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Bilateral Nephroblastoma & Nephroblastomatosis (About 2 Cases)

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Abstract: The nephroblastomatosis is defined by the presence of multiple or diffuse nephrogenic remains, regarded as precursor's nephroblastoma and appear in up to 90% of bilateral Wilms, nephroblastoma is the first renal tumor of the child. Our work is a retrospective study of 2 cases of bilateral Wilms and nephroblastomatosis. The average age was 20 months, both are female. The circumstances of discovery were the finding of abdominal distention, fever or hematuria with Beckwith-Wiedmann diagnosed syndrome. At the end of the assessment, particularly by ultrasound and abdominal CT scan diagnosis in two cases of bilateral Wilms tumor non metastatic and nephroblastomatosis is made. The treatment consisted of preoperative chemotherapy, the former having responded well to chemotherapy then secondary tumor progressed, that led to an extended unilateral nephrectomy followed by chemotherapy and radiation therapy postoperatively. The second case has also responded well to chemotherapy currently stands tumor progression with paraspinal extension thus changing the treatment with chemotherapy nephroblastoma at high risk. At the end of this work and in the light of the most recent data from the literature, we conclude that the nephroblastomatosis precursor nephroblastoma including their genetic and pathological characteristics similar making it difficult to differentiate, medical imaging of bilateral Wilms and nephroblastomatosis plays a role primary diagnosis but cannot differentiate between the two. Therapeutically, the treatment strategy is to prolonged preoperative chemotherapy according to response to chemotherapy followed by unilateral nephrectomy with a postoperative treatment adapted to the local tumor stage.
Keywords: Nephroblastoma, nephroblastomatosis, nephrogenic remains, child.

INTRODUCTION

Kidney tumors are one of the most common groups of solid tumors of the child. For 30 years, the nosology of these tumors has progressed a lot. She owes it to work of the major series brought together by the National Wilms Tumor Study (NWTS) for North America, and the International Society of Pediatric Oncology (SIOP) for Europe, as well as the progress of molecular genetics which has upset the understanding of these tumors. Nephroblastoma is an embryonic tumor that occurs in infancy.

It is exceptional in adults. Bilateral localization, either from the outset, or secondarily is rare, it represents 4 to 8% of all Wilms tumors. This shape occurs in younger children, often associated with nephroblastomatosis. Nephroblastomatosis is defined by the presence of nephrogenic remains that are evidence of the presence of embryonic tissue in the developing kidney. These lesions are precursors of nephroblastoma and are found in 25% to 40% of patients with nephroblastoma and also meet in syndromes predisposing to nephroblastoma.

Diagnosis is often made in front of a typical clinic and imaging data in order to start the treatment but the diagnosis of certainty remains histological which conditions postoperative practice and prognosis. Treatment consists of a homogeneous therapeutic approach combining chemotherapy, surgery and radiotherapy. The rarity of bilateral nephroblastoma associated with nephroblastomatosis explains the variability of therapeutic proposals and the lack of codified protocols. The care must be multidisciplinary and must meet two contradictory imperatives: on the one hand to be as curative as possible, and on the other hand to preserve the maximum renal parenchyma to prevent progression to renal failure.

MATERIALS & METHODS

Our work consists of a retrospective study concerning 2 children, followed in the service Pediatric Oncology, one of which was operated on the Pediatric Visceral Surgery Department "A" at the Children's Hospital of Rabat.

The purpose of this study is to analyze the characteristics of such a location on the clinical and radiological plan, to discuss the choice of the surgical

technique and to study the relationship between nephroblastoma development and nephroblastomatosis.

Case n°1

3-year-old girl with no particular pathological antecedents, no notion of consanguinity, admitted for an abdominal mass whose history dates back to 1 month before admission by the observation of the parents of a progressive abdominal distension evolving in a context of apyrexia and conservation of the general state. The parents consulted where an ultrasound showed a suspicious looking bilateral nephromegaly. The clinical examination finds this mass of the left flank of firm consistency and painless without any other clinical abnormality.

