

ЗАМІТКИ ІЗ ПРАКТИКИ

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Small Cell Variant of Renal Oncocytoma – a Case Report of Unusual Histopathologic Entity

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Abstract

Renal oncocytoma (RO) accounts for 3–7% of all renal cells tumors. It typically consists of large eosinophilic cells (oncocytes) with abundant cytoplasm, which constitute the crucial diagnostic feature. In 2001, the Czech authors first described an unusual small cell variant of RO and until now, only a few reports of such cases have been published. In the current article, the author presents an additional new case. 40-year old male with macroscopic hematuria as a clinical symptom was diagnosed to have solitary tumor in the upper third of the right kidney. He underwent a nephrectomy. On light microscopy, the tumor was predominantly composed of uniform small cells („oncoblasts“) with scant cytoplasm, hyperchromic nuclei and high nuclear-to-cytoplasmic ratio. In addition, it also contained characteristic oncocytes typical for oncocytoma. Tumor was strongly immunoreactive for EMA, sporadically positive for CK7 and negative for RCC antigen, vimentin, S100, WT1, chromogranin and synaptophysin. Proliferative activity did not exceed 1% and mitotic activity was virtually absent. No necrosis or aggressive growth features were found. The spectrum of histopathologic and immunohistochemical findings was consistent with a diagnosis of small cell variant of RO. The author focus on histopathological aspects and differential diagnostic pitfalls of this unique lesion.

Keywords: renal oncocytoma, oncocytes, „oncoblasts“.

Background

Renal oncocytoma (RO) is a distinct benign tumor accounting for approximately 3-7% of all renal cells neoplasms [1,2]. The occurrence is higher in men, with the peak incidence in the seventh decade of life [1-5]. Despite it is considered benign (ICD-O code 8290/0), it may occasionally manifest aggressive histopathologic features, such as extension to perinephric fat or vascular invasion [4-6]. Although this tumor shows highly variable microscopic appearance [1,4,5,7], in a common biopsy practice, it is usually easily recognizable in its „classic“ form. Histomorphologically, solid-nested, alveolar and tubular formations comprise the most characteristic patterns, but another microarchitecture (papillary, microcystic, acinic, trabecular, or adenomatoid) is also frequently seen [1,4,5,7]. Oncocytomas typically consist of large eosinophilic cells (oncocytes) with abundant granular cytoplasm filled with mitochondria. In the majority of cases, this cellular component forms the entire tumor tissue and constitutes the crucial diagnostic feature. Besides the classical oncocytes, a population of small neoplastic cells with scanty pale-pink cytoplasm, high nuclear/cytoplasmic ratio and dense hyperchromatic nuclei (so called „oncoblasts“) may also be present at various extent [1]. On occasion, some RO may predominantly consist of these „oncoblasts“ and for such cases, the term small cell variant of RO was proposed [8]. To date, only a few case reports and small series of the cases have been published in the literature [8-12]. Here, an additional new case with focus on histopathological aspects of lesion is reported.

Case presentation

Clinical Synopsis

40-year old male was sent by his regional urologist to the Department of Urology in the Faculty Hospital in Žilina for macroscopic hematuria lasting about 3 weeks. Physical investigation and other laboratory tests were unremarkable. Abdominal CT scan revealed an inhomogeneously enhancing tumor mass of 6 cm in the largest diameter, arising in the upper third of the right kidney. It was solid and relatively well demarcated. No regional lymphadenopathy was noted. The patient underwent a right-sided nephrectomy and biopsy specimen was sent for histopathologic examination. A presumptive clinical diagnosis was a tumor of the kidney with an uncertain biologic behaviour. The postoperative course of the patient was uneventful and he was discharged 6 days subsequent to surgery.

Pathology, Histomorphology and Immunohistochemistry

Grossly, the kidney revealed a solitary well-circumscribed intraparenchymatous tumor without apparent spreading into the hilus or perinephric adipose tissue. It measured 55x50x45 mm. It has yellowish-brown color and rubber consistency. An inconspicuous scar in the centre and focal hemorrhages were seen (Fig. 1). The tissue sections were routinely processed in paraffin blocks and stained with hematoxylin and eosin (H&E). An immunohistochemical analysis was also performed.

