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# Extrarenal Nephroblastoma: A Report of Two Cases

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**Abstract** **Case Report**

In children, the most common solid tumours is nephroblastoma, but the extrarenal nephroblastoma exists and it is especially rare. It is defined by extrarenal location and histological confirmation. There are many symptoms of extrarenal nephroblastoma and it depends on the location. The diagnosis is based on histology after the resection of the tumor. The treatment of the extrarenal nephroblastoma is similar to the treatment of intrarenal nephroblastoma.

**Keywords:** Nephroblastoma, extrarenal location, children.



## INTRODUCTION

Nephroblastoma or Wilms's tumor, is a common solid tumour in children, it represents 8-10% of all neoplasms, ranking third after neuroblastoma and CNS tumours [1, 2]. It is also the most frequent tumour found in paediatric kidneys. It is generally found in pre-school children, between 1 to 5 years of age [3, 4]. Nephroblastoma arises almost exclusively from the kidney and in 5% of cases it affects both kidneys at the same time [5, 6].

Extrarenal Wilms' tumour (ERWT) are extremely rare in adults and children and its occurrence without kidney involvement is extremely uncommon. The diagnosis is almost always made after surgical intervention [4, 7].

Only 300 cases have been reported to date from all over the world**.** The most common sites of extrarenal Wilms are the retroperitoneal space, the ovaries, the uterus, the cervix of the uterus, the loin, the sacrococcygeal region the mediastinum and it is found in children with the horseshoe kidney [8, 9].

The mechanism of extrarenal nephroblastoma is not known. The clinical manifestations vary by its location because of pressure effects on the adjacent vital structures such as blood vessels, nerves, ureter, bladder, and bowel [4].

The final diagnosis is histopathological, but the radiological examination plays an important role in the evaluation of the lesions for the extent. The chemotherapy for extrarenal nephroblastoma is the same that is used for the intrarenal nephroblastoma [3].

## TWO CASES

### Case Report 1

D.A is a 12 years old girl, without any particular medical history. She was addressed to our Pediatric oncology center for further exploration and management of her painful abdominal mass. In fact, for the past 2 months, the patient has been suffering from chronic pelvic pain associated with a deterioration of her general condition, asthenia, and a weight loss (up to 4kg in 3 months). The patient has experienced worsening of her symptoms, complicated by an intestinal obstruction syndrome made of: Abdominal pain, bilious vomiting, and a total inability of defecation and passing gas. These symptoms had led the patient to check up in a nearby hospital where an abdominal ultrasound was performed. It has revealed a massive left-sided abdominal-pelvic mass. On ultrasound, the mass appeared heterogeneous with both tissue and liquid components associated with hemorrhagic areas.

Also, the mass compressed ureters which lead to a mild bilateral ureterohydronephrosis (UHN). Based on these ultrasound features, an ovarian tumor was highly suspected. Moreover, the abdominal and pelvic CT scan confirmed the presence of a massive left-sided abdominal-pelvic mass, compressing ureters and invading the uterus (Figure 1). Thus, these images of CT scan first evoked an ovarian tumor.

Due to the worsening of her symptoms, the patient was urgently admitted to the OR where a surgical biopsy was performed. Then, she was addressed to our Pediatric oncology center for further case management.

After admission, physical examination showed a conscious patient with cutaneous/ conjunctival pallor, apyretic, eupneic but cachectic weighing 29kg (-2DS). Her abdomen was soft, with a 9cm mass in the left hypochondria. The clinical examination of superficial lymph nodes and the rest of the physical examination were normal. Tumoral markers were normal on blood tests: BHCG < 0.10 UI/L AFP 4.13 UI/ml

A thoracic, abdominal, and pelvic CT scan was reperformed and has shown on the thoracic level: 2 nodules, one is localized in the subpleural area on the posterior basal segment and measuring 4mm, while the other is intraparenchymal in the lingular segment, measuring 7mmx7mm. Whilst on the abdominal level, a massive abdominal mass appeared measuring 110×189×244 mm. The CT described a well-delimited mass, with both tissular and mainly liquid components with intratumoral septal enhancement, besides fatty areas. The mass appeared to invade ureters causing a left UHN and a right pyelic ectasia. Moreover, the CT showed multiple nodular hepatic lesions that appeared hypodense and well delimited (Figure 1).

The MRI revealed the presence of a massive encapsulated cystic abdominal-pelvic mass (left ovarian mass) with a left lateral uterine starting point without signs of renal invasion; sized 148*106*214 mm (Figure 2).