We realised an Ultrasound who showed a left renal tissue injury process with inferior cortical development, well encapsulated and well-limited, containing areas of necrosis, without calcification or vascular invasion and measuring 85.4 x 77.2 mm. There were three other hypoechogenic, heterogeneous and well-limited nodules associated with it: - On the left, one super-inner polar and the other medio-renal, measuring 16.3 and 18, 3 mm.

A right upper polar, measuring 26 x 21 mm. There was no dilation of the pyelo-calicielles cavities. (Figure 1)

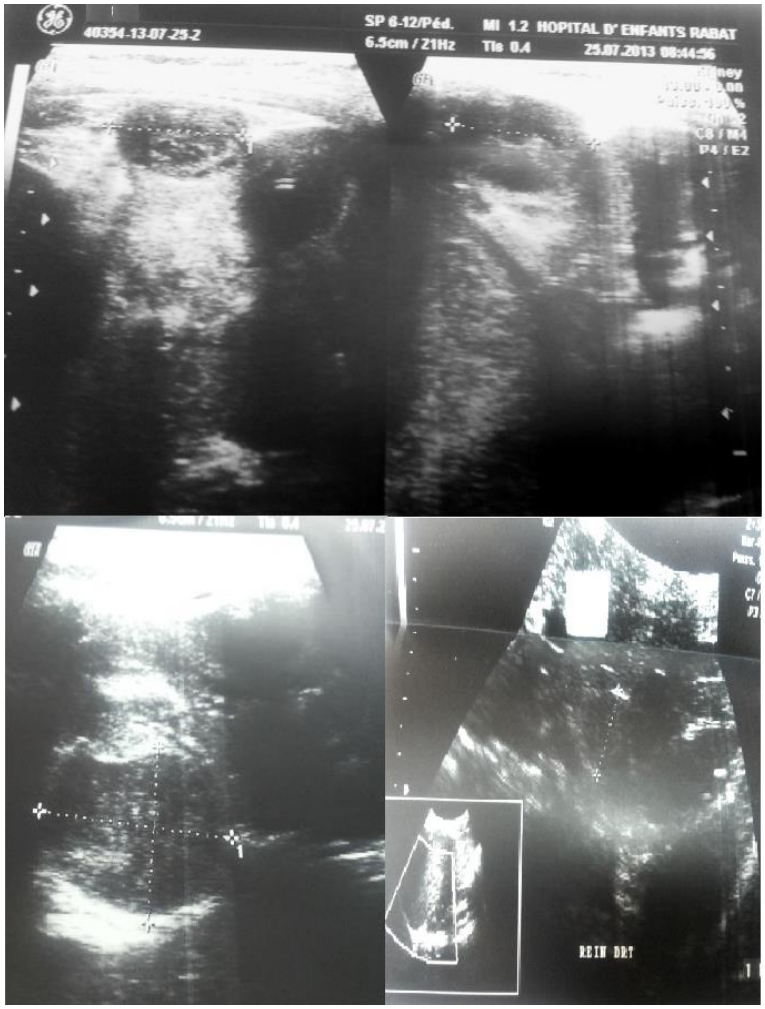

Fig-1: Abdominal ultrasonography showing renal nodules on the right and left

A pelvic abdominal CT was then performed (Figure 2), showing a large, well-defined, heterogeneous tissue mass enhancing after contrast measuring 113 x 81 x 70 mm. Two other hypodense left renal tissue formations, well 14 x 11mm and 13 x 11 mm. Tissue lesion of the right kidney in superior polar, isodense, well limited, enhancing after the contrast, measuring 20 x 19 mm. Urinary catecholamine dosing was normal and the extension balance was negative.

