyhydramnios, renal tumor

Date of Acceptance: 11-Jun-2013

Introduction

Neonatal tumors are generally rare occurrences. Congenital mesoblastic nephroma (CMN) although a rare tumor is the most common neonatal renal tumor and it accounts for 3-10% of childhood renal tumors.^[1,2] Histologically, two main variants are recognized, the classic and cellular variants.^[3] A third variant, mixed type, combines the features of the two main variants.^[3,4] In general, prognosis is very good and in most cases, surgery alone may effect a cure.^[4] The more aggressive behavior has been observed in the cellular or mixed variants with documented cases having recurrence and metastasis.^[5] We report a case of CMN in a preterm neonate who was delivered via a cesarean section on account of polyhydramnios, but had respiratory difficulty, cyanosis and a left flank mass CMN discovered at birth. Prenatal diagnosis of CMN was not made. She died 13 h after birth while being treated at the intensive care unit (ICU) following, which a consented autopsy was carried out.

Case Report

She was a 30-week-old preterm female neonate who was born to a 26-year-old gravida2/para1 (1 alive) woman through

emergency cesarean section on account of polyhydramnios and a previous cesarean section. The polyhydramnios was diagnosed antenatally by ultrasonography and the birth weight was 1.6 kg with an Apgar score of 4 in the 1st min and 8 in the 5th min. Examination findings at birth included respiratory difficulty, acrocyanosis and a palpable solid abdominal mass in the left abdominal region (10 cm × 8 cm). An assessment of a pre-term neonate with respiratory distress and multi-cystic dysplastic kidneys was made. She was admitted to the neonatal ICU. While she was in the neonatal ICU, she was given intravenous fluids, antibiotics and intranasal oxygen, but had cardiac arrest terminally and died 13 h after delivery.

At autopsy, the body of a female neonate with head circumference of 28 cm, crown heel length of 42 cm, crown-rump length of 29 cm, chest circumference of 24 cm and abdominal circumference of 26.5 cm was received. There were no dysmorphic features, but there was central and peripheral cyanosis. The lungs were subcrepitant with features of collapse. The main finding was in the urogenital system with a firm, well-circumscribed, smooth-surfaced left kidney mass measuring 5 cm × 5 cm × 3 cm and weighing

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Access this article online

Quick Response Code:



Website: www.njcponline.com

DOI: 10.4103/1119-3077.127573

PMID: 24553043

75 g [Figure 1]. The cut sections through the mass showed tan colored whorled surfaces. Histological examination showed interlacing fascicles of spindle shaped tumor cells with bipolar cytoplasmic processes and bland nuclear appearances entrapping tubules and glomeruli [Figure 2]. The tumor cells showed positive reactivity to vimentin [Figure 3] and thus the diagnosis of CMN, classical type was made. Patient died as a result of complications of prematurity, which is known to be associated with polyhydramnios.

Discussion

CMN is a rare renal tumor presenting usually within the first 3 months of life and accounts for 3-10% of all pediatric renal tumors.^[1] In a previous study performed at the Lagos University Teaching Hospital Nigeria over a decade ago, CMN was found in one case (0.7%) of 131 nephrectomies (adult and children), occurring in a 2½-month-old male infant.^[6] In a South African study, CMN was seen to comprise 17.6% of pediatric non-Wilms' renal tumors, second to clear cell sarcoma of the kidney (33.8%).^[7] The United Kingdom Children's Cancer and Leukemia Group reported 47 (3.5%) cases of CMN out of 1346 registered renal tumors. The median age at diagnosis was 30 days (ranging from birth to 3.8 years) with the majority occurring within the first 3 months of life.^[8] Texas Children's Hospital in the United States reported 7 cases (6.9%) of CMN out of 101 resected renal tumors occurring in children less than 6 months and it was shown that CMN was the commonest renal tumor presenting within the first 6 months of life.^[2] Few cases of adult mesoblastic nephroma have also been reported; one in a 20-year-old woman in South Africa and another in a 54-year-old Ethiopian woman.^[9,10]