On light microscopy, the tumor was predominantly composed of uniform small cells resembling „oncoblasts“ with scant cytoplasm, hyperchromic nuclei and high nuclear-to-cytoplasmic ratio (Fig. 2). They were arranged mostly in solid-lobular fashion with occasional tubular and acinar formations. Subjectively, this cellular population constituted about 80 % of the total tumor volume. In addition to small cell component, the tumor also contained oncocytic cells with voluminous eosinophilic granular cytoplasm typical for oncocytoma. In some parts, areas of small cell population gradually merged with the nests of classic oncocytes. In other regions, there was a relatively well visible boundary between these two cellular populations (Fig. 3). Immunohistochemical study of tumor showed diffuse reactivity for EMA (clone E29, Dako) (Fig. 4) and only sporadic (cca 5%), but strong cytoplasmic expression of CK7 (clone OV-TL 12/30, Dako). All other markers we have investigated, i.e. RCC antigen (clone SPM314, Dako), vimentin (clone V9, Dako) (Fig. 5), protein S100 (clone 15E2E2, BioGenex), WT1 (clone 6F-H2, Dako), chromogranin A (clone LK2H10, BioGenex) and synaptophysin (clone Snp88, BioGenex) were negative. Proliferative activity (Ki-67, clone MM1, Leica) of the neoplastic cells did not exceed 1%. The mitotic activity was virtually absent throughout the tumor. No necrosis or aggressive growth features were found. The spectrum of histopathologic and immunohistochemical findings of tumor was consistent with a diagnosis of small cell variant of renal oncocytoma.

Discussion

Although oncocytoma is the most common benign epithelial tumor of the kidney [2], the cases with a preponderance of small cell („oncoblastic“) population are very rare. These cells as a



Figure 1. The kidney (post fixation in formalin) shows a well-circumscribed tumor mass

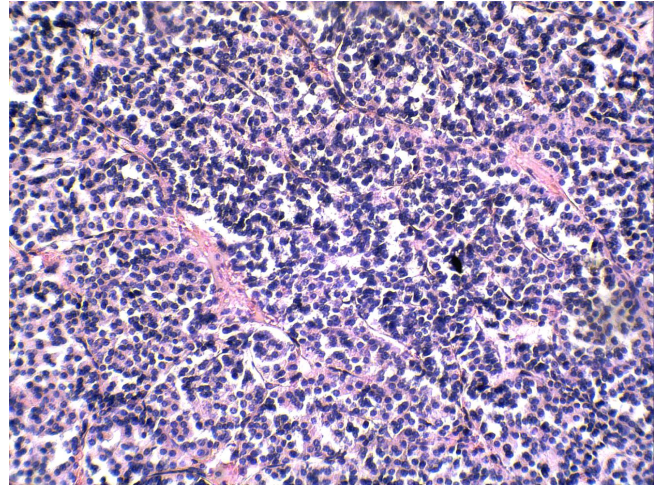


Figure 2. Detail on population of small neoplastic cells with dense hyperchromic nuclei and scant cytoplasm (H&E, magnification x400)

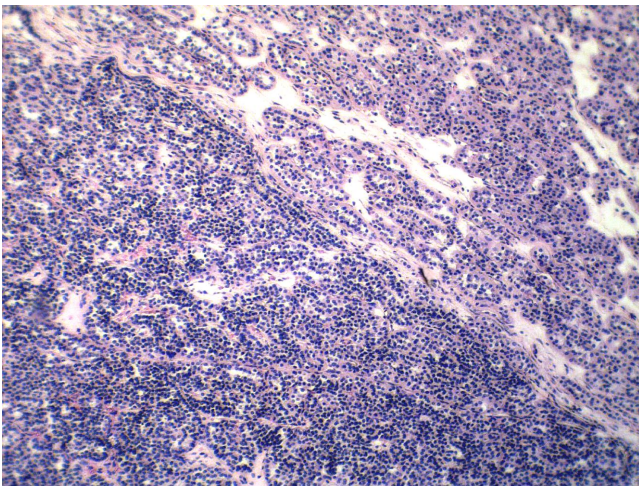


Figure 3. Visible boundary between the small cell („oncoblastic”) population (lower part) and classic eosinophilic oncocytes (upper part). (H&E, magnification x200)

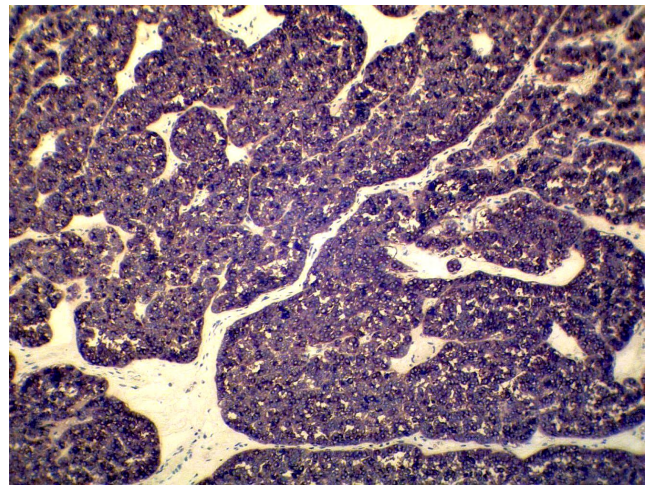


Figure 4. Diffuse strong immunoreactivity of tumor for EMA (magnification x200)

