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PRIMARY RENAL MASSES IN CHILDREN IN CAMEROON: A PLEA FOR PRE-TREATMENT HISTOLOGY

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ABSTRACT

Although multidisciplinary therapy (combinations of chemotherapy, radiation and surgery) has improved the prognosis of children with renal malignancies, the sequence of application of these various modalities is still not standardized. In Cameroon, there are two approaches to the management of paediatric renal masses: the treatment protocols of the Societé Internationale d'Oncologie Pédiatrique (SIOP) and the National Wilm's Tumor Society (NWTS) protocols. The main difference between the NWTS and SIOP protocols is initial chemotherapy of renal masses in children without a histologic diagnosis championed by SIOP. We reviewed the histology of paediatric renal tumors to determine if the tumor cell type was identical to that found in Europe. Our objective was to determine if patients should receive chemotherapy on clinico-radiologic bases, without a histologic diagnosis. This was a retrospective review of all cases of paediatric renal tumors collated from the pathology register at the Yaoundé General Hospital and Yaoundé University Teaching Hospital over a 15-year period. Clinical data and histology results were entered into an Epi-Info 5.1 database and analyzed. There were a total of 29 patients, 18 (62.1%) males and 11 (37.9%) females. The mean age was 6.4 years, median 5 years and the range from 1 to 20 years. Twenty-eight (96.6%) patients had a palpable mass, 16 (55.2%) haematuria, 8 (27.6%) anaemia, 5 (17.2%) weight loss, 2 (6.9%) bone pain, and in 1 (3.4%) the renal mass was detected on an ultrasound of the abdomen for suspected urinary tract infection. The symptom duration before presentation ranged from one to seven months with a mean of 2.5 months. Twelve patients (41.4%) presented within two months. Twenty-seven (93.1%) patients had malignancy, whereas two (6.9%) had benign tumors. Twenty-one (72.4%) had nephroblastomas, 4 (13.8%) had lymphomas, 2 (6.9%) had adenocarcinomas and one (3.4%) each had mesenchymoma and angiomyolipoma. Survival data was available in 18 of the 27 patients with malignant tumors. Two patients with lymphoma survived more than 3 years (33.3%) and one patient with papillary adenocarcinoma survived 7 years (16.7%). Fifteen of 21 patients (71.4%) with nephroblastoma survived past 5 years. We conclude that, while the nephroblastoma is the most common tumor cell type, lymphomas and adenocarcinomas occur in over 20% of children with renal tumors. Therefore, prior to chemotherapy and radiotherapy, it is imperative to make a histologic diagnosis so as to determine the most suitable treatment protocol.

INTRODUCTION

Multidisciplinary therapy (sundry combinaions of chemotherapy, radiation and surgery) has improved the outlook and prognosis of children with renal malignancies, especially nephroblastoma. Unfortunately the sequence with which these various modalities are applied is still not standardized. Some groups uniformly apply systemic chemotherapy, then followed by either radiation and/or surgery. Others perform surgery and then use complementary or adjuvant radiation and/or chemotherapy[1].

In Cameroon, there are two approaches to the management of paediatric renal masses: the treatment protocols of the International Society of Pediatric Oncology (SIOP) and the National Wilm's Tumor Society (NWTS) protocols. The main difference between the NWTS and SIOP protocols is the treatment of renal masses in children based on the presumptive (clinical and radiological) diagnosis of nephroblastoma in the SIOP protocol[1].

Herein we describe the histology of primary renal tumors in children and compare clinical and radiological with the final histological diagnosis. We recommend that chemotherapy should be given to children with renal tumors in Yaoundé only after the histology has been established.

PATIENTS AND METHODS

This was a retrospective review of cases with a histological diagnosis collated from the pathology registers and medical records of patients treated at the Yaoundé General Hospital and the University Hospital Center from 1985 to 1999. These free-for-service institutions are teaching hospitals of the Faculty of Medicine of the University of Yaoundé I. The macroscopic and microscopic description of the renal lesion and the histological diagnosis were retrieved from the pathology register. The following data was obtained from the medical record: age, sex, size of the renal mass, haematuria, pain, kidney involved, presence of masses in other organs or lymph nodes, other symptoms or absence of same, duration of illness prior to consultation, results of ultrasonographic and CT scans, diagnostic procedure performed (needle biopsy, aspiration biopsy and nephrectomy), order of treatment and follow up. This data was entered into an Epi Info 5.1 file from the CDC, Atlanta, for statistical analysis.

