

## Childhood renal cell carcinoma

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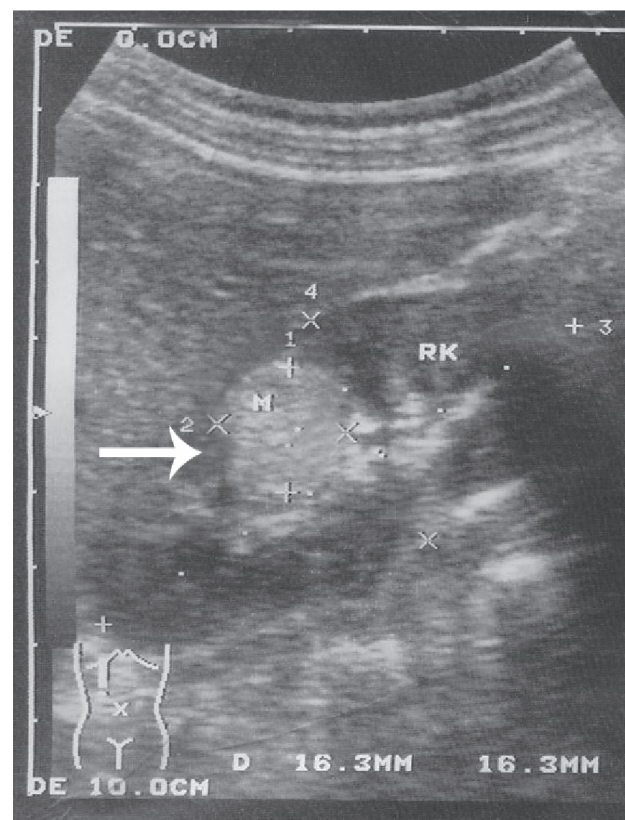
**R**enal cell carcinoma (RCC) in children is seldom found.<sup>1-8</sup> The incidence of this tumor in childhood is estimated to be 0.1-0.3% out of all neoplasms and 2-7% out of all malignant renal tumors.<sup>1,3-8</sup> The Third National Cancer Survey reported an incidence of only four cases of RCC per year compared to 117 per year of Wilms' tumor.<sup>1</sup>

The incidence of RCC has not been reported in Indonesia. This is the first case of childhood RCC found in our institution. To the best of our knowledge, this is the first report of childhood RCC in Indonesia.

### Report of the case

A 6.5-year-old boy presented with a 6-month history of intermittent right flank pain and hematuria. The patient had no family history of renal tumors or any syndromes associated with renal tumors. On physical examination, the patient was afebrile with blood pressure of 120/70 mmHg. No palpable masses or enlargement of regional lymph node were present. Laboratory results showed hemoglobin of 13.7 g/dl and abundant red blood cells/high power field on urinalysis. Blood urea and creatinine were within normal limits at 18 mg/dl and 0.75 mg/dl, respectively.

Ultrasound showed solid mass on the middle part of the right kidney measuring at 16x16 mm (**Figure 1**). Computed tomography (CT) scan revealed a solid mass on the middle area of the right kidney measuring at 20x20 mm with enhancement after contrast



**FIGURE 1.** ULTRASOUND SHOWS SOLID LESION ON MIDDLE POLE OF THE RIGHT KIDNEY.

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injection (Figure 2). No liver or lung metastases were found.

A radical nephrectomy of the right kidney was performed. Intra-operatively, there was an enlargement of the paraaortic lymph nodes and lymph node dissection was performed. The kidney was incised longitudinally and the tumor was found in the middle pole of the kidney with extension to the renal vein. Post-operatively, the patient's general condition was good and surgical wounds recovered without complications.

Macroscopically, the tumor was located on the cortex and medulla of the kidney measuring at 1 cm in greatest dimension with brittle and whitish appearance. Histologically, the tumor consisted of a group of large cells with clear and eosinophilic granular cytoplasm. There was also psammomatous calcification. Morphology of the tumor cells was polygonal, columnar, and cuboidal with pleomorphic nucleolar. The ureteral margin was negative for tumor and the Gerota fascia was intact. Histopathological examination showed high grade, clear, and granular cell which concludes renal cell carcinoma. There was an invasion to the renal vein and paraaortic lymph nodes (Figure 3).

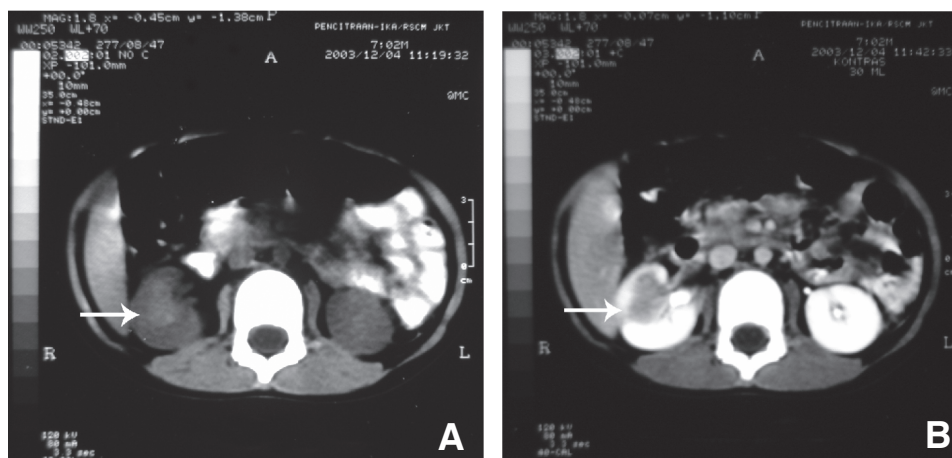
The tumor staging was T<sub>3b</sub>N<sub>1</sub>M<sub>0</sub>, high grade according to Tumor Node Metastasis (TNM) Union Internationale Contre le Cancer (UICC) 2002 staging system. No additional treatment was administered. The patient is alive and well with no clinical or radiographic evidence of tumor recurrence or metastasis until 27 months after initial presentation.