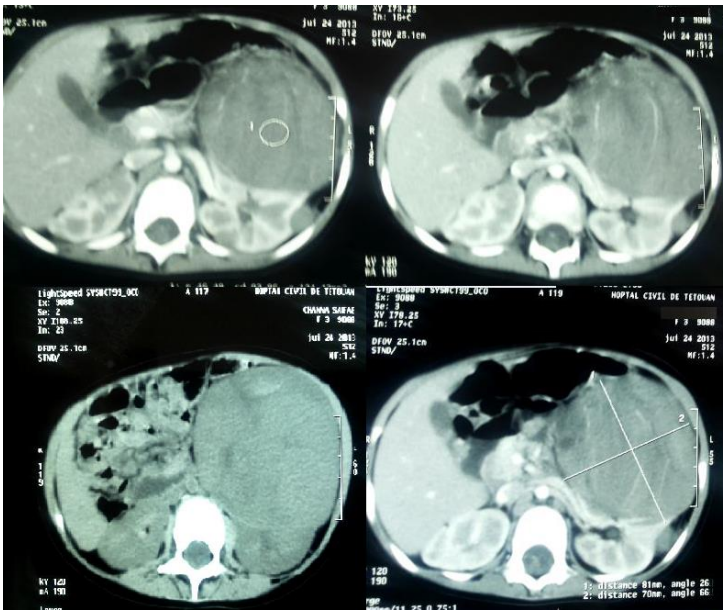

Fig-2: Abdominal CT showing bilateral tumor processes in favor of Bilateral nephroblastoma on nephroblastomatosis

Case n°2

Daughter of 2 years and 6 months, without notion of consanguinity, having as antecedents a syndactilie of the right hand, admitted for abdominal mass whose history dates back to 2 months before admission by the progressive increase of the abdominal volume with vomiting complicating of episodes of hematuria, the whole evolving in a context of unencrypted fever and slimming.

The clinical examination found a child in fairly good general condition, apyretic, slightly discolored conjunctiva, with a palpable mass in the left flank measuring 5 cm in large diameter, firm consistency, painless on palpation. Pleuropulmonary examination finds bilateral whines at auscultation. The rest of the examination objected to macroglossia, acromegaly, the face as well as the right forearm.

An abdominal Ultrasound was performed (Figure 3), showing:

- The right kidney is enlarged in size (10 cm in length) with multiple nodules the biggest ones sit in:

* Upper polar: mostly cystic, measuring 30 x 25 x 30 mm.
* Medi-renal peri-sinus / heterogeneous tissue measuring 27 x 24 mm.

- The left kidney is very enlarged in size (15 cm long) with multiple masses nodular, the largest of which are sieges:

* Upper polarity: tissue with cystic areas, 77 x 65 x 66 mm.
* Medio-renal: heterogeneous tissue, 57 x 55 x 51 mm.
* lower polar: tissue, 40 x 35 x 40 mm.

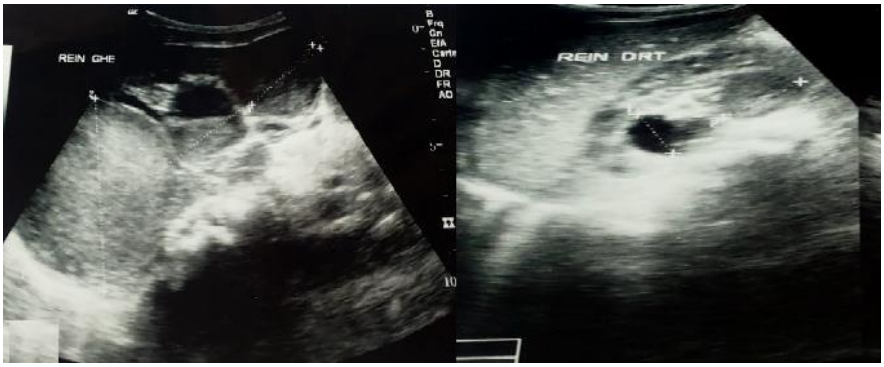

Fig-3: Abdominal ultrasound showing right and left renal nodules

These renal masses reach the left medial retroperitoneal region, repress the splenic pedicle, and exert a mass effect on the left excretory pathways (which are dilated in places wit endoluminal echo of possible superinfection) and on the pedicle renal vascular left which remains permeable.

