

Cystic nephroma in pediatrics

Nefroma quístico en pediatría

Leonardo M. F. de Souza^a, Débora D. C. de Q. Turíbio^b, Jeovana P. F. de Souza^b, Raiane S. Oliveira^b, Isadora C. Lopes^b, Ana K. da C. Dantas^a, Thais M. Cruz^c, Fabio M. de Azevedo^d

^aDepartment of Pediatrics, Child and Adolescent Health Care Unit, Hospital Universitário Onofre Lopes, Federal University of Rio Grande do Norte, Brazil

^bFederal University of Rio Grande do Norte, Brazil

^cChild and Adolescent Health Care Unit, Hospital Universitário Onofre Lopes, Federal University of Rio Grande do Norte, Brazil

^dDepartment of Pathology, Hospital Universitário Onofre Lopes, Federal University of Rio Grande do Norte, Brazil.

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What do we know about the subject matter of this study?

In this case, the research evidence indicates an unusual presentation of cystic nephroma, considering that most cases have no symptoms and, therefore, are incidentally diagnosed.

What does this study contribute to what is already known?

The trials allowed us to discuss a disease whose prevalence is still barely known and requires further research, as well as improving the differential diagnosis for a better decision making.

Abstract

Cystic nephroma is a rare benign renal tumor of uncertain etiology. In children, it can manifest as a palpable abdominal mass, hematuria, and recurrent urinary infections. Imaging tests such as ultrasound and computed tomography assist in the diagnosis, but confirmation is made through anatomopathological study. Treatment is surgical and may be partial or total nephrectomy, with a good prognosis. **Objective:** To report a rare case of pediatric cystic nephroma, its clinical manifestations, radiological and histopathological aspects, as well as the treatment used and its evolution. **Clinical Case:** Pre-school, male, with a history of recurrent urinary infections in the first year of life. At 2 years and 8 months, he presented nodulation in the right hypochondrium with local pain on palpation, associated with urinary disorders and hematuria. An ultrasonography showing enlarged right kidney due to multiseptated cystic formation. Computed tomography showing multiloculated cystic expansive formation in the right kidney. At 2 years and 10 months, he underwent partial right nephrectomy for excision and anatomopathological study, which was compatible with Cystic Nephroma. He evolved with regression of hematuria and recurrent episodes of urinary infections, maintaining renal function preserved. Currently, at 4 years and 6 months, asymptomatic. **Conclusions:** Cystic nephroma is a rare entity, generally with a good prognosis. The association of clinical findings, radiological images, and anatomopathological study are fundamental for the establishment of diagnosis and a better definition of therapeutic conduct.

Keywords:

Cystic Nephroma;
Benign Renal Tumor;
Multilocular Cyst;
Pediatrics

Correspondence:
Jeovana P. F. de Souza.
jeopfs@gmail.com

Introduction

Cystic nephroma is a rare, benign renal tumor of uncertain etiology, first described in 1892 by Edmunds in an 18-year-old girl¹. Among renal neoplasms, its prevalence is still undefined, estimated between 2 and 4%². It is a condition characterized by small multiple cysts, separated by septa and enclosed in a single cyst, with a well-defined capsule that separates it from the underlying renal parenchyma³.

With a bimodal distribution, it mainly affects children under 4 years old, being 75% male and over 30 years old, will affect mainly women (87%) in this case, an 8: 1 ratio to males^{3,5}. Currently, pediatric and adult cystic nephromas are considered completely different entities, with different morphological, histological, immunohistochemical, and genetic characteristics⁶.

Genetically, the relationship between cystic nephroma and other tumors with the DICER1 gene mutation is well established, with a high prevalence (86%) of such mutations in pediatric cases, compared with approximately 10% of nephroma adult cysts^{9,10}.

The diagnosis of cystic nephroma is based on clinical manifestations, imaging tests, and anatomopathological study. In children under 10 years of age, it usually presents as a palpable abdominal mass or on the sides. After this age group, it can be manifested by abdominal pain or is detected in imaging studies. Hematuria and urinary tract infections can occur in all age groups⁷. Among the imaging tests that can be used are simple radiography, ultrasound, computed tomography (CT) scan, and magnetic resonance imaging (MRI). In the anatomopathological study presents a characteristic macroscopic aspect ("honeycomb" appearance), and variable histology³.

