Case Report

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Renal cell carcinoma with MiTF/TFE3 translocation in children: Report of a case at the stage of lymph node involvement

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ABSTRACT

Renal cell carcinoma (RCC) is rare in children. Unlike nephroblastoma, however, it does not respond well to chemoradiotherapy. Its treatment is therefore based on surgical removal of the tumour. However, lymphadenectomy for RCC is controversial, and its prognosis is unclear. The authors report a case of RCC with MiTF/TFE3 translocation at the stage of lymph node involvement without metastasis in a boy of age 12, who was treated with radical nephrectomy and limited lymphadenectomy. This tumour constitutes a newly individualised entity in the World Health Organization's 2004 classification. Eighteen months after the operation, the patient was presented with no sign of recurrence. This case aids in showing that lymph node involvement in RCC with translocation in children is not associated with a poor prognosis and that lymphadenectomy during surgery for enlarged nephrectomy is essential.

Key words: Child, lymph node involvement, MiTF/TFE3 translocation, renal cell carcinoma

INTRODUCTION

Renal cell carcinoma (RCC) represents 2–3% of all cancers in adults. In children, it is rare. Indeed, only 0.3–1.3% of RCCs occur during childhood, representing 2–6% of renal tumours in children against 85–87% for nephroblastoma.[1-3] Unlike nephroblastoma, RCC is resistant to chemotherapy and radiotherapy.[4] Treatment occurs mainly through surgical removal of the tumour. Therefore, distinguishing between these two types of tumours before treatment is very important, but in practice, this differentiation is hard to accomplish. Moreover, the role of lymphadenectomy during RCC surgery is controversial,[4,5] and the prognosis of this type of cancer is not clear. The authors report a case of RCC with MiTF/TFE3 translocation at the stage of lymph node involvement. This type of tumour is a newly described entity in the World Health Organization's 2004 classification. Malouf *et al.* suggested that RCC translocations in adult patients are more aggressive than those in children and young adults.[6] Vascular endothelial growth factor-targeted agents appeared to demonstrate some efficacy in adult-onset translocation-associated metastatic RCCs.[7] North American series have shown that they are more frequent in female patients and particularly in patients of African-American ancestry.[8] But to our knowledge, no case has been reported in African countries.

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CASE REPORT

The subject is a 12-year-old boy with no particular medical history, who was presented with lower right abdominal pain. Pain duration was 11 months. The patient had a good general condition and was not febrile. Physical examination revealed a lumbar mass on patient's right side. An ultrasound scan of the urinary tract showed a renal tumour on patient's right side. A computed tomography of the abdomen and pelvis confirmed the existence of a right-side renal hypodense tumour, absorbing weakly the contrast product and measuring 67.6 × 53.1 mm. It also showed a gross paracava lymphadenopathy [Figure 1]. There was no invasion of perirenal fat, nor metastasis. The tumour was classified as T1b N1 M0 according to the TNM's 2002 classification of the International Union Against Cancer. A right radical nephrectomy was performed. The intraoperative abdominal exploration found, in addition to the renal tumour, a gross paracava lymphadenopathy on patient's right side. In addition to the nephrectomy, a lymphadenectomy limited to the interaortico-cava and retropara-cava areas was performed. Pathological examination of the surgical specimen revealed a macroscopic tumour nodule measuring 7.5 × 6 × 6 cm. Histological examination was suggestive of a clear

cell carcinoma with translocation, nest for necro-hemorrhagic alterations and affecting approximately 90% of the tumour's surface. The tumour was composed of cylindrical cells of slightly unequal size with a clear cytoplasm with acidophilic content. The nuclei were rounded or ovoid, irregular, and filled with a fine chromatin and sometimes prominent nucleoli. Few mitotic figures were observed, mainly in the acidophilus areas. These elements were arranged in lobules, or tubular structures, separated by a thin endocrine stroma [Figure 2]. The tumour reached the medullar without infiltration, avoiding and not affecting the excreto-urinary tract. There was a capsular infiltration with no signs of overrun. The excreto-urinary tract and the hilar and perirenal fat were not infiltrated. The hilar vessels were permeable, and the ureteral sections were normal. The tumour's immunohistochemical study showed an expression of TFE3. A cytogenetic analysis was not performed. The examination of the lymph node sample showed complete involvement. The tumour deposit in the lymph node measured 3.5 × 2.5 cm.

The immediate postoperative after-effects were uneventful. The patient received no adjuvant therapy. Eighteen months after the surgery, the patient showed no clinical sign of tumour recurrence, and a control abdominopelvic computed tomography revealed no tumour recurrence, nor a recurrence of adenopathy or metastasis.

