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Research Article

Congenital Mesoblastic Nephroma: Our Experience in the Last 26 Years

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ABSTRACT

Congenital mesoblastic nephroma (CMN) is the most common type of renal tumor in the neonatal period. It is rare in the general population and usually benign, and the treatment protocol is poorly defined. The aim of the present study is to present a retrospective analysis of the cases of mesoblastic nephroma treated at our centre during the last 26 years. A retrospective study was conducted of 11 patients diagnosed with congenital mesoblastic nephroma between 1st January 1990 and 30th September 2016 at our centre. A review of the patients' clinical records was carried out, analysing the demographic, clinical, diagnostic, therapeutic, survival and follow-up variables. Nine (81.8%) were males; one patient was diagnosed prenatally, 9 patients in the first three months of life, and one patient when he was two years old. The most common presentation was a palpable abdominal mass in 10 patients, 2 had haematuria, 6 of them had arterial hypertension, and one had hypercalcaemia. The pathological findings were: 3 cases classic of classic CMN type, 4 mixed type and 4 cellular type. Regarding the tumor stage, 7 patients were at stage I, 3 were at stage II and 1 was at stage III. In all patients, the treatment of choice was radical nephrectomy, and 3 patients received neoadjuvant chemotherapy. Only one patient presented a local recurrence and all of the patients are still alive without any death related to the tumor. CMN is a rare renal tumor but it is considered the most frequent renal tumor in the neonatal period, generally of benign behaviour, but recurrence is possible, and its obstetric and perinatal complications can compromise life.

Introduction

Congenital mesoblastic nephroma (CMN) is a rare renal tumor that accounts for approximately 3-10% of renal neoplasms in childhood, but it is considered the most frequent renal tumor in the neonatal period. It is usually evident in the first weeks of life as a palpable abdominal mass. Although the tumor is usually benign – especially the classical variant – it might, in some cases, recur locally and even metastasize. The treatment of choice is radical nephrectomy, although in cases with worse prognosis, chemotherapy can be prescribed [1-4]. The incidence of this tumor is very low, and the series published up to now have only reported a small number of cases. Some aspects, such as management, adjuvant treatment and prognosis related to this type of tumor, therefore, remain uncertain. We present a retrospective study of the cases of mesoblastic nephroma treated at our centre (a tertiary hospital specializing in pediatrics) over the last twenty-six years, and we review the method of diagnosis and the associated clinical protocols and treatments.

Materials and Methods

A retrospective study that included 11 patients diagnosed with congenital mesoblastic nephroma (confirmed by pathological anatomy) between 1st January 1990 and 30th September 2016 was conducted.

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Initially, we had a sample of 71 patients, of which we ruled out 49 cases because the final diagnosis was Wilms tumor and 11 cases of multilocular cystic nephroma.

A review of the patients' clinical records was carried out, analyzing the demographic, clinical, diagnostic and therapeutic data and follow-up variables, which allowed us to characterize the cases of congenital mesoblastic nephroma presented at our centre during this period.

Results

Eleven patients were found with an anatomopathological diagnosis of congenital mesoblastic nephroma. Nine of them (81.8%) were males, and two (18.2%) were females. The right kidney was affected in six cases (54.5%) and the left kidney in five cases (45.5%). The diagnosis was prenatal in one of the patients, it was done in the first three months of life in nine patients and at two years in one patient.

Clinically, all but one had palpable abdominal mass at the time of the consultation at our centre. Six of them had arterial hypertension, two had haematuria and one had hypercalcaemia. Renal function was normal in all of them. Two of the cases presented tumor rupture (18.2%), one of them perinatally and another during surgery.

The most commonly used radiology technique was ultrasonography, which was given to ten of the patients (90.9%). Computed tomography (CT) was carried out in eight cases (72.7%) and magnetic resonance imaging (MRI) in the four most recent cases. Cysts were observed in six of the patients, haemorrhages in two of them, and necrosis in two others. From radiology, only one case presented suspicion of metastasis on CT, which disappeared in subsequent examinations performed after surgery and adjuvant chemotherapy treatment.

The treatment of choice in all cases was radical nephrectomy; resection of adjacent adenopathy was carried out in five cases. The pre-surgical presumptive diagnosis was of Wilms tumor in 3 patients, CMN in 4 patients and tumor of an extrarenal origin in 4 other cases, although the pathological anatomy finally diagnosed the 11 patients with congenital mesoblastic nephroma. Patients were classified into cellular CMN type (four cases, 36%), mixed type (four cases, 36%) and classical type (three cases, 28%). Regarding the tumor stage, seven patients (64%) were at stage I, three were at stage II and one was at stage III (who received chemotherapy). The nodes analyzed were negative for neoplastic cells in all patients. In two of the patients (those diagnosed in the last year) the presence of chromosomal translocation was evaluated, with no alterations in any of them.

Regarding the chemotherapy treatment, one patient received neoadjuvant chemotherapy with Vincristine and Actinomycin for radiological suspicion of pulmonary metastasis, and in another case, only Vincristine was the administered adjuvant. Only one of the patients (with a classical histological variant) presented a local recurrence within 2 months of nephrectomy, requiring surgical re-operation and adjuvant treatment (Vincristine, Doxorubicin and Cyclophosphamide).

At present, all patients studied are alive and free of disease.