Retroperitoneal Ganglions and Adenomegalies Blocking the Renal Vascular Pedicle left forward which remains permeable. The Spleen increased in volume to 11 cm, homogeneous and without focal lesion. A thoraco-abdominopelvic CT scan was performed (Figure 4), showing on the thoracic stage a left basal alveolar focus, then on the abdominopelvic floor:

- Left kidney increased in size, seat of several tissue hypodense lesions heterogeneously enhanced after contrast, the largest of which: superior polar (70 x 80 mm), medio-renal (50 x 48 mm) and inferior polar (40 x 36 mm), they push back the bassinet with moderate hydronephrosis.
- Right kidney, of subnormal size, seat of tissue lesions: at the level of the lip anterior (24 x 31 mm), posterior lip (17.5x12 mm), medio-renal cortex (11x9mm). Presence of an upper polar cyst of 24x22mm.

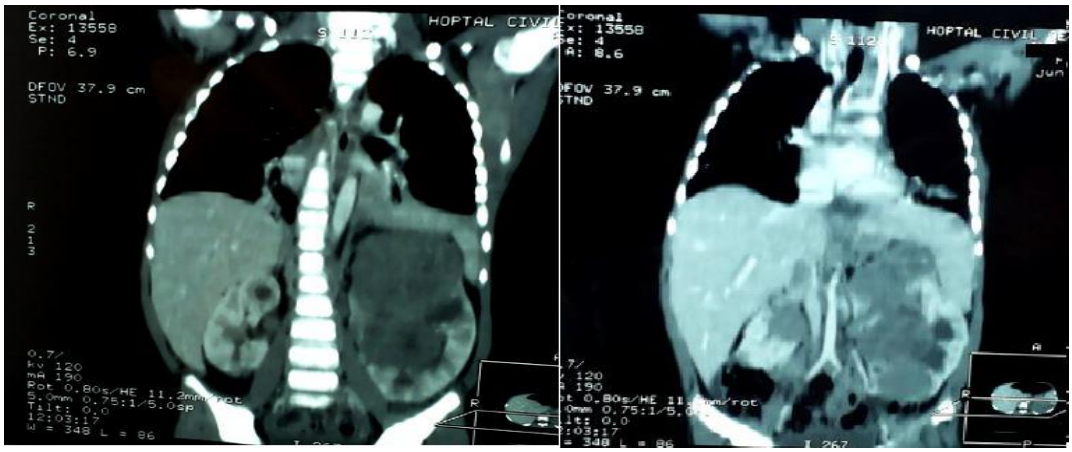

Fig-4: CT TAP showing bilateral renal masses

Respect of the renal vessels and the IVC. The extension assessment was negative; however it was a bilateral nephroblastoma probably on nephroblastomatosis on Beckwith Weidman syndrome.

RESULTS

Vincristine-based preoperative chemotherapy was started weekly and Actinomycin D every 15 days up to a maximum reduction of one side with volume stabilization for one month; with the goal of a less aggressive surgical treatment and however the most conservative possible.

