

**OCULAR METASTASIS OF EOSINOPHILIC RENAL CELL CARCINOMA: CASE REPORT AND LITERATURE REVIEW**

Falone Amoussou\*, Hajar Lemsyeh, Edith Ngbwa, Sara Naciri, Siham Lkhoyaali, Saber Boutayeb, Ibrahim El Ghissassi, H. M'rabti and H. Errihani

Medical Oncology Department at the National Institute of Oncology in Rabat.



\*Corresponding Author: Falone Amoussou

Medical Oncology Department at the National Institute of Oncology in Rabat.

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**ABSTRACT**

Low-grade eosinophilic cell renal cell carcinoma (CRIBGCE) is a recently described rare tumor of the kidney, not included in the WHO classification, as are orbito-choroidal metastases of renal cancer, which are rare and unusual. We report the case of a 68-year-old patient who presented with nausea and left lumbar pain. Investigations revealed a clear-cell renal cell carcinoma, which underwent surgery. The evolution was marked by the appearance of metastases, including a rare ocular metastasis.

**KEYWORDS:** carcinoma, kidney, eosinophilic cell, ocular metastasis.**INTRODUCTION**

Renal cancer is the 3rd most common urogenital cancer, after bladder and prostate cancer.<sup>[1,2]</sup> Worldwide, and particularly in Africa, its frequency varies between 8.5 and 13.54% of urogenital cancers.<sup>[3]</sup> It affects both men and women. In 2004<sup>[3]</sup>, the World Health Organization stated that renal cell carcinoma (RCC) is the most common kidney tumour, and classified it into several types, including the very rare eosinophilic carcinoma of the kidney, which accounts for around 4-6% of tumours. Metastases are possible in several organs, with a predilection for the lungs, lymphatics, bones, liver, adrenal glands and brain.<sup>[4]</sup> Metastatic orbital and choroidal localizations are rare and unusual, accounting for 3.2% and 2% according to Parnes and al and Shields CL and al respectively.<sup>[5,6]</sup> We present a case of ocular-choroidal metastases in a 68-year-old patient.

**CASE REPORT**

Our patient is 68 years old, hypertensive, well-monitored diabetic, with a history of prostatic adenocarcinoma treated with radio-hormone therapy and a surgically-treated dorsal melanoma. He presented with lumbar pain and nausea. A CT scan showed a voluminous left renal mass with thrombus of the renal vein coming into contact with the inferior vena cava and doubt about a nodule of peritoneal carcinosis. A nephrectomy was performed and the biopsy showed eosinophilic renal cell carcinoma: the lesion was classified as pT3aN0 with vascular embolism. The appearance of tibial pain prompted a bone scan, which showed tibial hyperfixation. Bone biopsy confirmed an eosinophilic carcinoma of renal origin.

Radiotherapy was performed on the bone lesion and the patient received 1st-line immunotherapy. The patient progressed after 4 months of treatment and was put on Carbozantinib in 2nd line. The 3-month CT scan showed mediastinal adenomegaly with bilateral pleural effusion, pulmonary micronodules and liver nodules, with bone scintigraphy showing bone progression. The patient was started on 3rd-line sunitinib. Within a month of starting treatment with Sutent, the patient presented with severe weight loss and chest pain, for which the chest X-ray showed bilateral diffuse micronodular alveolar interstitial syndrome with bronchial syndrome and minimal effusion in the left posterior cardio diaphragmatic cul de sac. Treatment was suspended and the patient received symptomatic treatment. The evolution was marked by a decrease in visual acuity in the same period, although the patient had no previous ophthalmological history. Cerebral CT to explore the symptomatology showed thickening of the posterior wall of the right eyeball, probably secondary to metastatic choroidal involvement. Fundus examination confirmed the diagnosis. The patient underwent radiotherapy to the eyeball.

**DISCUSSION**

Low-grade eosinophilic cell carcinoma of the kidney (CRIBGCE) is a recently described rare tumor of the kidney, not included in the WHO classification, and morphologically very similar to oncocytoma. It is little known to most pathologists and clinicians. Histopathologically, CRIBGCE is composed of oncocytic cells arranged in diffuse patches, without cell nests, which differentiates it from oncocytoma, and it