It is important to make the differential diagnosis of cystic nephroma with other pediatric renal masses, such as Wilms' Tumor, which represents 6% of childhood cancers⁸. The search for a correct differential diagnosis increases the diagnostic accuracy by ruling out other hypotheses, thus avoiding unnecessary therapeutic procedures⁸. However, it is worth mentioning that the preoperative imaging and macroscopic examination are not completely reliable to differentiate it from a malignancy, therefore, elective surgical treatment (partial or total nephrectomy) with histological analysis is the diagnostic confirmation method^{9,10}.

Given the unusual nature of the pathology, few studies, and the limited number of cases described in the literature, the interest in studying and describing this case becomes imperative and justified. Therefore, this article aims to report a pediatric case of cystic nephroma, its clinical manifestations, radiological and histopathological aspects, as well as the treatment used and

its clinical evolution, emphasizing the importance of differential diagnosis with other renal masses, to define the best therapeutic approach.

Clinical Case

Male preschooler, born by normal delivery, full-term (39 weeks and 4 days), Apgar 9/9, Head circumference 34 cm ($Z = 0$: appropriate for age), Weight 2972 g ($-2 < Z < 0$: appropriate for age), Length 51 cm ($0 < Z < 2$: appropriate for age). Pre-natal, peri-delivery, and immediate neonatal period without complications. During the first year of life, he presented 3 episodes of urinary tract infection (UTI), treated with first-generation cephalosporin (cephalexin).

At 2 years and 8 months of age, he was referred to the Pediatric Nephrology outpatient clinic of the *Hospital Universitário Onofre Lopes* (HUOL) with a 1-month history of nodulation in the right hypochondrium, associated with local pain on palpation, evolving with a gradual increase in size. Orange-colored urine (questioning whether macroscopic hematuria) and strong odor, with voiding effort and intermittent urinary stream. Normal general physical examination. Weight 12.8 Kg ($-2 < Z < 0$: appropriate for age), height 92.5 cm ($-2 < Z < 0$: appropriate for age), BMI 14.8 ($-2 < Z < 0$: appropriate for age). Normal blood pressure 80 x 60 mmHg (Mean value 0 - 4 years: 85 x 60 mmHg). Palpable abdominal mass in the right hypochondrium 6 cm from the costal rim, round-shaped and with an irregular surface. He presented an altered urine test (EAS), with 20 red blood cells per high power field (normal value: $< 3-5$ RBC/HPF), and a negative urine culture. Abdominal ultrasound showed a right kidney enlarged by multiseptated cystic formation (7.29 x 7.17 cm), of undefined etiology, and bladder with thickened walls and without evidence of hydronephrosis (figure 1).

Complementary CT scan showed an expansive multilocular cystic formation involving the right kidney, measuring 8.6 x 6.4 cm in its major axes; left kidney without morphological abnormalities, with both kidneys concentrating and eliminating symmetrically and satisfactorily the contrast medium, showing no signs of lithiasis or hydronephrosis (figure 2). A Static Renal Scintigraphy with 99mTc-DMSA showed preserved renal tubule function in the left kidney and moderately depressed in the right one, next to the extensive hypofunctional area in the lower pole of the right kidney (probably a cystic area). Normal left kidney (figure 3).

At 2 years and 10 months of age, the patient underwent partial nephrectomy of the right kidney for excision and anatomopathological study of the lesion.



Figure 1. Abdominal ultrasound: multiseptated cystic formation (yellow line), measuring 7.29 x 7.17 cm, bladder with thickened walls and no evidence of hydronephrosis.

There was an oval, cystic, grayish mass, measuring 7.5 x 7.0 x 5.0 cm, with a multiseptate cavity, complete, measuring 5.0 x 4.0 cm, filled with liquid and citrin content. The microscopic examination showed a cystic lesion with fibrous septa, associated with a mononuclear inflammatory process in the wall and, to a greater extent, a hobnail, cuboidal epithelium (figures 4 and 5), compatible with Cystic Nephroma.

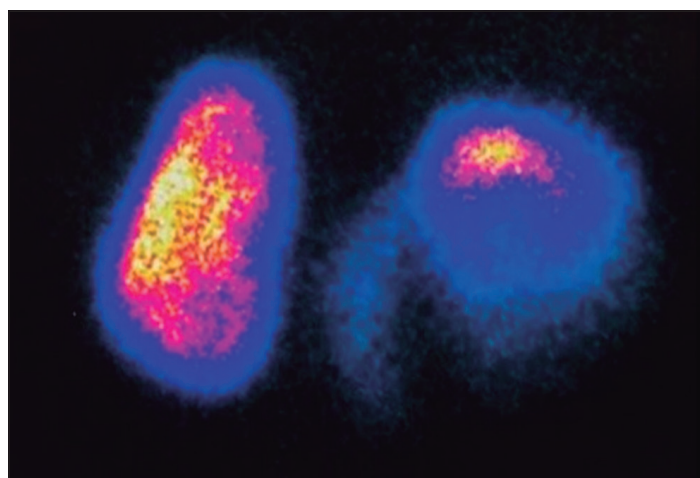


Figure 3. Static renal scintigraphy - DMSA-^{99m}Tc: tubular function preserved in the left kidney and moderately depressed in the right one, along with an extensive hypofunctional area in the lower pole of the same, corresponding to the cystic area.