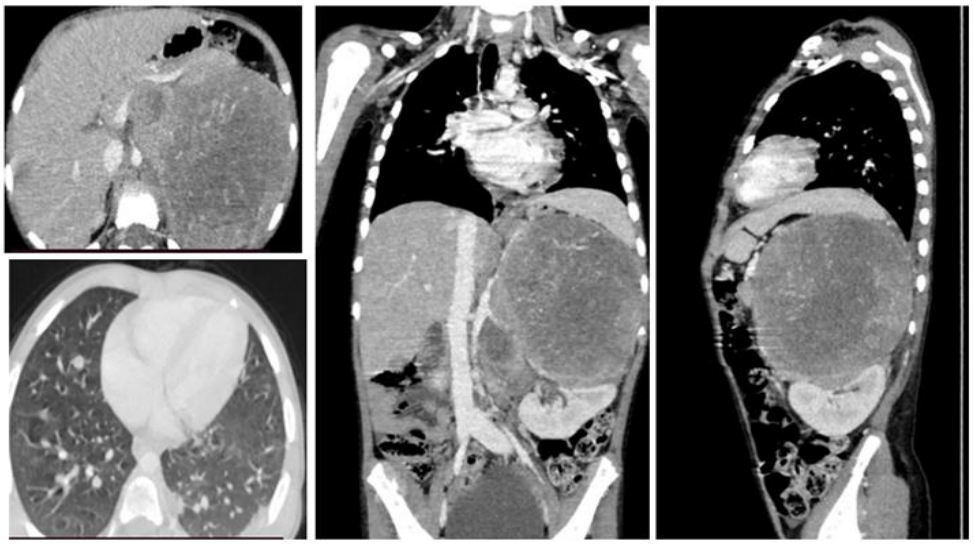
This case management consisted of the administration of neoadjuvant chemotherapy, followed by surgical resection and cytological analysis of the peritoneal liquid. The operation led to the resection of a massive retroperitoneal mass weighing 2,5 kg. The mass was found fissured on the initial biopsy site, with the presence of fibrosis and calcification (Figure 3). However, there weren't any signs of peritoneal carcinomatosis. The 2 ovaries and 2 kidneys weren't invaded.

On the macroscopic level, the tumor was totally resected and seemed encapsulated. The histological analysis reported a regressive extra-renal nephroblastoma staged 3 according to the SIOP classification (reviewed in 2016), with the presence of necrotic areas estimated up to 70%. There wasn't any focal anaplasia reported.

The patient has been put on the therapeutic protocol of a high-risk nephroblastoma (Wilms Tumor) alternating cycles of VP16/CARBO and ENDOXO/ADRIA: -VP 16 150 mg/m2/j -carboplatin 200mg/m2/j -Cyclophosphamide 450 mg/m2/j -Adriamycin 50 mg/m2/j . Furthermore, radiotherapy has been indicated in this case.

The patient is currently in the 7th week of the high-risk protocol. Surveillance under chemotherapy included:

- Thoracic CT scan performed on the 26th July 2021, that hasn't revealed any particular findings
- Pelvic MRI performed on the 27th July 2021 has shown a regression of the secondary hepatic lesions (priorly described on a CT scan performed on 27th May 2021).



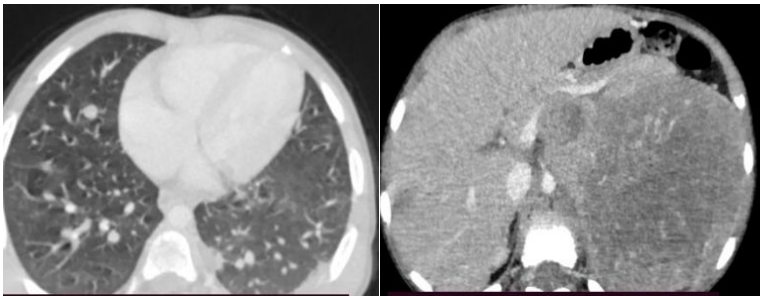


**Figure 1: Abdominal and pelvic CT scan confirming the presence of a massive left-sided abdominal-pelvic mass, compressing ureters and invading the uterus**