RESULTS

During the study period a histological diagnosis of renal tumors was made in a total of 29 children with renal masses. The male to female ratio was 3:2 and the mean age was 6.4 years, median 5 years, and the range from 1 to 20 years. Most patients presented late, the symptom duration prior to presentation ranged from one to seven months, with a mean of 2.5 months. Twelve patients (41.4%) presented to the doctor within two months of illness. Twenty-eight patients (96.6%) had a palpable mass, 16 (55.2%) haematuria, 8 (27.6%) anaemia, 5 (17.2%) weight loss, and 2 (6.9%) had bone pain. Of the 29 patients, 27 (93.1%) had malignant and two (6.9%) benign tumors. Twenty-one (72.4%) had nephroblastoma, 4 (13.8%) lymphoma, two (6.9%) adenocarcinoma and one (3.4%) each mesenchymoma and angiomyolipoma.

Of the 29 patients, there was a concordance between the clinico-radiological and histological diagnosis in only 17 (63%). Six patients (21%) who could afford chemotherapy received it for presumed nephroblastoma (without prior histology). The final histology in these cases following surgery was nephroblastoma in 4, lymphoma in 1 and mesenchymoma in the other. The 23 (79.3%) other patients had surgery before any subsequent chemotherapy. Varying combinations of vinblastine, adriamycin and cyclophosphamide were administered to the patients. Due to poverty, many were unable to complete the chemotherapy protocols. Eight patients received postoperative chemotherapy, 6 had postoperative radiation therapy to the kidney bed. The choice of therapy and the sequence depended often on the specialist who saw the patient first (surgeon, oncologist or radiotherapist) and the patient's ability to pay.

Adequate follow-up and survival data was available only in 18 (66.7%) of the 27 malignant cases. 15 (71.4%) patients with nephroblastoma survived at least 5 years. Two patients with lymphomas survived more than 3 years (33.3%) and one patient with papillary adenocarcinoma who had a single positive hilar node has survived 7 years without evidence of disease. The latter patient had radiation to the renal bed after radical nephrectomy.

Table 1: Illustration of Inaccuracy of Diagnosis in 4 Cases.

Case	Sex	Age	Clinical Diagnosis	Radiological Diagnosis	Histological Diagnosis
1	male	10 yrs	rt. renal mass & haematuria	ultrasound angiomyolipoma	papillary adenocarcinoma
2	female	20 yrs	solid rt. kidney mass with hepatic matastases	CT systemic lymphoma	metastatic adenocarcinoma kidney
3*	female	15 months	solid left renal mass	- CT solid unique mass - nephroblastoma - 2 cycles of vinblastine & adriamycin - without histology	non-Hodgkin malignant lymphoma
4	female	14 months	solid left renal mass	multicystic kidney disease on ultrasound & CT	cystic nephroblastoma

* Patient actually received two cycles of chemotherapy for presumed nephroblastoma

The importance of establishing a diagnosis prior to planning any multimodal therapy is illustrated by four cases in Table 1. The final histological diagnosis in these cases was different from the preoperative impressions.

DISCUSSION

From a purely clinical perspective, the renal mass in a child can be anything from a congenital malformation, compensatory hypertrophy, unilateral multicystic kidney, infantile polycystic kidney disease, multicystic displasia secondary to distal obstruction, a benign tumor such as mesoblastic adenoma, to malignant tumors such as Wilm's, clear cell sarcomas and rhabdoid tumors[2]. This broad range of diagnostic possibilities is narrowed down to either good or poor prognostic outcomes depending on the histology. Since obtaining tissue for histology is invasive and, therefore, attendant with significant risks, some authors figure the decision to treat can be made from clinico-radiological basis. The usual approach is to perform an ultrasound of the kidney mass, and often computer tomography as a preoperative staging method.

Ultrasonography of the renal mass usually distinguishes benign cystic conditions from complex cystic masses as opposed to solid masses, the latter usually inferring a malignancy. Radiologists often suggest non-operative management of multicystic kidney disease purely on the ultrasonic appearance. This non-operative approach, however, is not usually recommended when the cystic mass has solid elements within, for this may herald a cystic nephroblastoma for instance. Whereas a solid renal mass in an infant may not necessarily carry a somber prognosis (mesoblastic nephroma, renal duplication, fetal lobulation etc.), malignancy needs to be ruled out. Renal ultrasonography, therefore, permits the identification of the solid (malignant) renal tumor[3].

When there is access to computer tomography, the nature of the mass is further refined. Calcification, subcapsular haematoma, lobular appearance, centrally located heterogeneous mass suggests central tumor necrosis and haemorrhage in rhabdoid Wilm's tumor[4]. However, psammomatous calcifications also occur in benign adenomatous tumors in children[5]. Cystic tumors on CT scan may be cystic nephroma, cystic partially differentiated nephroblastoma (CPDN), Wilm's tumor with cystic formation due to haemorrhage and necrosis, cystic renal cell sarcoma, multicystic displastic kidney and segmental multicystic dysplasia in a duplicated collecting system[6]. Although there are distinctive CT patterns, none would distinguish clear cell sarcoma of the kidney from most common renal neoplasms of childhood[7]. Tumor vascularity can be assessed (whether it takes up contrast), and the volume (extent of disease), especially lymph nodal involvement, and other organ involvement are usually determined on CT.

