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Case Report

Solitary Clear Cell Renal Cell Carcinoma Metastasis to the Eyelid: A Case Report

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Keywords
Eyelid tumor · Eye metastasis · Renal carcinoma

Abstract
Introduction: This study is a case of solitary clear cell renal cell carcinoma (ccRCC) eyelid metastasis in a 66-year-old man as the first sign of a primary tumor. ccRCC usually spreads to the lungs, mediastinum, bones, liver, and brain, while ocular metastases are rare. ***Case Presentation:*** Solitary metastasis presented as a solid mass in the central third of the upper eyelid, which has been growing for 3 weeks. Treatment included tumor removal and blepharoplasty. Histopathological examination showed metastasis of clear cell renal carcinoma. A thorough examination revealed a primary tumor on the lower pole of the right kidney. A right nephrectomy was performed, and histopathology showed ccRCC. Postoperative examinations showed no signs of local or systemic disease. Sunitinib malate was administered to the patient. ***Conclusion:*** The eyelid metastasis in this case was still solitary and had been discovered before the existence of the primary tumor was known. Ocular metastasis of renal carcinoma is a rare initial manifestation of the disease and therefore requires a multidisciplinary approach in the treatment of these patients.

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Introduction

Renal cell carcinoma usually spreads to the lungs, mediastinum, bones, liver, and brain, while eye metastases are rare. It is usually asymptomatic, and the most common form is clear cell renal cell carcinoma (ccRCC) [1, 2].

Basal cell carcinoma, squamous cell carcinoma, meibomian gland carcinoma, melanoma, metastases, Kaposi's sarcoma, and Merkel cell carcinoma are the most common tumors of the eyelid, but not all tumor forms on the eyelid are some of these tumors [3]. Eyelid metastases can present with different clinical features and can mimic different eyelid tumors. Metastatic ccRCC of the eyelid usually presents as a painless, rapidly growing mass that may appear as a capillary hemangioma due to marked vascularization [4]. Eyelid metastases of ccRCC can also present as a typical fast-growing chalazion unresponsive to topical therapy and recurring after routine incision and curettage [5]. Patients with systemic malignant tumors usually have multiple metastatic sites, ocular and non-ocular [6].

Case Report

This is the case of a 66-year-old man with a history of an enlarging mass on the upper eyelid of the right eye for the past 3 weeks. The primary ophthalmologist characterized the mass as a chalazion. His functions and habits were normal – no blood in the urine and no painful micturition. Past medical, family, and psychosocial history was normal. Ophthalmological status showed normal visual acuity and intraocular pressure in both eyes. Slit-lamp examination revealed a hard, pearl-like mass with a diameter of 7 × 10 mm in the central part of the upper eyelid margin of the right eye. The mass is red in color, covered with telangiectasias, with preserved eyelashes at the tumor site (Fig. 1). Initial nuclear cataract and normal fundus status were present. The findings of the left eye were unremarkable.

The patient underwent complete extirpation of the tumor tissue and blepharoplasty with stitches on the upper eyelid of the right eye. The pathohistological findings showed the following: material covered with partially ulcerated epidermis, made of trabecularly arranged, polymorphous, polygonal cells with clear cytoplasm. The tumor is well separated from the surrounding tissue, the tumor cells are mitotically active, and there are pathological mitoses. No necrosis was found. Histology and immunohistochemical expression indicate metastasis, most likely kidney cancer. The tumor does not reach the edges of the skin sample in the examined histological sections (Fig. 2).

After obtaining the pathohistological findings, we performed a total physical examination to determine the origin of the primary tumor. Complete blood count was normal, except for slightly elevated leukocytes (12.7×10^9/L) and segmented neutrophils (9.0×10^9/L). Chemistry laboratory findings showed elevated values of bilirubin (37.8 μmol/L), blood glucose (7.7 mmol/L), and C-reactive protein (16.3 mg/L). Urine tests, including microscopic examination, were normal.

Abdominal ultrasound revealed an expansive formation, located in the area of the lower pole of the right kidney, with the largest diameter of about 7.5 cm, which mostly indicates a neoplasm. A fatty liver was diagnosed without focal liver pathology, while the findings of the left kidney, pancreas, bile ducts, and spleen were normal.