Case n°1

The patient received 2 months of chemotherapy

- Ultrasound control showing a reduction of 26% → decision to add 1 month of chemotherapy.
- CT scan showing a 90% reduction of the left target lesion (Figure 5) → add 1 month of CMT.
- CT scan not done for technical reasons → add 1 month of CMT.
- CT scan showing the regression of 40% left target lesion and stationary aspect of the right → add 2 months of CMT.
- CT scan: slight progression of the volume of the left lesion → add 2 months of CMT.
- CT scan: left tumor progression of 68% (Figure 6) → continue CMT for 2 months.
- Scan control at 1 month: progression to 40% of the last control

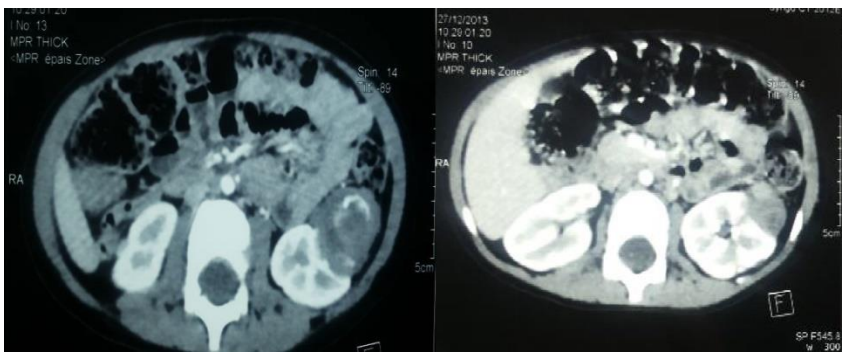

Fig-5: Abdominal CT demonstrating a significant regression with necrosis of the renal lesions

Ultrasonographic examination: progression of the left lesion and stationary aspect of the right lesion.

= Total of 11 months of chemotherapy.

⇨ Decision of the surgeons at the multidisciplinary staff of a total left nephrectomy in front of tumor progression on this side.

The pathological study concluding in a blastematous nephroblastoma necrotic to 20%. Hile and infiltrated sinuses, Limited tumor excision. Absence of nephrogenic remains and latero-aortic ganglionic infiltration.

→ Tumor classified Stage III of the SIOP 2001.

Postoperative chemotherapy was performed according to the same protocol. The clinical evolution was favorable with a decline of three years. The last ultrasound and CT scan is normal with complete regression of nephroblastomatosis lesions.

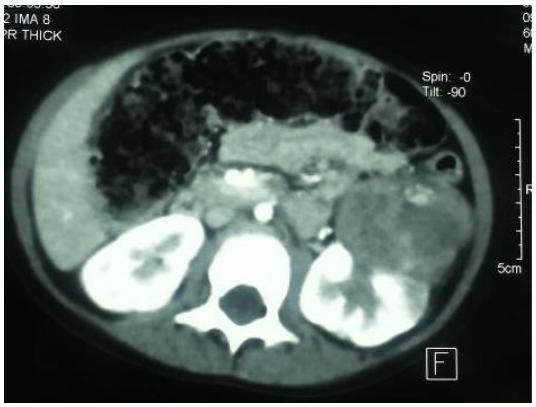

Fig-6: Abdominal CT showing tumor progression on the left

Case n°2

The child received 26 weeks of chemotherapy,

- **Clinically**

The child has a fever with a dry cough, erythemato-pultaceous tonsillitis with greenish deposits, treated with protected amoxicillin and antipyretic per os without improvement, encouraging intravenous therapy with 3rd generation cephalosporin for 3 days with relay bone with protected Amoxicillin, and return to apyrexia.

- **Biologically**

Regular biological monitoring is continued by checking the blood count and renal function without particularity except for hemoglobin anemia 8.2 g / dl for which a transfusion of 1 packed red blood cell is made.

- **Radiologically**

On the abdominal ultrasound, there is a tumoral process of the left superior polar kidney, with heterogeneous tissue echo, with calcifications and zones of necrosis, measuring 12 x 11 cm (versus 80 x 67 mm), an increase of 56%.

On the same side, it is associated with latero-aortic adenopathies, the largest of which measuring 42 x 38 mm. Right renal nodular lesions with the largest voluminous slightly necrotic upper pole measuring 42 mm long axis (versus 30 mm) is an increase of 40%.

