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Case Report

Low-Grade Oncocytic Tumor of the Kidney: A Distinct Emerging Pathological Entity: Report of One Case and Discussion

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Abstract: Low-grade oncocytic tumor (LOT) of the kidney has recently emerged as a distinct diagnostic entity among eosinophilic renal neoplasms. Due to its notably slow clinical progression and "mismatch" immunoprofile (CK7+/CD117-), LOT must be differentiated from renal oncocytoma and chromophobe renal cell carcinoma (chRCC). In this report, we discuss the case of a 69-year-old male patient who presented with a solid enhancing mass in the right kidney, clinically suspected to be renal cell carcinoma. A right radical nephrectomy was performed, and histological and immunohistochemical features were consistent with LOT.

Keywords: Assessing, Barriers, Early Antenatal Booking, Reproductive Age, Rural Areas.

INTRODUCTION

Over the last ten years, the diagnostic landscape for eosinophilic renal neoplasms has undergone a major paradigm shift. In the past, renal oncocytic tumors were classified in a binary manner, with benign renal oncocytoma (RO) and malignant chromophobe renal cell carcinoma (chRCC) receiving the most relevant classification [1]. On the other hand, the identification of "grey-zone" tumors showed that tumors in grey-zone have morphological characteristics of both entities, and that at present a "new" clinicopathological unit is recognized as Low-grade Oncocytic Tumor (LOT) [2]. First described in detail by Trpkov *et al.,* in 2019, LOT is defined as a non-invasive, distal nephron-derived neoplasm [2, 3]. It is of paramount clinical significance because it occupies a unique place: it presents the low-grade cytologic hallmarks of an oncocytoma but also has widespread immunohistochemical expression of Cytokeratin 7 (CK7), a characteristic reserved for chRCC. This “immunophenotypic mismatch” frequently resulted in the early misdiagnosis of LOT as an eosinophilic form of chRCC and may have brought patients over-treatment and unwarranted oncological distress [4, 5]. Molecularly, LOT is distinguishable by its prevalence of somatic mutations of both the mTOR pathway (particularly MTOR, TSC1, and TSC2 genes) or CCND1 rearrangements which prevent it from being detected as the chromosomal losses (monosomies) of chRCC [6, 7]. Notwithstanding such genetic changes, LOT's clinical behavior is extraordinarily sedentary [5-3]. No evidence has been documented of aggressive progression, recurrence, or metastatic potential, nor in cases managed using nephron-sparing surgery to date in the literature [6]. The purpose of this article is to describe the specific morphological features, the critical function of the CK7+/CD117- immunoprofile, and the differential diagnostic criteria for the definitive diagnosis of LOT. Differentiating this entity from its more aggressive mimics could allow clinicians to offer the more accurate prognosis, and conservative management approach.

CASE REPORT

A 69-year-old man presented to the urology department after incidental detection of a renal mass on

routine abdominal ultrasound for benign prostatic hyperplasia (BPH). He had a significant past medical history of hypertension and type 2 diabetes; no family history of renal cell carcinoma (RCC) or genetic syndromes. Computed Tomography (CT) with contrast showed a 6.7 cm, well-circumscribed, solid exophytic mass located in the lower pole of the left kidney. The lesion exhibited homogeneous enhancement with no indication of internal calcifications, necrosis, or fat content (Figure 1).

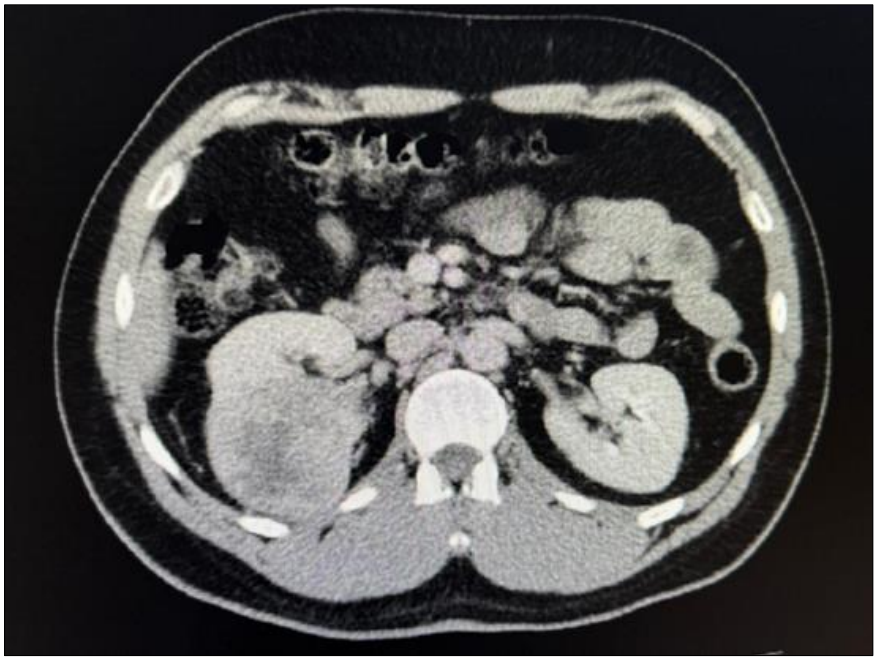

Figure 1: Contrast-enhanced CT scan revealing a 6.7 cm renal mass located at the lower pole of the left kidney

