Cellular congenital mesoblastic nephroma: case report

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Abstract

Introduction: Congenital Mesoblastic Nephroma (CMN) is a rare pediatric renal tumor. It comprises two histological subtypes, namely classic and cellular, with the second accounting for two thirds of all cases and being more often associated with poor prognosis. It remains a diagnostic challenge for pathologists due to its similarity with other more frequent pediatric kidney neoplasms. **Case report:** We describe the case of a 2-year-old girl who presented with a left renal mass. After nephrectomy, the specimen analysis showed, on gross examination, an extensive, granular and whitish tumor lesion occupying almost the entire kidney, invading the renal sinus, capsule and perirenal fat, with areas of hemorrhage and necrosis. Histologically, it was characterized by ovoid spindle cells, mitoses and no cell atypia, which led to a diagnosis of cellular mesoblastic nephroma. Adjuvant chemotherapy was carried out, but tumor recurrence occurred in the first year, presenting as an unresectable tumor that did not respond to adjuvant chemotherapy and the patient died at 4 years of age. **Discussion:** The cellular variant tends to be more aggressive, with a survival rate of 85% *versus* 100% for the classic variant. Recurrence generally occurs in the first year, particularly with the cellular variant.

Keywords: mesoblastic nephroma, kidney neoplasms, nephrectomy.

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Introduction

Most renal neoplasms in childhood are represented by Wilms' Tumor (WT) and predominantly occur in the age range between 1 to 4 years.[1] This fact makes this diagnosis the most probable one when an abdominal mass is detected in a child's kidney, very often leading to the treatment directed at WT, even without pathological confirmation.[2] Renal neoplasms in children younger than 6 months are less common. In this group, the congenital mesoblastic nephroma (CMN) is the most frequent one,[1] with 90% of the tumors being diagnosed within the first year of life and, virtually, never occurring after three years of age.[3] This tumor generally has a favorable prognosis.[4]

The CMN represents, approximately, 3-10% of all pediatric renal neoplasms and has two histological subtypes: classic and cellular. The cellular subtype accounts for 42-63% of all cases,[5] has larger tumor volumes, occurs significantly more often in older patients,[6] in addition to being more aggressive when compared to the classic subtype.[7]

Its diagnosis remains a challenge for pathologists, due to its similarities with other more common pediatric renal neoplasms. The lack of familiarity with this rare entity can lead to a misdiagnosis.[4]

We report on the case of a two-year-old child with an aggressive CMN and its recurrence.

Case Report

A female child, aged two years and nine months, was referred to a Medical Oncology Service in July 2007, due to the presence of abdominal mass. The father reported hematuria episode eight months

before, and approximately 20 days before the consultation, he had observed an increase in the child's abdominal volume and vomiting. An ultrasonographic assessment brought by the patient's parents indicated the presence of a mass in the left kidney. The patient was then submitted to a nephrectomy.

The specimen analysis showed that the kidney measured 11.5 x 8.0 x 7.0 cm and weighed 266 g. There was perirenal, renal sinus and capsule involvement. At cross-sectioning, the kidney was almost entirely occupied by a tumor lesion (7.0 x 7.0 x 6.0 cm), grayish-white in color and granular appearance with extensive areas of necrosis and hemorrhage (Figure 1). There was no ureteral invasion. Histologically, the tumor was characterized by ovoid or fusiform cells, with monotonous nuclei without atypia, infiltrating the surrounding renal parenchyma, low mitotic activity and scarce collagen deposition (Figure 2). Eleven lymph nodes were resected, which were not compromised. The diagnosis was cellular-subtype mesoblastic nephroma. A thoracic and abdominal computed tomography (CT) was requested, which showed normal results.

Adjuvant chemotherapy was started and the patient was submitted to a series of imaging assessments. One month after the end of the chemotherapy, in March 2008, an abdominal ultrasonography disclosed retroperitoneal nodular images compatible with lymphadenomegalies of up to 2.1 cm in size. A thoracic and abdominal CT was then requested. The thoracic CT suggested pneumonia and the abdominal assessment disclosed a solid lesion, 10.6 x 9.6 cm at the largest diameters in the left renal fascia, dislocating large abdominal vessels and pushing against bowel loops that were indissociable from the ipsilateral paravertebral muscles. A pediatric surgical assessment was then requested.

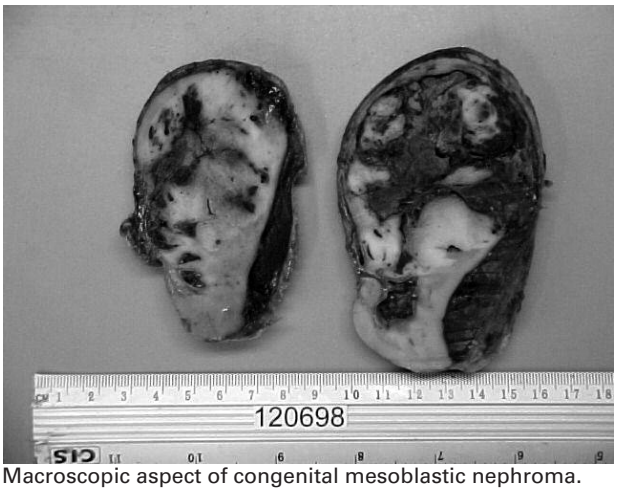
During surgery, it was observed that the tumor was adhered to the bowel loops and pancreas, being unresectable. A mass biopsy was performed, which revealed a cellular subtype mesoblastic nephroma (recurrence). The immunohistochemical analysis showed that the tumor cells were positive for vimentin. Adjuvant chemotherapy was carried out; however, there was no decrease in tumor mass. The patient developed severe malnutrition, fever and neutropenia and died at four years of age, in October 2008.