heterogeneously expresses cytokeratin 7 (CK7). Low-grade eosinophilic cell renal cell carcinoma (CRIBGCE) is an entity recently proposed by Prof. Argani (Department of Surgical Pathology, The Johns Hopkins Hospital, Baltimore, USA) in the context of eosinophilic cell renal tumours.<sup>[7]</sup> Described only once in the literature by Argani et al. in 2014, it remains unknown to pathologists. Although it has not been included in the 2016 WHO classification, it seems important to raise it as a differential diagnosis of oncocytoma, which it closely resembles.<sup>[8]</sup> These tumors must be distinguished because CRIBGCE is a malignant tumor unlike oncocytoma. Their histological profile is similar, but the architecture is denser and CK7 positivity more diffuse in CRIBGCE. Cytogenetically, renal oncocytoma frequently shows loss of chromosomes 1, 14 and Y and, in 25% of cases, a rearrangement of the CCND1 gene. To date, CRIBGCE has received little molecular attention.

All organs can be affected by metastases of kidney cancer, but the preferred sites are often the lung, bone, liver, brain, adrenal gland, skin and subcutaneous tissue.<sup>[9]</sup> Ocular metastases (OM) have become extremely rare since systemic treatment of certain cancers has prolonged patient survival. The most frequently implicated cancers are breast cancers, for which the frequency of ophthalmic localization is said by some authors to be as high as 30%, with a prevalence of 11,000 cases per year in the United States. Breast cancer is followed in order of frequency by bronchial cancer and metastatic adenocarcinoma of unknown origin.<sup>[9,10]</sup> Choroidal metastases of cancers in general represent the most common choroidal tumour, sometimes confused with choroidal melanoma.<sup>[9]</sup> In 8-30% of cases, they may precede the diagnosis of the primary cancer.<sup>[10]</sup> Renal cancer is responsible for 3.2% of orbital metastases and 2% of choroidal metastases, with a delay of between 10 months and 16 years after diagnosis.<sup>[11, 12]</sup> In a series of 3 cases, Kindermann et al<sup>[13]</sup> reported a delay of 15 months for palpebral metastases, 9 years for choroidal metastases and 15 years for orbital metastases. The early onset of our patient's metastases (around 2 months) may be explained by the histological type of our patient's primary tumour, which is an eosinophilic renal cell carcinoma. Most often, ocular localization appears before the discovery of the primary<sup>[14]</sup>, but in some cases, such as our patient's, it may appear much later or at the same time. The presence of numerous vessels in the choroid and the orbit, with lymphatic drainage for the latter, could explain the ophthalmological localization. Clinically, in the case of metastasis preceding the tumor, the primary site may not be found or may reveal itself late<sup>[15]</sup>, whereas in the case of metachronous metastasis, the patient, who has already been treated, may fail to specify such a history, or the practitioner may not take it into consideration at first. Symptoms in this case include a drop in visual acuity, which is very often unilateral, diplopia, exophthalmos, which is non-reducible and painful, or a palpebral mass. Diagnosis must be suspected at an early stage, in the presence of a drop in

visual acuity or any other ocular symptom. Diagnosis is confirmed by fundus examination, orbital ultrasound, CT scan, magnetic resonance imaging and, in our case, a fundus and CT scan. Local treatment is based on radiotherapy, which allows sufficient recovery of visual acuity in 72 to 94% of cases treated early. Early diagnosis and treatment of MO cancers helps to improve the quality of life of patients with metastasized cancer. The therapeutic management of a renal tumor depends on the nature of the tumor, its histological type, the progress of the cancer, the presence or absence of metastasis, and the patient's general condition. A treatment proposal is made after a RCP with all kidney cancer specialists. The general attitude is towards conservative treatment whenever possible. Surgery is often proposed if the cancer is localized or locally advanced, with a good prognosis. It may involve partial nephrectomy, multiple lumpectomies, or removal of the tumour with surveillance. If the disease is bilateral and affects both kidneys, then bilateral nephrectomy is required. Today, kidney tumours are diagnosed earlier and earlier, when the cancer is at an early stage and the tumours are still small. This contributes greatly to conservative management. In the presence of metastases, targeted therapy or immunotherapy can be administered, with or without surgery and radiotherapy depending on the case, if possible.

## CONCLUSION

Eosinophilic renal cell carcinoma is a very rare entity not included in the classification of renal tumors. Its diagnosis is purely based on immunohistochemistry. Most renal tumors are metastatic, but ocular metastases are very rare, especially in women. They can be functionally prognostic, while vital prognosis is highly threatened, with a very low five-year survival rate. The search for a primary tumour location in all choroidal lesions suspected of metastasis or tumour should therefore be a priority, in order to facilitate early management and, if possible, prolong survival.

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