There was no lymphadenopathy or venous involvement. It was considered to be cT1aN0M0 at clinical stage. According to the localization of the tumor and the age of the patient, a partial nephrectomy was done. Macroscopic examination of the specimen identified a 6,7 cm, unencapsulated, but sharply defined tumor. The cut surface was solid and uniformly pinkish white, absent a central stellate scar or hemorrhaging. It was found on microscopic view that the tumor consisted of nests and cords of cells containing ample amounts of eosinophilic granular cytoplasm. The nuclei were highly uniform and round, with no significant irregular membranes or perinuclear halos as in chromophobe RCC. The characteristic morphology was focal perivascular edema in which the tumor cells seemed to "pull away" from the delicate capillary structure (Figure 2).

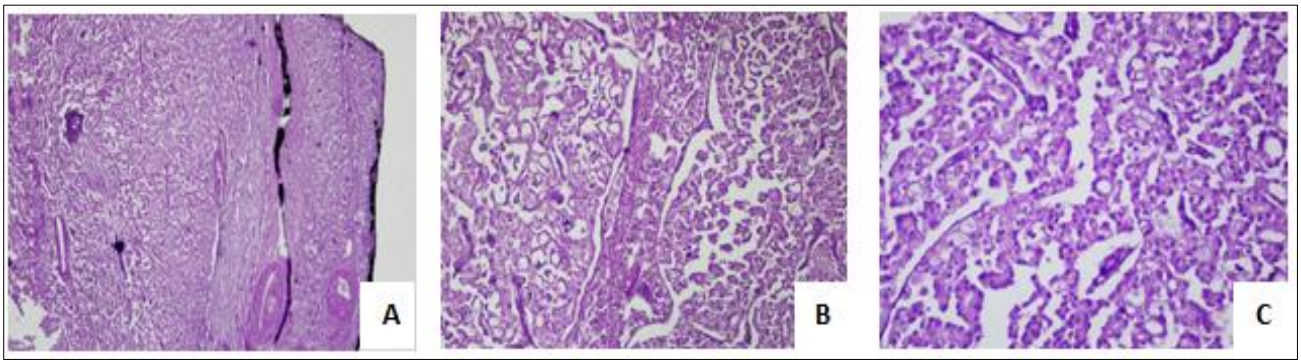

Figure 2: Histopathological examination of the tumor. Representative hematoxylin and eosin–stained sections are shown at magnifications of ×4 (A), ×10 (B), and ×40 (C).

A diagnostic immunohistochemical (IHC) stain was performed to establish the diagnosis. CK7 showed strong and diffuse membranous positivity (100% of cells) (Figure3A), as well as E-Cadherin (Figure 3D). CD117 (c-kit) was completely negative (Figure 3D) as well as CD10 (Figure 3C).