When the renal tumor is a solitary lesion limited within Gerota's fascia, that is stages I (kidney < 550g) and II disease, nephrectomy is usually recommended[8]. In the NWTS protocol, these patients would be further classified into the favourable and non-favourable histology group. A German study group has come up with three histologic classes: a favourable group consisting of congenital mesoblastic nephroma and CPDN, an intermediate group made up of classic nephroblastoma and fetal rhabdomyomatous nephroblastoma and the unfavourable class which includes anaplastic nephroblastoma, clear cell sarcoma and malignant rhabdoid tumor[9]. These classifications permit stratification of patients into treatment and prognostic groups[10].

When there is bulky disease, stage III and IV or bilateral renal or other organ involvement, most protocols offer chemotherapy and/or radiation first. Surgery is reserved for removal of residual disease and confirmation of cure. In the NWTS protocol, it is advised to obtain a histologic diagnosis prior to treatment. Various methods have been proposed to get material for diagnosis, with various advantages and disadvantages.

Needle biopsy of renal masses has been discouraged because it is attendant with bleeding and seeding of the tract with tumor cells. Further, the yield from cystic masses is poor. Aspiration of the renal mass lesion has been recommended as an alternative, since bleeding is less, and a definite tumor type can be identified in 93% of renal tumors studied[11]. However, seeding of the tract is still a problem, although it has been argued that the tract is within chemotherapy and radiation bed. A troubling disadvantage is the high false negative rate of the aspiration procecedure, even when the aspirated material is not the necrotic center of the tumor[12]. It is partly for these reasons that the SIOP protocol precludes a histologic diagnosis prior to chemotherapy[13].

Nephroblastoma is the most common renal tumor of childhood, 6% of all childhood cancers in the USA[14]. It is the fifth commonest paediatric malignancy, with an annual incidence of 6-9 per 10^6 in whites[15]. However, there is great variation in incidence worldwide. There is a threefold difference in incidence between age-standardized annual rates (10 per 10^6) in African Americans versus Nigerians, and 3 per 10^6 in East Asia. However, the age distribution is the same between blacks and whites, with a peak age of 2 years at diagnosis. Variations along ethnic rather than geographic lines suggest a high genetic predisposition. This in in contrast with renal cell carcinoma (RCC) of childhood which is rare throughout the world without international variation, although in East Asia it has a high proportion relative to the lower rate of Wilm's. However, RCC has been reported in a child with haemoglobin SA disease, a genetic disease[16]. Further, hereditary papillary adenocarcinoma and familial renal oncocytoma have been reported[17].

In North America, nephrectomy is both a diagnostic and therapeutic procedure for solitary stage I or II disease. In the SIOP protocol, localized and bulky disease is treated without prior histologic diagnosis because nephroblastomas account for over 90% of renal tumors in the West[3]. These treatment approaches may not be obtained in Yaoundé for several reasons. Patients present late with advanced disease, therefore few are ammenable to curative nephrectomy. This tardiness is prejudicial to cure but more importantly, imposes onerous, expensive multimodal therapy. Due to poverty and unavailability of effective chemotherapeutic agents, the lot of these patients are not treated adequately. They are comforted in the belief that orthodox (modern) medicine is inefficacious. A vicious cycle is set where the lack of access (poverty and ignorance) leads to poor treatment outcomes, thereby sending away potentially curable patients.

Further, the epidemiology of renal tumors in children in Yaoundé is different than in Europe and North America. Yaoundé is in the lymphoma belt of sub-Saharan Africa. The commonest childhood tumors here are lymphomas[18,19]. In Nigeria, Burkitt's lymphoma is second to nephroblastoma as a childhood renal tumor[20]. The kidney is the commonest urinary organ involved with lymphoma[21]. Granted that the kidney is most often secondarily involved with lymphoma, the cases in our series show that primary renal lymphomas must be considered in the differential overview[21-24]. Since from one-third to one-forth of paediatric renal tumors in Yaoundé are not nephroblastomas[25], it is imperative that a histologic diagnosis be established prior to chemotherapy and/or radiation. More appropriate treatment is likely to lead to better therapeutic results, the latter which should attract patients early in the course of the disease.

Therefore, patients with stages I and II disease should be offered nephrectomy for diagnostic and therapeutic purposes, whereas stage III, IV and V patients should benefit from either fine needle aspiration or needle biopsy of the mass(es) prior to chemotherapy and radiation.

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