CMN has been associated with polyhydramnios and prematurity.^[11-14] The risk of preterm deliveries reaches up to 22% in pregnancies complicated by polyhydramnios and this risk is influenced by the underlying cause of hydramnios.^[15,16] In the case presented, severe polyhydramnios complicating undetected CMN necessitated preterm delivery in a previous cesarean sectioned mother. Blank *et al.* reported three cases of polyhydramnios and premature deliveries complicating deliveries of infants born with CMN.^[14] In a study of 28 children with prenatally diagnosed renal tumors (26 with CMN and 2 with Wilms tumor), polyhydramnios were observed in 11 fetuses (39%).^[17] Kim *et al.* however, reported a case of CMN occurring in pregnancy with oligohydramnios.^[18]

CMN most commonly presents as an abdominal mass, but could also manifest with hypertension or hypercalcemia.^[19] The hypercalcemia observed in some infants has been attributed to excessive production of prostaglandin E by the tumor cells.^[20,21] In cases with reported childhood hypertension, hyperreninism due to excessive production

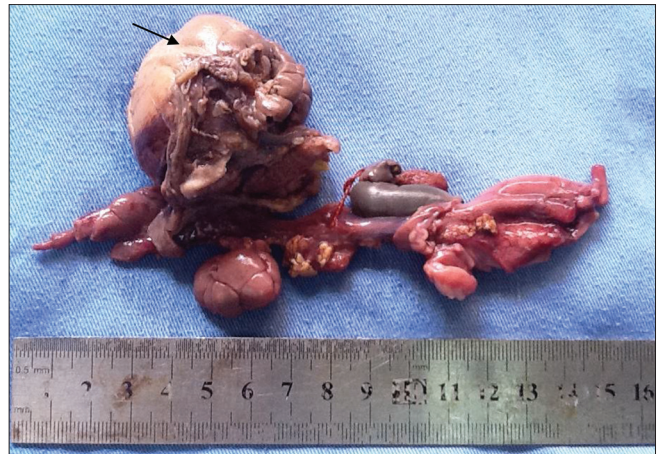


Figure 1: Gross picture of the left renal mass with smooth lobulated surface (arrow)

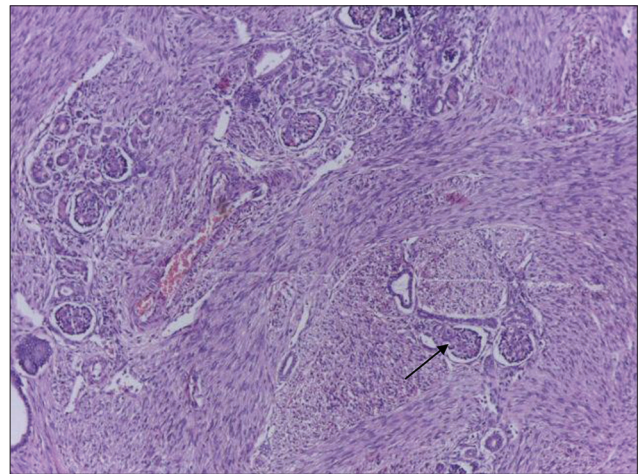


Figure 2: Photomicrograph showing tumor composed of interlacing fascicles of spindled cells entrapping renal glomeruli (arrow) and tubules (H and E, ×10)

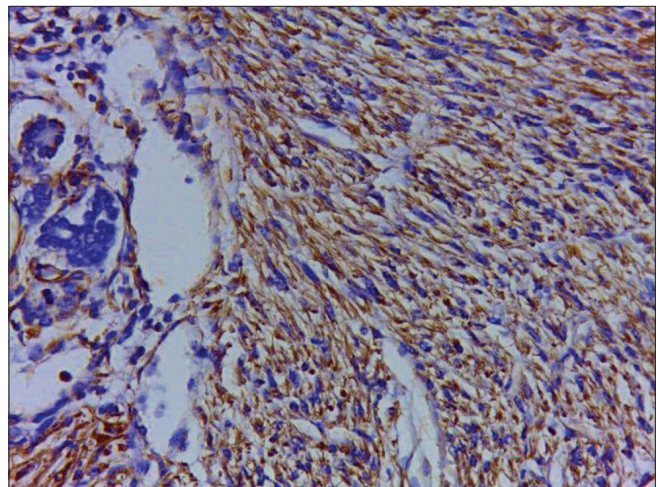


Figure 3: Photomicrograph of tumor with positive reactivity to vimentin (×40)