Abdominal computed tomography with intravenous contrast confirmed an expansive mass in the lower pole of the right kidney in transverse layers, with firm, undulating borders, 7.3 × 5.6 cm in diameter, with areas of necrosis and inhomogeneous contrast enhancement suggestive of a primary neoplastic process. The left kidney was unremarkable. There were no enlarged lymph nodes, ascites, and metastases (Fig. 3).

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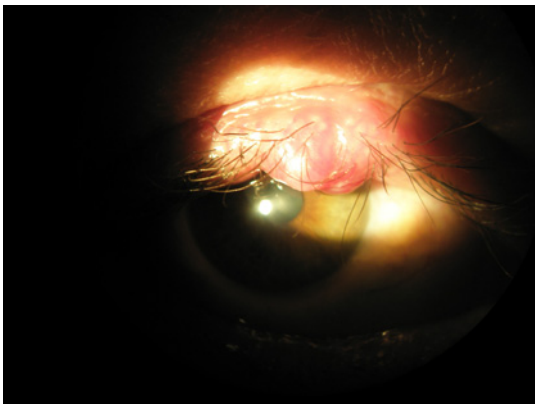

Fig. 1. Biomicroscopic view of a mass measuring 7 × 10 mm, with telangiectasias and preserved eyelashes.

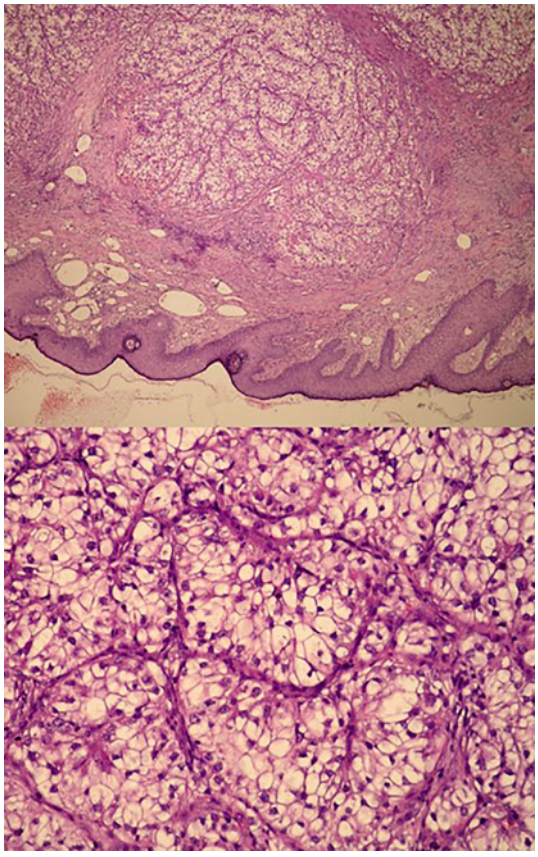

Fig. 2. Pathohistological finding of the eyelid tumor: material sheathed with partially ulcerated epidermis, made of trabecularly arranged, polymorphic, polygonal cells with clear cytoplasm. Tumor was well divided from the surrounding tissue, with pathologic mitosis and mitotic active tumor cells and without necrosis. The upper part is ×40 and the lower is ×200 magnification.

After examining the aforementioned findings, the patient was transferred to the Department of Urology. A total nephrectomy of the right kidney was performed. The pathohistological findings showed a kidney with dimensions of 13 × 5 × 6 cm, with a well-limited tumor with a diameter of 6 cm in the lower pole, gray in color, which macroscopically does not penetrate the capsule and with up to 20% necrosis (Fig. 4). There were no pathohistological findings on the adrenal gland, blood vessels, and ureter. Histologically, this finding, according to the WHO 2004 classification, indicates ccRCC of nuclear grade 3 [7]. The tumor was classified as stage T1bN0M1, according to the TNM cancer staging system [8].

