Ped. Med. Chir. (Med. Surg. Ped.), 2014, 36: 170-172

# Nephrogenic remnants: occasional ultrasound diagnosis and follow-up

*Residui nefrogenici: diagnosi ecografica occasionale e follow-up*

S. Caiulo,[1] C. Gargasole,[2] V. Gianfredi,[3] V. A. Caiulo[4]

*Key words: Nephrogenic remnants - Wilms tumor - ultrasound - kidney*


## Abstract

**Nephrogenic remnants (NRs) are nodular collections of undifferentiated renal blastema cells in the postnatal kidney that are recognized as putative precursor lesions of Wilms tumor (WT). NRs may remain stationary, undergo regression, or proliferate. In the last case, there is a high risk for the development of a WT. During infancy, they are most frequently of microscopic size, to be found only at autopsy in approximately 1% of infant kidneys. Approximately 1 out of 100 microscopic lesions persist and grow developing lesions large enough to be seen by ultrasound in the first months of life.**

**We report on a case of NRs in a six year old child, as incidental finding during abdominal ultrasound performed for other purposes. In consideration of the potential evolution in WT, after a period of close surveillance of 14 months, the lesion was resected. Histological examination revealed the presence of NRs, no neoplastic lesions were found. Currently the patient is 16 years old, in good health, and there have been no signs of recurrence.**



## Riassunto

I Residui Nefrogenici (RN) sono noduli di cellule indifferenziate considerati potenziali precursori del Tumore di Wilms. Tali lesioni hanno spesso dimensioni microscopiche, e sono individuate nell'1% delle autopsie. I RN possono rimanere stazionari, andare incontro a regressione, oppure possono proliferare. In quest'ultimo caso c'è un alto rischio che si sviluppi un Tumore di Wilms. Approssimativamente 1 su 100 delle lesioni microscopiche tende a crescere e può essere individuata con un esame ecografico nei primi mesi di vita.

Noi riportiamo un caso di RN in un bambino di 6 anni, individuato come reperto occasionale nel corso di un esame ecografico eseguito per altri motivi. Considerando la potenziale evoluzione verso un tumore di Wilms, dopo un monitoraggio di 14 mesi, la lesione è stata asportata chirurgicamente. L'esame istologico non ha evidenziato cellule neoplastiche. Attualmente il paziente ha 16 anni e non ha avuto alcun segno di recidiva.





Figure 1.
hyperechoic formation at the upper pole of the right kidney


[1] Department of Pediatrics, Vita-Salute San Raffaele University, IRCCS San Raffaele Hospital, Milan, Italy
[2] Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Mangiagalli, University of Milan, Italy
[3] Department of Pediatrics, Perugia University, Perugia, Italy
[4] School of Ultrasound of Italian Federation of Pediatricians, Brindisi, Italy

Indirizzo per la corrispondenza (Corresponding author):
Vito Antonio Caiulo
Address: Piazza Angeli, 3 - 72100 Brindisi, Italy
Tel.: +39 0831 591137; fax: +39 0831 537861
E-mail address: antoniocaiulo@inwind.it

## Introduction

Nephrogenic remnants (NRs) are nodular collections of undifferentiated renal blastema cells in the postnatal kidney that are recognized as putative precursor lesions of Wilms tumor (WT).
They usually occur along the perimeter of a mature renal lobe (ie, perilobar nephrogenic rest), within the lobe itself (ie, intralobar nephrogenic rest), or both (ie, combined). NRs may remain stationary, undergo regression, or proliferate. In the last case, there is a high risk of development of a WT, the most common malignant neoplasm of the urinary tract in children.[1,2]
The suggestion that NRs could be a precursor lesion of WT was proposed in the mid-1970s.[3,4] Today, it is well accepted that NRs are found in 25% to 40% of kidneys presenting WT.[5] Thus, NRs are considered to be clinically significant entities requiring close surveillance when detected.[2] The cause of malignant transformation of NRs to WT is not known. Multiple pathways to Wilms tumorigenesis have been proposed recently, but are beyond the scope of this discussion.[6]

## Case report

A six year old boy was admitted to our Institution for parotitis and suspected pancreatitis. The patient had been healthy since birth, with normal growth and development.
An abdominal ultrasound was performed and it showed the presence of a hyperechoic formation at the upper pole of the right kidney, as incidental finding. The lesion had an ovoidal shape, with well-defined margins and a maximum diameter of 26 mm (fig. 1).
At computed tomography (CT) the lesion presented a homogeneous enhancement following contrast injection. There was no lymphadenopathy. These findings were consistent with the diagnosis of NRs. As the patient was completely asymptomatic and no malignancy was suspected it was undertaken regular follow-up with ultrasound.
During the first year of follow-up there was a slow increase in the dimension of the lesion (from 26 to 28 mm). In the subsequent two months there was an increase in the rate of growth of the lesion that reached the maximum diameter of 35 mm.
In consideration of the increased growth rate of the lesion, we opted for surgical removal. Surgical intervention had a regular course, in the absence of postoperative complications.
Histological examination revealed the presence of NRs, without neoplastic lesions.
Currently the patient is 16 years old, in good health, and there have been no signs of recurrence.