Discussion

The most frequent causes of palpable abdominal mass in a neonatal patient are hydronephrosis and multicystic renal dysplasia. However, tumor origin should be taken into account in the differential diagnosis. Within this group, congenital mesoblastic nephroma (CMN) is the most frequent renal tumor. Also called fetal renal hamartoma, CMN was first described in 1967 by Bolande [5-7]. It is considered the most frequent renal tumor in children under six months, representing 3-10% of all kidney tumors in childhood [5-8]. It most frequently affects boys (1.5: 1 male: female ratio) and the right kidney, which is supported by the data in our series [1, 6]. The fusion of the ETV6-NTRK3 gene has been reported in some patients with CMN, also seen in childhood fibrosarcoma [9]. On the other hand, translocation 12; 15 (p13; q25) is characteristic of cellular subtype CMN [2, 6]. In our sample, two of the 11 cases were analyzed to determine the alteration in the ETV6 gene, being negative in both.

Clinically, most cases, as also in our study, begin with palpable abdominal mass (94%). Patients might also present with haematuria (18%) or paraneoplastic syndromes such as hypercalcemia – due to the release of prostaglandins and parathyroid hormone by the tumor itself – or secondary hypertension – secondary to the activation of the renin-angiotensin-aldosterone axis [2, 10-12]. It should be noted, however, that in recent years, there has been an increase in diagnoses at the prenatal stage, with up to 70% of the patients having polyhydramnios in the final weeks of gestation [1, 6, 10]. Our study group has one patient with prenatal diagnosis (9%), one of the most recent cases.

There are three anatomopathological variants – classical or typical (24%), cellular or atypical (66%) and mixed (10%) [1, 4]. In our series, we found a higher percentage of the mixed type and a lower percentage of the cellular type. The classical mesoblastic nephroma is similar to leiomyoma and fibromatosis in children; hence it is also known as renal leiomyomatous hamartoma and usually has a more solid consistency [1, 6]. The cellular variant is more heterogeneous, with a high mitotic index and great cellularity [2, 6]. It affects older patients and is usually a larger tumor [5]. It often presents areas of haemorrhage, necrosis or cystic areas [1, 4]. Due to its characteristics, it is related to childhood fibrosarcoma and it has been called malignant Bolande's tumor [1, 9].

CMN is generally considered benign, although the cellular variant occasionally may become malignant, resulting in local recurrence or even metastasis in up to 18% of cases [2, 3]. The most frequent location in these cases is lung, being rare in the central nervous system, liver, heart and bone [1]. In our study, as mentioned, one patient received adjuvant treatment for pulmonary metastases, and another required further intervention due to local recurrence (although this was a classical subtype, usually less aggressive according to the literature). On the other hand, cases of spontaneous tumor regression linked to the chromosomal translocation (12; 15) (p13; q25), have been described, although we have no data from our sample.

As it is a non-encapsulated tumor, rupture is reported in about 20% of the patients, which would contribute to the local extension. In fact, this has led some practitioners to recommend a scheduled C-section delivery,

although this is not widespread [9]. In our analysis, two cases of rupture were recorded (18.2%), one during surgery and the other perinatally.

The differential diagnosis should be established with Wilms tumor, which is very similar clinically and radiologically to CMN, especially the cellular variant, although less than 2% of Wilms tumor cases occur in patients younger than 3 years [1]. Other less frequent renal tumor strains in this age range, such as rhabdoid and clear cell tumors, should also be considered [2, 4, 5].

The most commonly used diagnostic tests for this type of mass are abdominal ultrasound and computerized tomography (CT), although in recent years, given the increase in prenatal diagnosis and with the intention of reducing the radiation received by the patient, Magnetic Resonance Imaging (MRI), has become more popular. This tumor can be characterized on echography by echogenic and hypoechogenic concentric rings in the periphery of the tumor – a Chan sign – vascular ring, typical of the classical variant. On CT, it is shown as an intrarenal mass, with a non-specific attenuation model and a mass density that can be homogeneous or heterogeneous able to present a sign of the echogenic ring. MRI also shows a mass effect with no specific pattern, generally showing low intensity in T1 and high intensity in T2 [5, 6, 13]. Although not currently popular, intravenous urography and abdominal X-ray have also been used, which can deform the urinary tract and / or intestinal tract, respectively. However, the definitive diagnosis is established after the anatomopathological study [2, 6].

As for the therapeutic approach, surgery is the initial treatment of choice [11]. Radical nephrectomy is currently recommended, although cases treated with partial nephrectomy or even enucleation have been reported. For all patients operated on at our centre during the period described, open radical nephrectomy was carried out, although laparoscopic procedures have been reported [2]. As for lymphadenectomy, it may be indicated in selected cases, but not routinely. The use of adjuvant treatment is controversial. Today, it is usually used after surgery in cases of incomplete resection, advanced stages with cell lineage, lymph node involvement or recurrence. The usual protocols used in most centres are those used with sarcoma or Wilms tumor (based on Vincristine, Doxorubicin and Cyclophosphamide), also used in our hospital in the cases that required it [1, 10].

Regarding the prognosis, some perinatal complications secondary to dystocia during childbirth have been reported, with the possibility of tumor rupture, haemorrhage and shock, as well as the appearance of fetal arterio-venous shunt [5]. However, these are rare, and the prognosis of this type of neoplasia is currently favorable, with survival above 96% [1]. Complete resection and age less than 3 months are favorable prognostic factors [2]. In this study, good prognosis reported in the literature corresponds to that of our series of patients, since at the present time all are alive and free of disease, including cases of local recurrence and metastasis.

Conflicts of Interest

None.

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