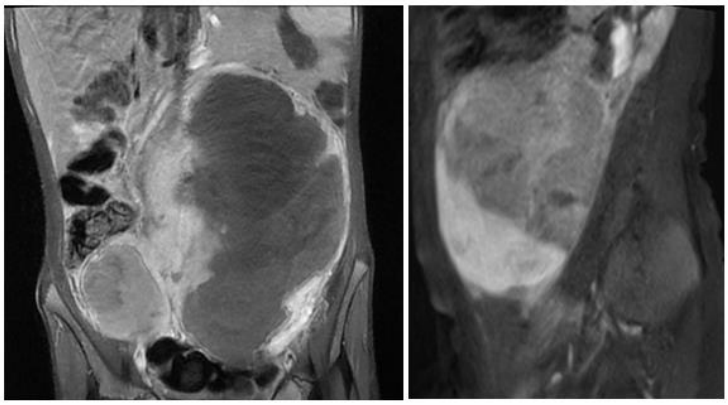


**Figure 2: MRI revealing the presence of a massive encapsulated cystic abdominal-pelvic mass (left ovarian mass) with a left lateral uterine starting point without signs of renal invasion; sized 148*106*214 mm**

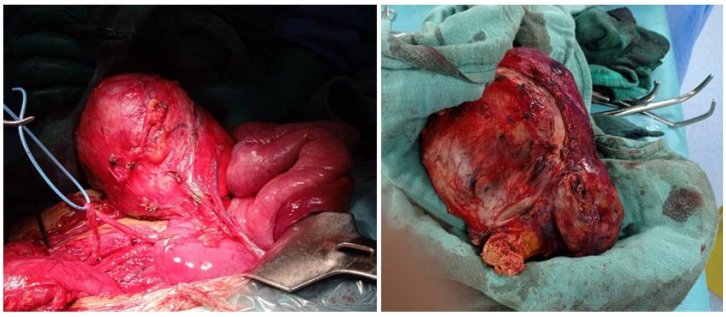


**Figure 3: The retroperitoneal mass weighing 2,5 kg**

## Case Report 2

D.N is a 7 years old girl, without any particular medical history. She has been admitted to our hospital unit for management of her abdominal pelvic mass. The patient's symptoms go up to 1 month with the discovery of a right abdominal pelvic mass associated with dysuria. Neither constipation nor rectorrhagia was reported. The patient has first checked up at a general practitioner who performed an abdominal-pelvic ultrasound. The ultrasound showed a right abdominal-pelvic mass with both cystic and tissue components. The mass measures 108×94 mm and seems to be from a right ovarian starting point with ureters compression leading to ureterohydronephrosis (UHN). An MRI was performed and showed a sub-uterine right-sided mass measuring 12×10cm. Indeed, the mass has both cystic and tissue components being originally from Ovaries and is associated with a right ureterohydronephrosis (UHN) The mass has been staged ORADS4 (Figure 4).

The patient was addressed to the Pediatric surgical Emergency unit, where an intraoperative exploration has revealed a pelvic mass. The mass seemed to reach the inferior renal pole without invading it. The mass has been completely resected. The patient was then addressed to the Pediatric oncology center for further exploration and case management.

After admission, physical examination showed a conscious patient with normal skin/conjunctive, apyretic, eupneic, weighing 20kg (-1DS). Her abdomen was soft, with a laparotomy scar on the right iliac region. The clinical examination of superficial lymph nodes and the rest of the physical examination were normal. Tumoral markers were normal on blood tests: BHCG and AFP.

The histology analysis came out favorable to an extra-renal blastematous nephroblastoma (Wilms Tumor), staged 3 according to SIOP (2001) (Figure 5).

The therapeutic scheme, in this case, includes a Postoperative Chemotherapy with:- Vincristin: 1,5 mg/m² - Adriamycin: 45µg/Kg Et doxorubicine: 50 mg/m². Furthermore, radiotherapy has been indicated in this case.

The patient is currently on her 20th chemotherapy cure. The treatment surveillance includes a Thoracic abdominal and pelvic CT scan associated with a pelvic MRI. They haven't reported any residual tumor tissue, or signs of recurrence, nor secondary neoplastic localizations.