## Discussion

To date, the NRs frequency in the general population is not well defined. In our previous publication, the incidence of NRs detected by ultrasound screening for kidney anomalies at two months of age was found to be 2 out of 17.783.[7]
During infancy, they are most frequently of microscopic size, to be found only at autopsy in approximately 1% of infant kidneys, according to Beckwith et al.[1] In most cases NRs regress or remain stationary, remaining subclinical. According to Beckwith, approximately 1 out of 100 microscopic lesions persist and grow developing lesions large enough to be seen by US in the first months of life (1). Many more can be expected to do so during the ensuing 15 years. For example, NRs were identified in children with WTs up to 111 months of age by Beckwith et al.[1] These data indicate that most NRs will regress or remain stationary without becoming appreciable clinically. However, some remnants will undergo progressive enlargement as hyperplastic NRs.[1] A small fraction will give rise to a WT, accounting for about 1/3 of the total population of WTs in the childhood population, which is about 1:10,000.[1]
Overt NRs may have a mixed appearance, manifesting themselves as hypoechogenic, hyperechogenic, or isoechogenic nodules. Computed tomography or magnetic resonance imaging rather than US are thought to be the more appropriate means of reaching a definitive diagnosis when needed in patients with NRs.
To date, there is not a uniform approach to the problem. A number of variables such as number and location of lesions, age at discovery, family anxiety, should be taken into consideration in the decision making. In consideration of the accelerated growth rate of the lesion, we recommend elective surgery because of the potential evolution in WT.[8-10]
In conclusion, NRs can be incidentally identified in a preclinical stage in the course of a sonographic exam done for other purposes. Most will regress, but when detected, serial abdominal US in a specialized center are mandatory.
This insures detection of malignant transformation at an early stage should it occur. We have defined this as a "wait and see" policy, which we advocate in such cases.

## References

1 Beckwith JB, Kiviat NB, Bonadio JF. Nephrogenic rests, nephroblastomatosis, and the pathogenesis of Wilms' tumor. Pediatr Pathol. 1990;10:1–36.

2 Hennigar RA, O'Shea PA, Grattan-Smith JD. Clinicopathologic features of nephrogenic rests and nephroblastomatosis. Adv Anat Pathol. 2001;8:276–289.

3 Bennington JL, Beckwith JB. Tumors of the kidney, renal pelvis, and ureter. In: Firminger HI, ed. Atlas of tumor pathology. Second series, Fascicle 12. Washington, DC: Armed Forces Institute of Pathology; 1975.

4 Bove KE, McAdams AJ. The nephroblastomatosis complex and its relationship to Wilms' tumor: a clinicopathotogic treatise. Perspect Pediatr Pathol. 1976;3:185–223.

5 Pianezza ML, Rubin S, Bass J, et al. Wilms' tumor at the Children's Hospital of Eastern Ontario: 1990–2001. Can J Urol. 2004;11: 2151–2156.

6 Breslow NE, Beckwith JB, Perlman EJ, et al. Age distributions, birth weights, nephrogenic rests, and heterogeneity in the pathogenesis of Wilms tumor. Pediatr Blood Cancer. 2006;47:260–267.

[7] Caiulo VA, Caiulo S, Gargasole C, Chiriacò G, Latini G, Cataldi L, Mele G. Ultrasound mass screening for congenital anomalies of the kidney and urinary tract. Pediatr Nephrol. 2012 Jun;27(6):949-53

[8] Fukuzawa R, Reeve AE. Molecular Pathology and Epidemiology of Nephrogenic Rests and Wilms Tumors. J Pediatr Hematol Oncol _ 2007; 29: 589-594

[9] Cooke A, Deshpande AV, La Hei ER, Kellie S, Arbuckle S, Cummins G. Ectopic nephrogenic rests in children: the clinicosurgical implications. Journal of Pediatric Surgery 2009; 44:13–16

[10] Antoniou D, Loukas I, Papadakis V. Ectopic nephrogenic rest in the inguinal canal in a 6-month-old girl and a review of published studies. Ann Saudi Med 2012; 32(6): 649-651