Discussion

The CMN generally presents as an asymptomatic abdominal mass, sometimes accompanied by hematuria. In most cases, the diagnosis is made still in the neonatal period, as it can lead to polyhydramnios (71% of the gestations associated with the tumor), hydropsy and premature birth, in addition to hypertension (as a result of the increase in renin levels by renal infiltration) and hypercalcemia (due to the tumor's secretion of a substance similar to parathormone).[1,3,5] The ultrasonographic assessment discloses, in general, a solid mass affecting the renal sinus, with cystic and hemorrhagic areas, as well as infiltration of local tissue.[5]

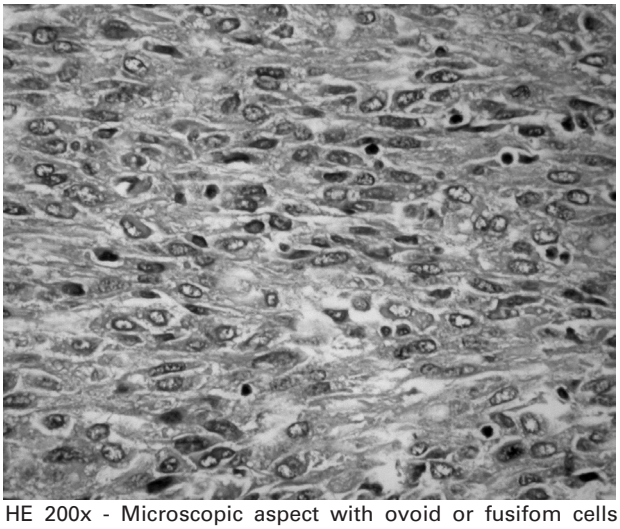
The CMN probably originates from nephrogenic mesenchymal proliferation.[5] The classic variant is similar to the leiomyoma,[1,5,6] described predominantly as solid, firm, of yellowish color, without capsule, with poorly defined margins,[5] fusiform spindle cells and rare mitoses.[6] Cystic areas and necrosis can eventually occur. In contrast, the cellular variant is

Figure 1. Kidneys with extensive areas of necrosis and hemorrhage.



Macroscopic aspect of congenital mesoblastic nephroma.

Figure 2. Ovoid or fusiform cells, with monotonous nuclei without atypia.



HE 200x - Microscopic aspect with ovoid or fusifom cells infiltrating the surrounding renal paraenchyma.

recognized as a distinct subtype, although both can coexist (mixed subtype).[5] The cellular variant shows high cellularity, mitosis, necrosis,[1] hemorrhage[6] and consists of solid ovoid or fusiform spindle cells with decreased cytoplasm.[3,5] This tumor type can invade adjacent structures and tends to be more aggressive.[7] Both variants are immunoreactive to fibroblastic markers (vimentin, smooth-cell actin, desmin) and negative for epithelial markers,[2] although the diagnosis is based on morphological criteria, only.[3] In the reported case, the immunohistochemical analysis was positive for vimentin, only, in the absence of immunoreaction for desmin and smooth-cell actin.

Recent studies have shown that the classic and cellular variants have genetic differences. Only the cellular variant shows translocation (12; 15) (p13; q25), which leads to the ETV6-NTRK3 gene fusion. There have been varied findings in mixed subtypes.[5,6] Identical translocation has also been reported in infantile fibrosarcoma (IFS), suggesting that the cellular subtype CMN would represent an intrarenal IFS[3] and that it would not be related to WT or renal clear cell carcinoma (RCC), as initially associated.[8] However, when fusiform cells predominate in a child's kidney, the differential diagnosis must include WT, clear-cell type RCC (fusiform cell pattern) and CMN, in addition to other entities that are less common in children.[2]

The CMN must be treated with radical nephrectomy to reduce the risks of local recurrence. This treatment alone is usually enough, as the tumor has low malignancy potential. Only 5% of the patients have recurrence, usually within the first year after the nephrectomy and most of them have the cellular subtype. Therefore, during the first year after the nephrectomy, the patient must be submitted to a series of ultrasonographic assessments, in order to detect early signs of local recurrence.[1,3,9] The cellular variant is associated with a worse prognosis, with a survival rate of 85%, when compared to 100% for the classic variant.[9] Metastatic disease, mainly into the lungs, liver, brain and heart and an extensive area of local recurrence are rare events.[6,7,9] Risk factors for recurrence are positive surgical margins, tumor rupture during resection,[1] cellular subtype and patient's age.[6] Patients older than 3 months presenting the cellular variant, with positive surgical margins, tumor rupture during resection or patients with vascular microinvasions are candidates to adjuvant chemotherapy.[9] The chemotherapy can also be carried out in cases of local recurrence, metastatic disease or patients with inoperable tumors, as some cases of CMN are chemosensitive.[8,9] The combinations of vincristine, cyclophosphamide and doxorubicin (VCD),[9] vincristine, doxorubicin and actinomycin D (VDA),[8] isophosphamide, carboplatin and etoposide (ICE)[9] can be used successfully. However, the ICE combination is nephrotoxic and therefore it is reserved as a second-line therapy.[8,9] Nevertheless, the literature shows that not all these tumors are chemosensitive, as observed in the reported case, or respond to the combinations of chemotherapy drugs. Moreover, the small number of patients available for analysis makes it difficult to identify the clinical or biological factors than can predict the response to chemotherapy. The ideal therapy to control recurrence is yet to be clarified, and, as the patients in general receive a multimodal therapy, it is difficult to determine whether the chemotherapy or the radiotherapy, or both are active against the tumor.[8]

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