of renin by entrapped renal elements is the main mechanism.^[22-24] Tejedor Sánchez *et al.* reported four cases

of CMN in which all presented with abdominal masses while two also presented with hypertension.^[25] Out of the seven cases of CMN recorded in the Texas children's hospital, four cases presented with hypertension and one had hypercalcemia.^[2] Daskas *et al.* reported a case of a premature male neonate with CMN who presented with hypercalcemia from the 1st day of life even though parathyroid hormone levels were normal. Resection of the tumor was followed by normalization of calcium levels.^[26] Fung *et al.* reported similar findings and he proposed that hypercalcemia may be the mechanism of polyhydramnios associated with CMN. Hypercalcemia can cause polyuria in the fetus and this could be the probable cause of polyhydramnios, though the exact mechanism remains unknown.^[27] The prematurity and preterm labor are induced by the polyhydramnios.^[28]

CMN is usually detected prenatally by ultrasonography. Shibahara *et al.* reported a case of CMN occurring after transfer of a cryopreserved embryo, which was diagnosed at 28 weeks' gestation when polyhydramnios associated with fetal renal tumor was detected using ultrasonography.^[29] Schild *et al.* also reported a case of CMN diagnosed prenatally using 3D-ultrasound and were able to reliably estimate the size of the tumor by volume calculation using the 3D technique.^[30] An increasing number of cases have been diagnosed antenatally especially with the widespread use of antenatal ultrasonography.^[26,31] However, in the index case, prenatal diagnosis of renal tumor CMN was missed by the Sonologist thus precluding antenatal counseling of the expectant parents for early surgical removal of the tumor. In addition to ultrasound diagnosis, magnetic resonance imaging (MRI) has been found as a useful and relevant adjunct to the determination of the tumor origin and morphology.^[32]

Grossly, CMN range in size from 0.8 cm to 14 cm in greatest dimension with a mean of 6.2 cm.^[33] CMN usually presents as a solid tumor with a smooth, firm or rubbery external surface and a lightly colored or yellow-tan whorled cut surface such as was seen in the index case. Cystic changes, hemorrhage and necrosis are present only in a minority of cases.^[34] Histologically mesoblastic nephroma comprises three variants, the first being the classic/leiomyomatous variant having interlacing bundles of spindle cells with elongated nuclei and entrapment of renal glomeruli and tubules that was seen in the index case. Others are the cellular/atypical variant consisting of densely cellular proliferation of polygonal cells with numerous mitotic figures and a mixed variant showing both classical and cellular variants.^[33] This mixed type is referred to as a mixed mesoblastic nephroma.^[33] The classical variant is seen in 24% of cases and is considered to be morphologically identical to infantile fibromatosis while the cellular variant is seen in 66% of cases and considered to be identical to infantile fibrosarcoma (IFS).^[19]

Various studies have attempted to correlate the gross, histologic and radiologic features of CMN. Chaudry *et al.* in a study of 30 cases of CMN, showed that 5 of 7 cases of CMN with intratumoral hemorrhage and all cases with large cystic/necrotic components had pathology consistent with the cellular variant while most of those that were solid in the histologic classical variant.^[35] In an MRI based study of morphology and staging of CMN, Schenk *et al.* found that necrosis, cystic degeneration and midline crossing is the most commonly seen in the cellular type compared with the classic type and mixed variant is intermediate.^[36]

Though CMN is largely a benign tumor with a vast majority of the patents being cured by surgical resection, cases of metastases, especially of the cellular variant, have been documented.^[4,37] The Gesellschaft fur Pädiatrische Onkologie und Hämatologie reported a case of metastases to the brain, lung and liver.^[38] Patel *et al.* reported a case of isolated metastases to the liver.^[39] Vujanić *et al.* reported a case of CMN in a 14-month-old girl with metastases to the lungs and heart.^[40] In a larger study by Fitchev *et al.* in which 415 cases of CMNs were analyzed, recurrences were documented in 29 of the cases of which 11 had distant metastases (lungs, brain, bone). They identified that the most significant factors associated with local recurrence and metastasis includes cellular variant, stage III or greater tumor and involvement of intrarenal or sinus vessels.^[41]