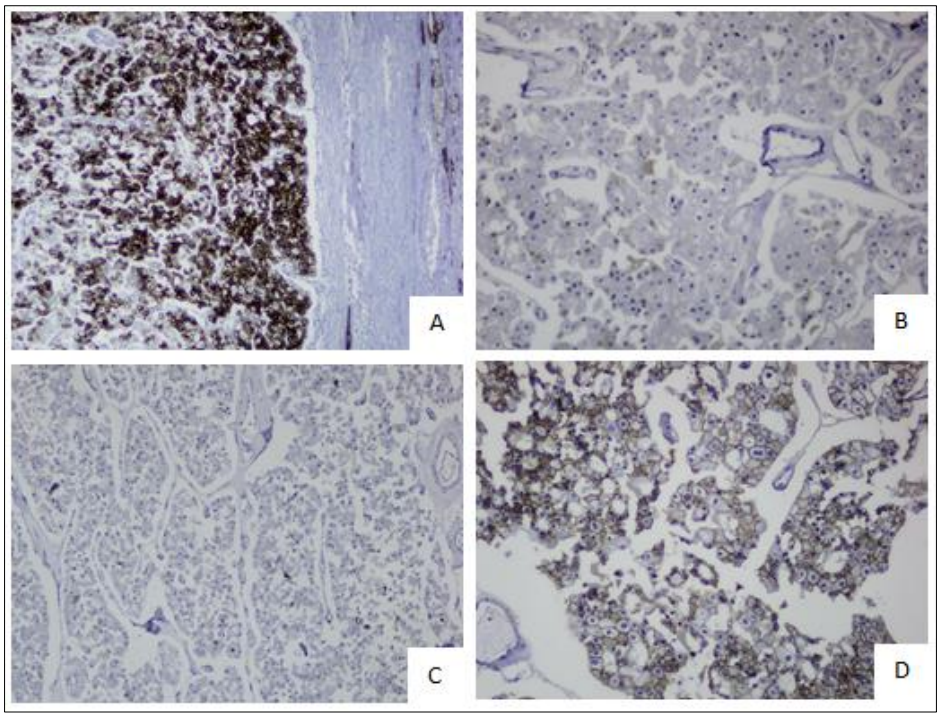

Figure 3: Immunohistochemical profile of the low-grade oncocytic tumor showing diffuse positivity for CK7 (A) and E-cadherin (D), with negative staining for CD117 (B) and CD10 (C).

On the morphology, and CK7+/CD117- "mismatch" immunoprofile, the definitive diagnosis of Low-grade Oncocytic Tumor (LOT) was made. The surgical margins of the patient were negative. At the 12-month follow-up he is asymptomatic and the patient does not present any local recurrence or metastatic disease on surveillance imaging.

DISCUSSION

Formal identification of Low-grade Oncocytic Tumor (LOT) as a specific diagnostic entity is a significant step forward for renal neoplasm classification [1, 2]**.** Historically eosinophilic (oncocytic) renal tumors have resulted in a diagnostic conundrum and an often-binary classification based on benign Renal Oncocytoma (RO) or malignant Chromophobe Renal Cell Carcinoma (chRCC) [1]**.** Our scenario of a 69-year-old male illustrates that although LOT shows morphological similarity to these entities, it has distinct clinicopathological and immunophenotypic characteristics which determine an indolent course [3]**.** Oncocytomas appear as homogeneous, well-defined renal masses on CT and MRI, but imaging cannot reliably distinguish them from renal cancer. Definitive diagnosis requires histopathology [9, 10]. Most notably, LOT is characterized microscopically by its remarkably homogeneous, low-grade cytology. LOT cells display round-to-oval nuclei with inconspicuous nucleoli compared to the "raisinoid" nuclei with characteristic perinuclear halos, and notable nuclear pleomorphism visible in chRCC [5]**.** The major challenge associated with LOT diagnosis is the reconciliation of its morphology with its immunohistochemical (IHC) signature. Historically, diffuse and strong membrane positivity for Cytokeratin 7 (CK7) has been indicative of chRCC. In contrast, CD117 expression is commonly found in both RO and chRCC. LOT does the opposite of this pattern by showing a "mismatch" profile: it has diffuse, strong CK7 positive expression, but is consistently negative for CD117 [4]**.** In the current situation, that IHC profile was vital. Considering the patient's age and the symptomatic features (hematuria and flank pain), a diagnosis of chRCC could have been entertained prematurely on CK7 alone. Nevertheless, the lack of CD117 expression and the presence of low-grade nuclear features is the pathognomonic evidence of LOT. Genomic characterizations of LOT have recently revealed a molecular basis for its indolent behavior. Though chRCC is characterized by several chromosomal aberrations (monosomies of 1, 2, 6, 10, 13, 17, and 21), LOT is remarkably stable at the chromosomal level. Several studies have shown somatic mutations to be prevalent in the mTOR signaling pathway involving the TSC1, TSC2, and MTOR genes [6, 7]**.** Additionally, some cases show CCND1 rearrangements as well. These results classify LOT in a new group of "mTOR-driven" renal neoplasms **[7]**. Being that these mutations don't lead to the genomic instability characteristic of high-grade carcinomas, the clinical growth appears benign. Most LOTs are incidentalomas and yet, our patient's hematuria and flank pain indicates that these tumors can mimic the classic triad of renal cell carcinoma from time to time. There have been no reported LOT cases demonstrating lymphovascular invasion, recurrences, or distant metastases, including in the setting of symptomatic presentation and tumor volume greater than 4 cm. The identification of LOT is important to prevent over-treatment. It is a reason to apply partial

nephrectomy even in elderly patients because of the negligible long-term oncological risk.

CONCLUSION

This case highlights the need to include LOT in the differential diagnosis of any eosinophilic renal mass. The diagnosis is based on the interpretation of low-grade oncocytic morphology, evidence of perivascular edema, and the definitive CK7+/CD117- immunoprofile. Differentiating LOT from more aggressive versions such as chRCC gives clinicians the ultimate reassurance to patients regarding the indolent nature of the disease and prevents them from facing any morbidity due to aggressive oncological interventions.

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Conflict of Interest: The authors declare no conflicts of interest regarding the publication of this paper.

Ethics Statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical approval was not required for this type of study according to institutional policy.

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