Liver enlarged with a hepatic arrow at 15 cm. CT performed (Figure 7) objectifying: Multifocal bilateral nephroblastoma on nephroblastomatosis up to 40% with paravertebral and endocanalar extension with multiple tumor adenopathies without distant metastasis.

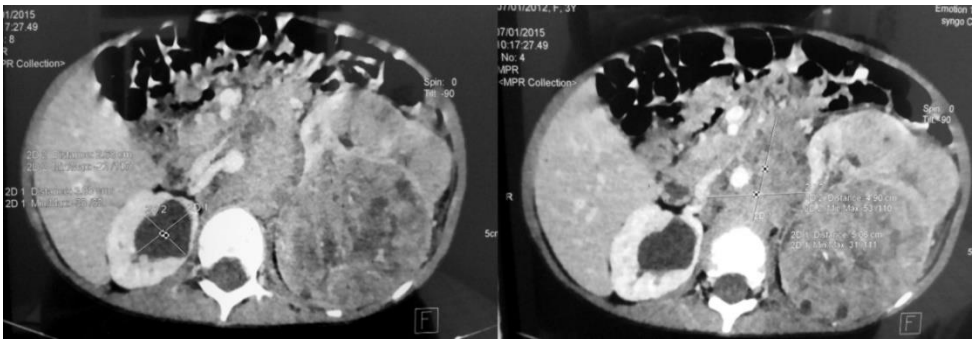

Fig-7: Abdominal CT showing the progression of bilateral renal tumor processes with endocalanar extension and retroperitoneal ADP

At the last multidisciplinary team the decision of a chemotherapy of the types of high risk was posed by Etoposide + Carboplatin followed 21 days after the association Cyclophosphamide + Doxorubicine. This treatment regimen is repeated a second time, ie 60 days, at the end of which a radiological assessment was made and before the significant regression of the tumor mass, a partial nephrectomy was performed for both sides.

Postoperative chemotherapy was initiated with radiological monitoring demonstrating significant regression of nephroblastomatosis lesions and absence of metastases.

DISCUSSION

Nephroblastomatosis is an anatomo-pathological entity rare, characterized by the abnormal persistence of metanephrogenic blastema beyond the 36th week of fetal life, date when complete maturation is completed. This is a problematic condition nosology. Several terms are used to to design the same affection. In 1976, BOVE et McADAMS proposed a classification that is based on on the variation of distribution of the metanephogenic blastema at the kidney level, which made it possible to define three histological types:

- Multifocal superficial nephroblastomatosis
- Diffuse superficial nephroblastomatosis
- The deep pancortical nephroblastomatosis which is an exceptional entity incompatible with life and death occurs by anuria in the perinatal period.

BECKWITH in 1990 introduced the term "leftover nephrogenic "for all lesions entering this frame. He thus distinguishes the nephrogenic remains perilobar and the intra-lobar nephrogenic remains that are localized and he reserves the term of nephroblastomatosis to multifocal or diffuse lesions. This term also refers to cases where the presence of remains nephrogenic can be inferred (Nephroblastoma bilateral or multifocal) [2].

Some associated malformation syndromes have been frequently reported in the literature represented mainly by the syndrome of Beckwith Weidman, body hemihypertrophy, syndrome of Drash and Perlman syndrome.

Nephroblastomatosis is rarely isolated and is often associated with nephroblastoma. Indeed, the study Pathology of parts of enlarged nephrectomy for unilateral nephroblastoma found a nephroblastomatosis associated in 17% to 44% and it reaches 99% of cases in bilateral nephroblastomas [2, 3, 10, 12]. All authors agree to consider nephroblastomatosis as a lesion precursor of nephroblastoma and this in front of their association frequent, their histological similarity and their common origin (metanephrogenic blastema) [5,10, 11].