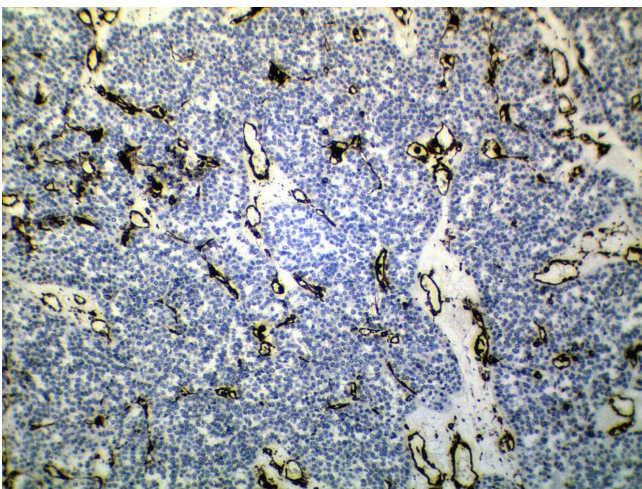


Figure 5. Lack of vimentin expression in tumor tissue. Blood capillaries are positive and may serve as internal control. (magnification x200)

minor tumor component in RO were previously observed by several investigators [4,5], but the small cell variant of RO as a distinct entity was first described by Czech authors [8] in 2001. They originally reported of 3 females with an unusual RO with a dominating small cell component and illustrated their histomorphologic, immunohistochemical and ultrastructural features. In contrast to previous papers the main difference was in that these organoid small cell areas had comprised a major cell population of tumors. Since then, other cases of this rare RO subtype have been published [9-12]. However, since the small „oncoblastic“ cells may be relatively frequently found in conventional ROs, there is no consensus, from what proportion of them should be the tumor defined as small cell variant of RO. In the present case, there was a marked preponderance of this neoplastic population (about 80%) and the tumor actually corresponded to the category of renal neoplasm that Hes et al. [8] have originally described. In their series, two of the three lesions consisted of more than 80% and remaining one of more than 50% of the small cell component. On the other hand, some papers [10,11] considered small cell variant of RO even those cases, in which the proportion of the small cells was below 50%. Therefore, it would be needed to exactly define and unify this

crucial histological diagnostic criterium (cut-off level).

Current knowledge on clinico-pathological characteristics of this uncommon tumor subtype is inadequate. In particular, there is not clear, as to whether an „oncoblastic“ population, as the name implies, represents an immature form of classic oncocytes. Even larger cohort study by Petersson et al. [10] did not add any further insight to the nature of these cells. Since the authors did not have any obvious evidence that „oncoblasts“ might be a developmental precursor to classic oncocytes, they proposed the more neutral term for them, the small oncocytic cells. They found a certain variation in the immunohistochemical profile between these two cell components, maybe indicating their histogenetic differences. Even Hes et al. [8] have previously demonstrated, the number of mitochondria was substantially lower in the small cells, compared to their classic counterpart. Although the histogenetic relationship between these two cell subtypes has not yet been explained, it rather seems, a small cell population does not have distinct biological behaviour. That means, this microscopic finding has probably no clinical significance and thus, it does not affect the patient management. On the other hand, it is much more important from the differential diagnostic aspects. An unusual extensive small cell component in RO may represent diagnostic pitfalls for certain kidney tumors with a preponderance of similar small cell population. Several entities should be considered, of which the well-differentiated neuroendocrine neoplasm (carcinoid), solid variant of papillary renal cell carcinoma, primitive neuroectodermal tumor, blastematos *Wilms'* tumor and metanephric adenoma are the most important. Besides basic histomorphology, diagnostic algorithm of these neoplasms strictly requires an immunohistochemistry. Each of the above-mentioned tumors produce certain molecular markers, which are crucial for diagnostics. Briefly, renal carcinoid typically express neuroendocrine markers (synaptophysin, chromogranin, CD56) and may be positive for CD99 [1]. *Wilms'* tumor is positive for WT1 and usually negative for chromogranin and synaptophysin [14]. Primitive neuroectodermal tumor of the kidney is immunoreactive for CD99 and negative for WT1 [15]. Metanephric adenoma is positive for WT1 and negative for EMA [16]. Compared to these neoplasias, RO neither express neuroendocrine markers, nor WT1 and CD99. Solid variant of papillary RCC is positive for EMA and alpha-methylacyl-CoA racemase and negative for WT1 [16]. The latter immunoprofile is also consistent with RO, however, papillary RCC is mostly positive for vimentin and RCC antigen, which are usually negative in RO [17]. It must be stressed, the immunoprofile results have to be interpreted comprehensively with the results of histomorphology and other investigation methods.

Conclusions

Small cell variant of RO is a unique tumor seen in a routine biopsy practice. Due to the rarity and hence the resulting diagnostic difficulties, the pathologists should be aware of this uncommon histopathologic entity to avoid a misdiagnosis of a malignancy. Especially in limited tissue specimens (core needle biopsy) containing exclusively a small cell population, distinguishing the tumor from another renal neoplasms may be very problematic. Such cases require complex differential diagnostic approach, in which a possible diagnosis of small cell variant of RO should be kept in mind.

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