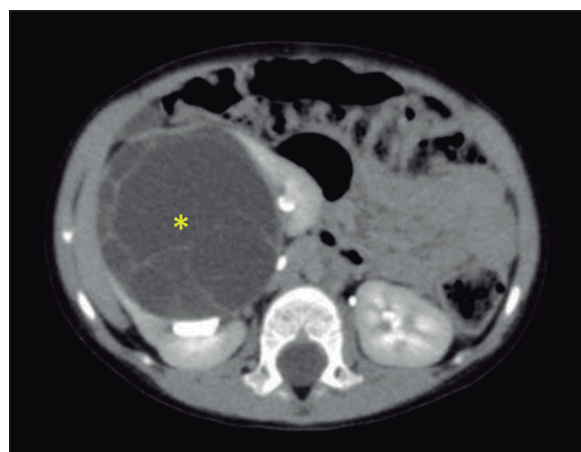


Figure 2. Computed tomography urography: multiloculate cystic (yellow asterisk) expansive formation involving the right kidney, measuring 8.6x6.4 cm in its major axes, concentrating and eliminating the contrast symmetrically and satisfactorily, without signs of lithiasis or hydronephrosis.

In a follow-up visit with pediatric nephrology, an ultrasound of the urinary tract showed topical kidneys with regular contours, the right one (with previous partial resection) was smaller than the left one, without evidence of hydronephrosis, lithiasis, cysts, or isolated masses. A year later, the patient did not present new episodes of UTI or hematuria. He maintained normal renal function, with urea 12 mg/dl (reference value 8-36 mg/dl) and creatinine 0.39 mg/dl (reference value 0.51-0.67 mg/dl). Current weight 19.2 kg ($0 < Z < 2$: appropriate for age); height 100 cm ($-2 < Z < 0$: appropriate for age); and BMI 19.2 (Overweight). Currently, at 4 years and 6 months of age, he remains asymptomatic.

Discussion

This article addresses the case of a male patient, under the age of 5, with a palpable, painful abdominal mass, associated with hematuria and recurrent urinary infections. In general, symptoms such as abdominal pain and hematuria are secondary to obstruction caused by the protrusion of one or more cysts in the renal pelvis. In some cases, arterial hypertension may occur due to the tumor itself or by the compression of the underlying renal tissue^{5,12}, which was not observed in our case. The age, sex, and clinical picture presented by the patient are in line with the researched literature.

Imaging tests combined with clinical history and physical examination are important for diagnostic suspicion and patient follow-up. A simple abdominal X-ray may show a large abdominal mass, displacing adjacent bowel loops. CT scan, in turn, is the method

of choice for the evaluation of this tumor, showing a multilocular cystic mass with thin septa, and peripheral and curvilinear calcifications¹³ (figure 2). It is important to note that other methods, such as ultrasonography (figure 1) and MRI, also describe multilocular cystic images, but they do not accurately differentiate them from other complex cystic renal masses¹³.

The anatomopathological study allows a certain diagnosis of cystic nephroma. Macroscopically, a circumscribed mass of cysts is observed, with a thick fibrous capsule, non-communicating fluid contents, separated by thin translucent septa (“honeycomb” aspect), where calcification, hemorrhage, and necrosis are uncommon³. In microscopy, it has a flat epithelium, with eosinophilic cuboidal cells areas projected to the lumen as a “hobnail”, containing mature tubules in its septa (figure 4).

Differential diagnosis with other renal masses is challenging since such tumors present with different radiological characteristics and highly variable prognosis^{5,14}. In this regard, malignant kidney tumors in pediatrics are rare, representing only 2% of the total neoplasms¹⁵. However, Wilms’ Tumor should always be suspected, a neoplasm that usually affects children under 5 years old, appearing as a palpable mass, and may be accompanied by hematuria and abdominal pain, evolving with an excellent prognosis in 90% of cases⁸.