In the associated form, the clinical picture is dominated by the abdominal mass and has no specificity compared to that of a classical nephroblastoma. For our two observations the circumstance of discovery was an abdominal mass. In case of nephroblastomatosis isolated, the clinical semiology is very poor in multifocal form; on the other hand in the diffuse form, the clinical picture is dominated by abdominal mass.

Radiologically, nephroblastomatosis lesions present on ultrasound as images often hypoechoic but can be hyperechoic, isoechoic or anechoic, nodular or cortical diffuse as the case of our two observations [13]. Computed tomography is more efficient as ultrasound by showing tumor lesions nodular or diffuse, isodenses that do not enhance not or weakly after injection of contrast [4, 5, 13]. Magnetic resonance imaging (I.R.M) is as efficient as the scanner in objectifying nephroblastomatosis in the form of Iso-intense lesions that become hypo-intense in T1 after gadolinium injection [10, 13]. These images do not that evoke the diagnosis and several authors advocate the practice of a renal biopsy [7, 9]. The differential diagnosis between nephroblastoma and nephroblastomatosis can remain complex even after biopsy.

In the form associated with a nephroblastoma, driving to hold is not confusing and the treatment is that of the tumor itself. But the particularity of these forms is the high risk of developing other contralateral nephroblastomas. For these reasons, some authors propose to perform a simple Tumorectomy or partial nephrectomy to preserve the no longer possible renal parenchyma [6, 8].

In isolated nephroblastomatosis, treatment is controversial. Although we can hope for a trend spontaneous regression, the risks of evolution towards nephroblastoma are elevated. This explains that the most authors agree to treat this pathology even in the absence of a nephroblastoma.

Currently the majority of authors are in favor of chemotherapy alone based on actinomycin D and oncovin [7, 14, 15]. The effectiveness of this chemotherapy is discussed and cannot be judged by the rarity of this affection. Some authors report results spectacular with a complete disappearance of lesions. Others report cases where chemotherapy was ineffective. But whatever the result of this chemotherapy, the malignant transformation always remains possible [1, 10, 12].

Monitoring must be strict and continued during a long time, faced with the risk of developing multiple nephroblastomas. However, it does not exist currently a standardized regimen as to the means and the pace of surveillance. This should be maximum between the age of one and five years, during which time the risk of

developing a nephroblastoma is elevated and must be continuous until the age of ten, the age at which this risk becomes important [14].

CONCLUSION

In the light of these data, the bilateral attack can be immediately (the two observations), or successively. He usually occurs in younger children than those with a unilateral form (2 years and 9 months average of our cases). Foci of nephroblastomatosis considered as precursors of nephroblastoma are more often found in cases of bilateral tumors.

These bilateral tumors often more frequently associated with abnormalities congenital which raises the hypothesis of a genetic origin of these nephroblastomas. This imposes the surveillance of the sibship of affected subjects, all we do not forget that parents, even distant, can be affected.

On the other hand, these congenital anomalies (aniridia, hemihypertrophy, Wiedemann-Beckwith ...) when they exist, associated with a unilateral nephroblastoma, should raise fears of bilateralisation.

Our 2nd case had Wiedemann-Beckwith syndrome.

Treatment should begin as soon as possible and as long as possible with continued low-dose chemotherapy, with careful, close, and highly prolonged, this surveillance makes complementary use of ultrasound and sequential imaging. In our study, the response to early favorable chemotherapy treatment is limited by secondary tumor progression requiring the change of drugs used in chemotherapy or the use of chemotherapy.

Surgical treatment should preserve the renal parenchyma as much as possible. The Postoperative treatment is stratified according to the local tumor stage. Today, great chances of healing are offered at the cost of minimal sequelae to the majority of patients with kidney tumors in industrialized countries. The healing remains a challenge in developing countries.

Recent advances in the knowledge of the biology of renal tumors are certainly allow in the future to define new prognostic criteria: patient groups with particularly favorable prognosis will thus still be able to benefit therapeutic de-escalation, while certain forms risk whose prognosis could be improved by new, more targeted approaches.

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