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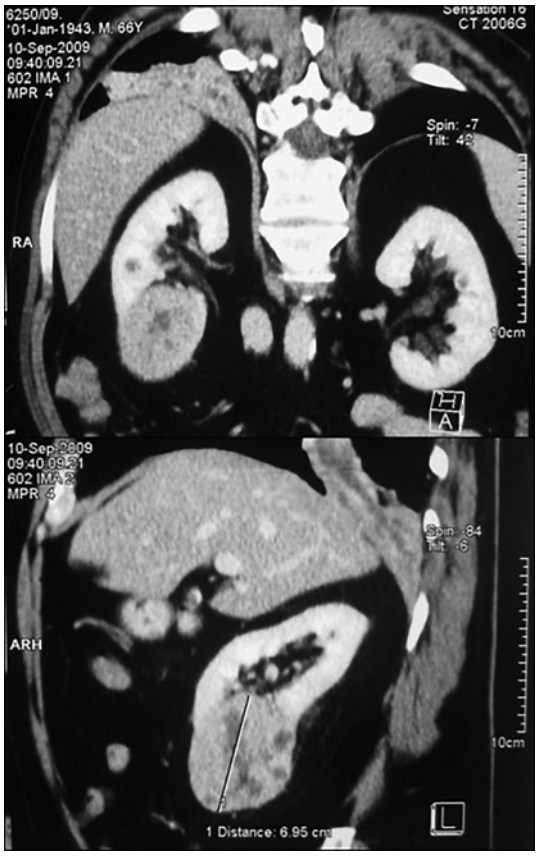

Fig. 3. Abdominal CT shows a confirmed, expansive mass at the lower pole of the right kidney.

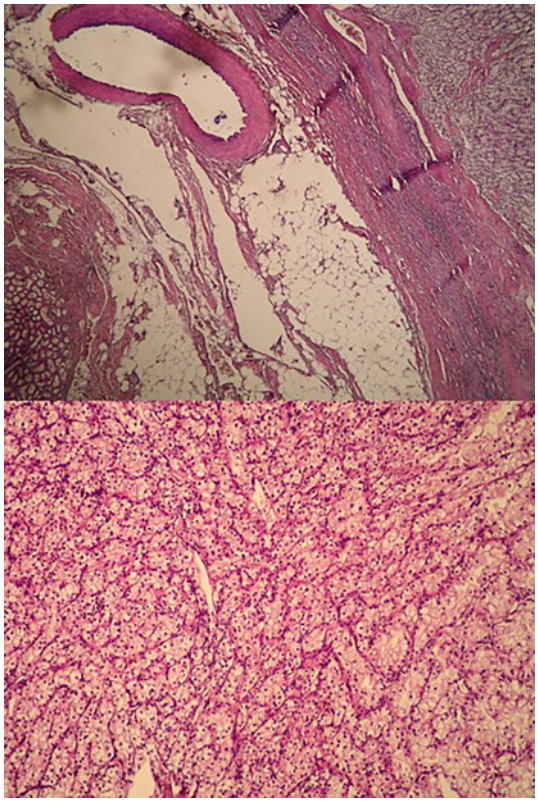

Fig. 4. Pathohistological findings were showing a kidney, measuring 13 × 5 × 6 cm, with well-bordered tumor in its lower pole, gray colored, with 6 cm in diameter, that macroscopically did not penetrate the capsule and with up to 20% of necroses. The upper part of the picture shows ×40 magnification, and the lower part shows magnification of ×100.

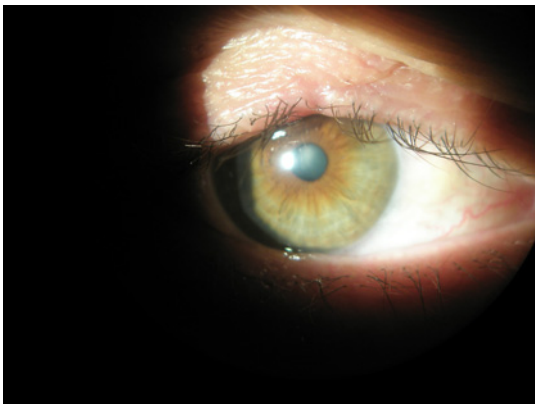

Fig. 5. There are no signs of local tumor recurrence or new metastases at the eye, as seen at 6 months after tumor excision.

One month after the nephrectomy, the patient was referred to an oncologist for the administration of the drug sunitinib malate, which inhibits receptor tyrosine kinase. The recommended dose of sunitinib malate was 50 mg orally daily for 4 weeks, followed by 2 weeks off treatment (4/2 schedule). Adverse and unanticipated events were not reported.