DISCUSSION

RCC is very rare in children in whom the majority of renal tumours are nephroblastoma.[3,4] Indeed, it represents only 2–6% of renal tumours in children against 85–87% for nephroblastoma.[1-3,9,10] In literature, most publications on RCC in children are clinical cases or small series.[10-13] To our knowledge, this is the first case reported in Senegal. Argani *et al.*[8] reported that most US cases occurred in African-American individuals. However, Malouf *et al.*,[6] in France, did not detect this ethnic predominance. Indeed, in this study, 63% of patients were of Caucasian ancestry. It is this not clear at the moment, if an ethnical predisposition to develop translocation RCCs exists.

Although difficult to accomplish without the use of histology, pre-treatment diagnosis of RCC is desirable. Unlike nephroblastoma, known for its high radiochemical sensitivity, this tumour is characterised by its low- to non-responsiveness to radiotherapy and chemotherapy, even in metastatic cases.[14] Recognising the RCC before treatment discards the need for preoperative chemotherapy, which, in addition to its inefficiency, has many side effects and delays surgical treatment.[3,12] Chemotherapy has also been implicated as a predisposing factor for secondary development of RCC. Fifteen per cent of RCC translocations occur in patients who received cytotoxic chemotherapy during childhood.[15] In addition, the incidence of RCC increases with age. While the peak incidence of nephroblastoma is around age 3, RCC peaks between the ages of 9 and 15.[4,14,16] In the literature, there is no gender nor right- or left-side predominance.[4,14,17] In more than 50% of the cases, RCC is symptomatic at the moment of diagnosis.[14,17] Back pain (27 to 61.5%) and massive haematuria (30–77%) are the most commonly reported signs.[4,14,17,18] Haematuria is more frequent in RCC than in nephroblastoma. Paraneoplastic syndromes are rare.[18] Medical imaging has limited value in the differentiation of nephroblastoma and other renal tumours in children.[16] Tumour calcification and hyperdense tumour areas are more frequent in RCC than in nephroblastoma. The arteriography of RCC is more vascularised than that of nephroblastoma. Our case meets with most of these clinical features of RC.



Figure 1: Right renal cell carcinoma and adenopathy. This figure shows a right renal tumour (RT) and a large hilar paracave adenopathy (A)

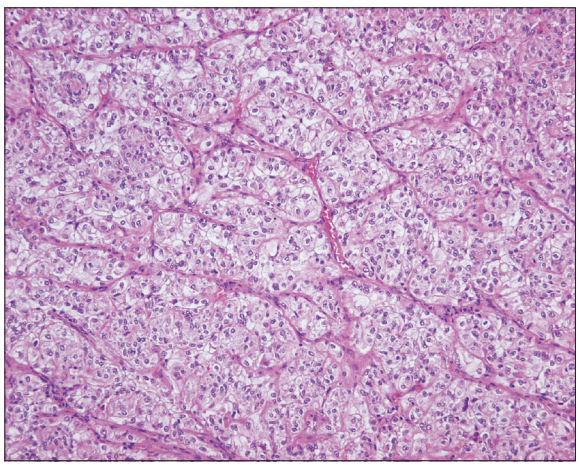


Figure 2: Histological section of the tumour

In spite of that we have not found any calcification or hyperdense tumour area with medical imaging. To date, the diagnostic aspects of RCC lack specificity, and the identification of this type of cancer without the use of histology remains difficult.

The prognosis of RCC is poorly known, yet it seems related to the tumour's stage. Our patient had a regional lymph node involvement. This invasion unanimously indicates a poor prognosis when found in adults. However, its prognostic value in children is controversial. According to several authors,[4,14] lymph node involvement in the absence of metastases is not necessarily a factor of poor prognosis. With these types of patients, adjuvant therapy is not recommended.[4] In agreement with these authors, we did not use it on our patient. However, this point of view is not shared by Indolfi *et al.*, who found that lymph node involvement was a factor of poor prognosis.[5] For this reason, other authors recommend lymphadenectomy and an adjuvant treatment. Unfortunately, these treatments have shown questionable effectiveness to date, in addition to numerous side effects.

Limited lymph node dissection was performed in our patient. In patients with N+M0, this dissection is recommended by several authors,[3,5,14] who indicate that it should be performed at the same time as the nephrectomy. If not, it is not necessary to perform it systematically later (after histological confirmation of RCC). However, if, at post-nephrectomy, images were to show any suspicious lymphadenopathy, a second dissection would be necessary.[4] In our patient, 18 months after surgery and without adjuvant therapy, no suspicion of lymphadenopathy was found upon examination and in images. This time, follow-up may seem short, but in literature, most recurrences or deaths were noted within 15 months after diagnosis.[19] However, RCC with MiTF/TFE3 translocation can show a late recurrence, as late as 30 years after diagnosis,[20] so follow-up in this case was too short to draw any definite conclusion.

RCC with MiTF/TFE3 translocation in children is a rare pathological entity, recently individualised in the World Health Organization's 2004 classification. Its prognosis is poorly known. This first case reported in our region shows that in this type of tumour, lymph node involvement is not always associated with poor prognosis, and that in these cases, lymph node dissection during enlarged nephrectomy is crucial.

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