Immunohistochemical studies of CMN show features consistent with myofibroblastic differentiation. The case presented showed strong positivity for vimentin, which has been reported in the other case studies. In a case described by Whittle *et al.*, the cellular variant of CMN was positive for vimentin and muscle specific actin.^[1] Siracusano also reported positive reactivity for vimentin and actin in a case of the classic variant of CMN. The tumor was also found to be positive for proliferating cellular nuclear antigen, an unusual immunohistochemical finding.^[42] In a report of three adult cases of mesoblastic nephroma, the spindle cells displayed cytoplasmic immunoreactivity for vimentin, desmin, panmuscle actin (HHF-35) and alpha-smooth muscle actin, but were non-reactive for keratin (AE1/AE3), epithelial membrane antigen and S-100 protein.^[43]

The cellular variant of mesoblastic nephroma has been reported to share cytogenetic features with IFS. Both are associated with polysomies for chromosome 8, 11, 17, 20 as well as translocation $t(12;15)(p13;q25)$, which fuses the E-twenty six variant 6 (ETV 6) or translocation ETS leukemia gene.^[1] In a study of five cases of IFS, two of CMN and one of mixed type (CMN and IFS), Adem *et al.* reported that 3 of the 5 cases of IFS had ETV gene rearrangements, but normal copy number of chromosome 11, one case each of IFS, cellular CMN and mixed type had both abnormalities while in the case of classical CMN neither trisomy 11 nor gene rearrangements was found.^[44] These studies imply a

common pathogenesis of cellular variant of CMN and IFS and some also believe that CMN is the visceral component of IFS as both conditions have similar clinical presentation, histologic features and response to chemotherapy.^[45] In contrast, no consistent genetic abnormality have been identified in the classical variant of CMN.^[33]

Classical variant of mesoblastic nephroma is treated by surgical resection. This would probably have applied to the index patient if she survived for few more weeks in the neonatal ICU to allow complete maturation of her lungs. The cellular variant, on the other hand, usually leads to recurrence and is often treated, with excellent results, by surgery with adjuvant chemotherapy. Of the four cases described by Tejedor *et al.*, three were treated by open surgery and one by laparoscopic surgery. All showed no subsequent evidence of disease recurrence.^[25] Dickerhoff described the case of a 3½-month-old girl whose tumor at laparotomy was found to have infiltrated the perirenal fat, right lobe of the liver and diaphragm. Partial nephrectomy was performed and the tumor was completely resected though adequate safety margins could not be achieved. She presented 11 months later with extensive local recurrence with infiltration of the perirenal fat, mesentery and the colon. She was treated with vincristine, actinomycin D and adriablastin and was free of the disease even at 38 months after relapse.^[46] In another case report of CMN with high mitotic index (characteristic of the cellular subtype) that had focally invaded the perirenal fat, the tumor was completely removed with free margins histologically and after 6 years of follow-up no recurrence was noted.^[33] Loeb *et al.* also reported a case of recurrent cellular CMN that completely responded to chemotherapy.^[47] As the standard treatment for CMN is immediate surgical resection, there have been few opportunities to study its natural history.^[1] However, cases of regression have been documented. Whittle *et al.* documented a case of cellular CMN that was untreated for 8 months, which showed significant degrees of regression. The original size as seen on the computed tomography scan was 11.5 cm × 9.2 cm × 8.8 cm without obvious necrosis, fluid or calcification. Eight months later, it was found to be 7.2 cm × 5.7 cm × 5.4 cm with large areas of intratumoral fluid and calcification. The tumor, which was initially deemed unresectable was resected with no evidence of recurrence.^[1] A clear surgical margin with or without chemotherapy depending on the histological variant is critical to disease free interval and survival.^[41]

Conclusion

Efforts should be made to diagnose potential congenital tumors including those of renal origin associated with polyhydramnios prenatally by ultrasound as this would assist in planning for delivery and counseling parents on the perinatal risks and pregnancy outcomes.

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How to cite this article: Anunobi CC, Badmos KB, Onyekwelu VI, Ikeri NZ. Congenital mesoblastic nephroma in a premature neonate: A case report and review of literature. *Niger J Clin Pract* 2014;17:255-9.

Source of Support: Nil, **Conflict of Interest:** None declared.