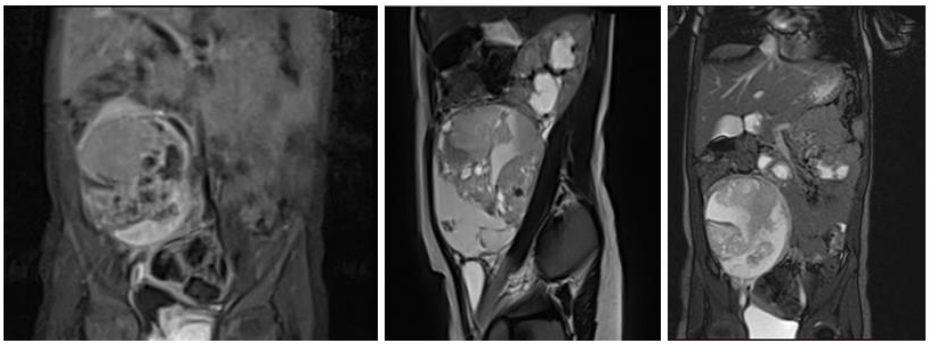


**Figure 4: MRI showing a sub-uterine right-sided mass measuring 12×10cm. The mass has both cystic and tissue components being originally from Ovaries and is associated with a right ureterohydronephrosis (UHN)**

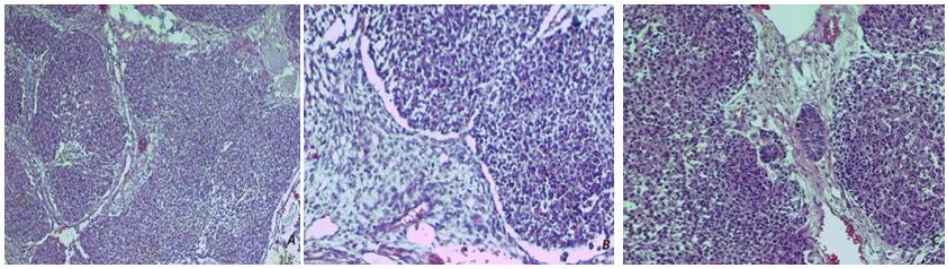


**Figure 5: A) Blastema cell nests. B) Blastme + primitive mesenchyme. C) Blastema nests + epithelial differentiation**

## DISCUSSION

Nephroblastoma is the next most common malignant abdominal tumor in childhood after neuroblastoma. It represents about 8-10 % of all childhood carcinomas. It arises almost exclusively from the kidney. Simultaneous involvement of both kidneys by nephroblastoma occurs in 5% of cases [1, 2].

Extrarenal nephroblastoma is extremely rare and the exact incidence is not known. According to Itoshima and al., there have been 300 well documented cases of extrarenal nephroblastoma [8]. There is no sex predominance. The age of appearance generally varies between 2 months and 10 years. Exceptionally young (an 8 day-old child) and old (77 year-old female) cases have also been reported [10]. In the United States, 73% of childhood cases are diagnosed before 5 years old, and 95% before 10 years old [9].

The exact mechanism of extrarenal Wilms tumor pathogenesis is not clear and there are various hypothesis and theoriesregarding the origin. Previous studies have suggested that extrarenal Wilms tumor from the ectopic metanephric blastema, this hypothesis is supported by the fact that the majority of the tumors occur in the retroperitoneal region. The Second hypothesis is the origin from the primitive mesodermal tissue: this hypothesis is based on the occurrence of ERWT in the cervix, vagina and inguinal canal, where there is a persistent mesonephric duct remnant. The third is the Connheim's cell rest theory: This is a common hypothesis where cells with persistent embryonal potential undergo malignant transformation at any point of time [4, 7, 10].

On the other hand, as WT-1 gene expression in 25% of extrarenal Wilms' tumors has been reported, mutation of this gene may be the reason for transformation of extrarenal primitive mesonephric or pronephric remnants into WT [6].

ERNBs can arise in different sites, more frequently in the retroperitoneal space [11]. The next most common locations are the uterus and inguinal region. Other sites include subcutaneous tissue, and muscles of the back, ovary, testis, pararenal space, sigmoid mesocolon, urinary bladder, prostate gland, and the lumbosacral area and frequently associated with spinal dysraphism, heart, thorax [6, 12].

There are no specific clinical criteria used to diagnose the extrarenal nephroblastoma because the clinical presentation may vary depending on its location with pressure effects on the adjacent vital structures such as blood vessels, nerves, ureter, bladder, and bowel. (7)

Extrarenal WT must be included in the differential diagnosis of abdominal, pelvic, and inguinal masses. The non-neoplastic association of this tumor is with horse-shoe kidney reported in six patients and spinal dysraphism in two cases. The most common presentation is a palpable mass. Patients with uterine ERWT may present with irregular menstrual bleeding [6].

In our first patient, the mass was attached to the ovary. However, in our second patient, the lesion was located in the lower pole of the kidney.