Six months after tumor excision, the patient was tolerating the therapy well. There are no signs of local tumor recurrence or new metastases in the eye or anywhere else in the body (Fig. 5).

A timeline summarizing the main events of this case is that the patient underwent total extirpation of the eyelid tumor the day after the ophthalmological examination. The pathohistological findings showed metastases of renal carcinoma, and the primary tumor was confirmed by ultrasound and CT. The patient underwent total nephrectomy and received sunitinib malate as adjuvant therapy. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000537860).

Discussion

Based on our previous literature search in PubMed, this is only the third case published so far with a solitary metastasis of primary ccRCC on the eyelid, as the first sign of the disease, while primary malignant tumor is still unknown [9, 10]. On the other hand, individual cases of ccRCC metastases in the eyelid have been recorded in patients with an already known primary tumor, usually after nephrectomy, as a sign of disease recurrence, as well as in patients who already have accompanying metastases in other locations [1, 6, 11, 12]. Two cases were recorded in which chalazion was primarily diagnosed, similar to our patient, which emphasizes the importance of a good ophthalmological examination [1, 5].

ccRCC is the most common type of renal carcinoma in adults, accounting for approximately 80% of cases [13]. It is also known to be the deadliest of all genitourinary tumors. Our patient had no risk factors for the development of ccRCC.

Initial treatment is usually radical or partial nephrectomy and remains the mainstay of curative treatment [14]. When the tumor is confined to the renal parenchyma, the 5-year survival rate is 60–70%, but this is lowered considerably where metastases have spread. Treatment of metastatic renal cell carcinoma with sunitinib malate has been shown to increase progression-free survival to 11 months versus 5 months with baseline interferon alpha treatment and to improve overall survival and quality of life (QoL) [15]. It is resistant to radiation therapy and chemotherapy, although some cases respond to immunotherapy. Current

treatment options for metastatic ccRCC are therefore limited and there is a need to identify novel and effective therapies. The results of new studies demonstrate the efficacy and manageable adverse-event profile of sunitinib malate as a single agent in second-line therapy for patients with cytokine-refractory metastatic ccRCC [16–19]. Mollica et al. performed a meta-analysis to evaluate the role of ECOG performance status (PS) in terms of survival in patients with ECOG PS 0 or ECOG PS 1 treated with immunotherapy, alone or in combination with other anticancer drugs. The pooled results showed that immunotherapy, either alone or in combination, reduces the risk of death or progression in both ECOG PS 0 and 1 populations [20].

Prognostic and predictive biomarkers for immunotherapy of patients with advanced cancer are extremely poor, and today it is based on clinical and laboratory factors such as hypercalcemia, neutrophil count, or Karnofsky PS. Programmed cell death ligand 1 (PDL1) expression level is a negative prognostic factor with an unclear predictive role for ICI response in carcinoma patients, while tumor mutational load and gene expression profile are promising predictors of ICI response [21]. Research is underway to identify additional prognostic and predictive biomarkers, which, however, are still far from validation and approval.

Analysis of the role of novel systemic treatments should include assessment of QoL, which is important for treatment evaluation benefits/risks, but is often not included among primary/secondary endpoints in clinical trials of renal cell carcinoma. There is still a large percentage of studies without QoL among the endpoints, and the correlation between treatment toxicity and QoL is of critical importance for clinical decision-making [22].

Metastasis on the eyelid in this case is still supposed to be solitary and has been detected prior of knowing the existence of the primary renal tumor, which could contribute to its better treatment. It is crucial to remember that not every red swelling of the eyelid is a chalazion. A careful examination of the patient is an essential element of any diagnosis and in some cases can lead to a complete cure of malignant diseases.

Statement of Ethics

This study protocol was reviewed and the need for approval was waived by Ethics Committee of Sestre milosrdnice University Hospital Center. Written informed consent was obtained from the participant for publication of the details of medical case and accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study conception and design: O.Z., I.K., and R.I.; data collection: M.M.R. and I.T.; and draft manuscript preparation: A.K. and Z.V. All authors reviewed the results and approved the final version of the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author A.K. upon reasonable request.

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