## Discussion

Renal cell carcinoma (RCC) is a malignancy thought to arise from epithelial cells of the renal tubule.<sup>1</sup> The mean age at presentation in children is approximately 8-10 years in most series,<sup>1,4</sup> the youngest patient reported was a child as young as 3 months of age.<sup>5</sup> RCC equally involves both sex without racial predilection.<sup>5</sup>

RCC has historically been classified according to cell types (clear, granular, spindle, or oncocytic) and growth patterns (acinar, papillary, or sarcomatoid). This classification gives little insight to the clinical behavior of the carcinoma.<sup>2</sup> A new histopathological classification proposed and accepted in the Heidelberg Workshop in 1997 is based on current genetic knowledge, correlated with morphological characteristics, and in line with the evolutive behaviour. Five types of carcinoma are distinguished according to this classification, i.e. conventional or common RCC, including clear and eosinophilic granular cell carcinoma, chromophobic RCC, papillary (or chromophilic) RCC, collecting-duct carcinoma with medullary carcinoma of kidney and unclassified RCC.<sup>11</sup> The cytologic grading was assigned according to the criteria proposed by Furhman *et al.*<sup>12</sup> This system uses nuclear grades based on size, irregularity of the membrane, and nucleolar prominence.

Cytogenetic studies have provided additional information and insight into genetic characterization of renal tumors. Conventional RCC (clear and/or



**FIGURE 2.** CONTRAST ENHANCED CT-SCAN OF ABDOMEN SHOWS SOLID LESION ON MIDDLE POLE OF THE RIGHT KIDNEY: (A) WITH ENHANCEMENT, (B) AFTER INJECTION OF THE CONTRAST.

granular cells) consists of familial RCC and tumor suppressor gene in the von Hippel-Lindau (VHL) disease, familial non-VHL RCC, and sporadic RCC.<sup>11</sup> In most cases, RCC occurs without any recognizable hereditary pattern. Several, rare, familial forms are characterized by autosomal dominant inheritance, young age at diagnosis, bilateral and multifocal tumors. The gene for VHL was identified at chromosome 3p25. This gene is a classic tumor-suppressor gene whose inactivation contributes to tumor development.<sup>2</sup> RCC with concurrent VHL disease in children has been reported by Parast *et al.*<sup>8</sup> Children with tuberous sclerosis (an autosomal dominant neurocutaneous disease) are also at risk for RCC with the onset of 20-30 years earlier than in the general population.<sup>9</sup>

The classic triad of flank pain, gross hematuria, and palpable mass is rare in children with RCC and found in only 6% of cases. The most common presentations in children are flank pain (50%), palpable mass (38%), and hematuria (38%).<sup>10</sup> In our patient, treatment was not immediately obtained which is revealed by intermittent hematuria and right flank pain for 6 months without prior medication. This condition is commonly found in developing countries.

Right radical nephrectomy was performed although a study by Indolfi *et al* showed that there was no significant difference between simple nephrectomy, radical nephrectomy, and survival rates.<sup>1</sup> Lymphadenectomy was performed in this case to determine the appropriate tumor staging, although the role of this procedure remains controversial. Lymphadenectomy may seem to be an overly aggressive procedure in children who remain most likely to have Wilms' tumor and undergo subsequent chemotherapy. However, it is generally impossible to distinguish RCC from Wilms' tumor on imaging. Thus, in a child without needle biopsy or frozen section confirmation of Wilms' tumor, an attempt to complete extirpation, including regional lymphadenectomy, may be prudent.<sup>4</sup>

Cytogenic morphology or microscopic features of clear cell/granular type showed polygonal or round cell with abundant cytoplasm. Granular cells have eosinophilic cytoplasm and abundant mitochondria. The larger tumors present variable amounts of necrosis, often with a pseudocystic aspect, hemorrhage or fibrosis, and calcifications. The extension of the tumor in the renal vein lumen or in the vena cava, with formation of neoplastic thrombus is characteris-

tic. The architectural pattern may be acinar, tubular (alveolar), cystic, or solid in a poor stroma, yet with a rich, delicate, and branching vasculature.<sup>2,11</sup> Most of these features are found in our patient.

No proper therapy has yet been defined for children with RCC. Surgery is the main treatment for localized and completely resected tumors. At present, the treatment of choice for RCC in children is radical nephrectomy.<sup>5</sup> RCC in children responds poorly to chemotherapy and radiotherapy. Biologic response modifiers, such as interleukin-2 and interferon have shown limited promise in adults with renal cell carcinoma, although it has not been demonstrated in children.<sup>5</sup>

The main prognostic factors seem to be staging and complete resection. Patients with tumor localized in the kidney have good prognosis compared to those with regional lymph node involvement or distant metastases.<sup>1</sup>

In summary, we can conclude that localized RCC in children continues to have good prognosis while managed by surgery alone. Therefore, clinical awareness of this disease in children with single symptom and sign, such as hematuria, flank pain, or palpable mass is very important and should be carefully managed since the classic triad is hardly ever to be found. Currently, localized, and completely resected RCC in children is best managed by radical nephrectomy while in the advanced stage, other modalities (chemotherapy, radiotherapy, and biologic response modifier) did not give any benefit and should be further investigated. Ideally, RCC should be further examined with cytogenetic studies to provide additional information of genetic characterization in renal tumors.

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