There are many possible differential diagnoses, such as renal cell carcinoma, clear cell sarcoma, cystic variants of mesoblastic nephroma, and multicystic dysplastic kidney, mainly the segmental form⁷. In anatomopathology, the hobnail epithelium containing mature tubules in its septa characteristic of the Nephroma is an important factor for differentiating from Nephroblastoma, which contains foci of blastema cells in the septa. Just considering the clinical aspects and imaging exams does not allow distinguishing these pathologies from each other⁷. In this respect, the differentiation with renal cell carcinoma is the absence of proliferating clear cells^{16,17}.

Another relevant differential method is the investigation of the DICER1 gene mutation, an alteration that also occurs in the anaplastic sarcoma of the kidney, an extremely rare malignant tumor, with about 25 cases reported in the literature, and may appear in renal regions where a cystic nephroma pre-existed^{18,19}. However, such research is not routine since is an exam that is not accessible, especially in the public health system. Therefore, it was not performed in the case studied.

Although Joshi and Beckwith have described the criteria for the diagnosis of cystic nephroma, to date, there are no guidelines or consensus on the treatment of it¹⁶. In general, nephrectomy is the procedure of choice since it allows a definitive diagnosis with anatomo-

pathological analysis and is also a definitive therapy. Partial nephrectomy is performed in small volume tumors, usually by laparoscopic approach¹¹; however, when this is not possible, total nephrectomy is performed²⁰.

As cystic nephroma is diagnosed and treated appropriately, the prognosis is good, usually without the involvement of underlying renal tissue¹³. The reported patient had an adequate diagnosis and treatment, progressing satisfactorily, with regression of hematuria, episodes of urinary infection, and preserved renal function, in line with the literature, and presenting an excellent prognosis after surgical treatment.

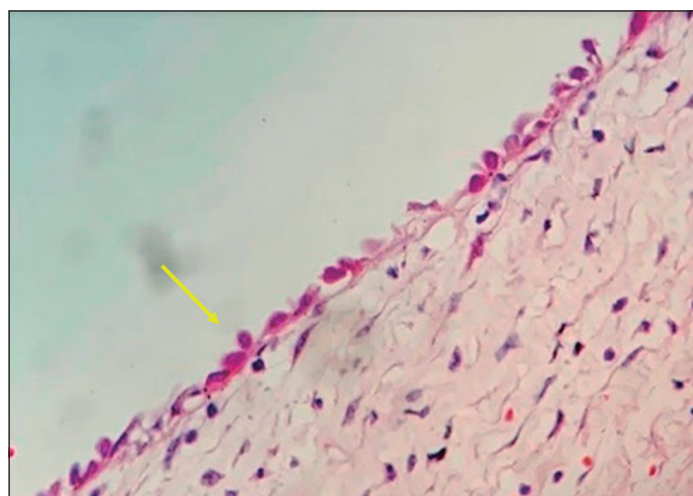


Figure 4. Histopathology of tumor mass in right kidney: epithelial lining with cuboidal epithelium and hobnail appearance (yellow arrow). HE, 400x.

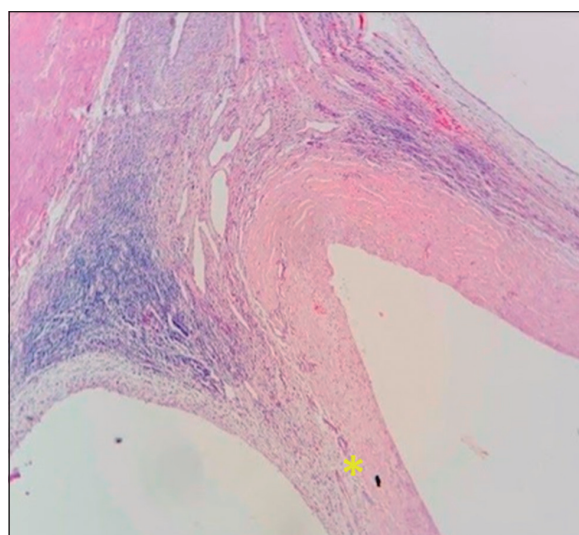


Figure 5. Histopathological analysis of tumor mass in right kidney: cystic lesion with fibrous septa (yellow asterisk). HE, 400x.

Conclusion

Pediatric cystic nephroma is a benign neoplasm with a good prognosis. Differentiation from other renal cystic lesions by imaging studies is still challenging. The combination of clinical, biochemical, and histological characteristics associated with radiological features is essential for diagnosis, as well as for better understanding the behavior of the lesion and defining the best treatment, thus avoiding unnecessary interventions. Since it is a rare and poorly studied pathology, it requires more research.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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