The initial imaging always begin with sonography, renal masses typically distort the normal renal parenchyma with a "claw sign" of the normal renal parenchyma surrounding the mass, whereas extrarenal masses displace the kidney.

Wilms tumours are usually large at diagnosis, measuring at least 5–10 cm in diameter. The margins of a Wilms tumour are smooth and well-defined. It grows by expansion and forms a pseudocapsule.

Theechogenicity of Wilms tumor can be highly variable depending on the degree of tissue necrosis/ intratumoral hemorrhage. It is usually heterogeneous with hypoechoic and anechoic areas caused by liquid haemorrhage/necrosis or cysts. Calcifications are less common, occurring in only 9% of patients.

Careful evaluation of the contralateral kidney is essential to evaluate for synchronous contralateral lesions and the renal vein and inferior vena cava because vascular extensionof the tumoris present in approximately 10% of cases.

CT and MRI have been shown to have equivalent diagnostic performance for locoregional staging of Wilms tumor [13, 14].

Wilms tumor typically shows less enhancement compared to the normal renal parenchyma andcan be heterogeneous in appearance from internal necrosis and hemorrhage. MRI is the preferred imaging modality in children with known bilateral Wilms tumors or known bilateral tumor predisposition. It is essential to have high-spatial- resolution post-contrast images of the renal parenchyma in the nephrographic phase because this aids detection of small Wilms tumors and nephrogenic rests.

The tumour usually demonstrates low signal intensity on T1-weighted (T1-W) sequences and hypo- or isointensity on T2-weighted (T2-W) images. The presence of haemorrhage, areas of fat, necrosis and cysts often make the appearance very heterogeneous. After injection of contrastagent, the heterogeneity of the tumour increases.

Diffusion-weighted images can aid in detection of small synchronous tumors/multifocal tumors. In addition, whole-tumor apparent diffusion coefficient (ADC) values have been shown to correlate with stromal subtype histopathology but not with blastemal predominant subtypes, which is a prognostic indicator in post chemotherapy tumors [15].

Preoperative diagnosis of extrarenal nephroblastoma is difficult because of the lack of specific tumor markers. It is usually diagnosed after operative removal and histopathological examination (after ruling out an extension from the intrarenal WT or a metastatic lesion). Itmust satisfy the following criteria: histologically confirmed nephroblastoma and extrarenal location. Beckwith and Palmer described the following criteria for pathologic diagnosis of extrarenal Wilms tumor: (1) extrarenal site of primary neoplasm, (2) primitive blastematous spindle or round cell component, (3) abortive or embryonal tubular or glomeruloid structure, and (4) noevidence of teratoma or renal carcinoma [10].

On histological examination, these tumors show similar to renal nephroblastomas. It comprises nephrogenic tissues, such as blastemal, epithelial (tubular and glomeruloid) and mesenchymal elements [12].

Extrarenal nephroblastoma is similar to intrarenal nephroblastoma in the staging and management protocols according to the National Wilms' Tumor Study (NWTS) protocol. (4) Surgical excision is the treatment of choice and all cases treated by surgery need postoperative adjuvant chemotherapy. The chemotherapy used for renal nephroblastoma is equally effective for extrarenal nephroblastoma [6, 10].

Radiotherapy should be reserved for those patients with unresectable gross residual tumor and those with distant metastasis [4, 7]

In our cases, we followed the recommendation of NWTS and first of all removed the mass surgically because it seemed possible to remove the mass totally, and after we complete by postoperative adjuvant chemotherapy.

The prognosis of ERWT is similar to the classical WT with the appropriate stage. The presence of anaplasia, characterized by extreme polyploidy, with nuclear and mitotic atypia, indicates poor prognosis as they show increased resistance to therapy. Metastasis have been reported in lungs, liver, pancreas and brain and is responsible for poor prognosis [7].

Fortunately, our cases reported show a benign prognosis because they did not have any evidence of any persistent metastasis and after the excision of the tumor they are doing well.

## CONCLUSION

Extrarenal nephroblastoma is an extremely rare and exceptional pathology requiring a multidisciplinary approach. The diagnosis is based on histology after tumor resection. The treatment of extrarenal nephroblastoma is identical to the treatment used for intrarenal nephroblastoma. The prognosis in adequately treated ERWT cases is quite good, and most cases have an excellent prognosis. Some cases with unfavorable histology have a poor prognosis despite complete tumor resection and adjuvant chemotherapy.

**Conflicts of Interest**: The authors declare no conflicts of interest.

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