Ocular adnexal metastases from renal cell carcinoma: An update and comprehensive literature review

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Abstract:

PURPOSE: The purpose of this study was to review the clinical presentation, systemic work-up, and outcomes of all previously reported ocular adnexal (OA) metastases from renal cell carcinoma (RCC).

METHODS: This was a literature review. PubMed and Google Scholar databases were searched for all well-documented cases of OA metastases from RCC.

RESULTS: Final analysis identified 44 patients with either biopsy-confirmed (41/44, 93%) or treatment response-documented (3/44, 6%) OA metastases from RCC. Thirty-four (77%) patients were male. The median age was 60 years (mean: 60, range: 22–87 years). The most common presenting signs were proptosis (19/44, 43%) and OA mass (14/44, 32%). Metastases most frequently involved the orbital bones (10/44, 23%) and adjacent extraconal fat, extending from the sinonasal tract in 7/10 (70%) of these cases. OA metastases were initial manifestation of RCC in 18/44 (41%) patients. At the time of primary tumor diagnosis, 22 of 30 (73%) patients had American Joint Committee on Cancer Stage IV disease with metastases to 2 or more sites in 13 (57%) patients. Seventeen of 42 (40%) patients underwent local therapy only, which most commonly included excision/exenteration with margin control (10/17, 59%). Twenty-five of 42 (60%) patients had systemic therapy, which included biologic agents and chemotherapy. The absolute 5-year survival rate was 66% with significantly improved survival in patients reported after 2006 (92% vs. 42%, $P = 0.04$) and in those with isolated OA metastases (100% vs. 27%, $P = 0.02$) at 30 months.

CONCLUSION: Although RCC metastases to OA occur in a setting of advanced disease, the recent advances in diagnostic modalities and targeted therapies resulted in improved survival.

Keywords:

Ocular adnexal metastases, ocular renal cell carcinoma, renal cell carcinoma eye, renal cell carcinoma ocular adnexal, renal cell carcinoma orbit

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Introduction

Renal cell carcinoma (RCC) is one of the most common cancers affecting both sexes in the United States.[1] According to the Review of the Surveillance, Epidemiology, and End Results (SEER) cancer registry, the overall incidence and mortality rates of RCC in the United States have steadily increased between 1992 and 2015.[2] The rise in RCC incidence has been attributed to an increase in the prevalence of RCC risk factors, such as smoking, obesity, and hypertension,[3,4] and to the higher rate of incidental detection of RCC driven by the increasing availability of the imaging studies. In recent years, however, the incidence rates of RCC have stabilized, and the mortality rates have decreased.[2] It is speculated that this decline in mortality is related to earlier detection and improved therapies for metastatic RCC.[2]

Approximately one-third of patients with RCC have metastatic disease at the time of diagnosis, with lung, bones, liver, and brain being the most commonly affected.[5,6] Ocular adnexal (OA) and intraocular involvement by RCC is infrequent.[7] To our knowledge, the most recent largest published systematic review by Shome *et al*. in 2008 included 33 patients with OA RCC metastases.[8] In light of changes in the

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epidemiology and treatment approaches to RCC over the last 15 years,[9-11] herein, we provide an updated comprehensive review of the published literature on the RCC metastatic to the OA to characterize its clinical presentation, systemic manifestations, diagnosis, and management.

Methods

Institutional review board approval was waived for this literature review. This study adhered to the ethical principles outlined in the Declaration of Helsinki as amended in 2013 and was Health Insurance Portability and Accountability Act of 1996 (HIPAA) compliant.

Literature search

A comprehensive review of the literature was performed with a systematic search of the PubMed and Google Scholar databases for all articles published between January 1957 and January 2021 using the following key terms: "renal cell carcinoma ocular adnexal metastases" or "renal cell carcinoma orbital metastases" or "orbital metastases kidney" or "renal cell carcinoma sinonasal metastases" or "renal cell carcinoma lacrimal gland metastases" or "renal cell carcinoma ocular muscle metastases" or "renal cell carcinoma eyelid" or "renal cell carcinoma conjunctival metastases" or "renal cell carcinoma eye" or "renal cell carcinoma ocular adnexa" or "renal cell carcinoma orbit" or "renal cell carcinoma sinonasal" or "renal cell carcinoma lacrimal gland" or "renal cell carcinoma ocular muscle" or "renal cell carcinoma eyelid" or "renal cell carcinoma conjunctiva." Additional articles were found by reference searching. Duplicates were removed. All articles published in all languages that met the eligibility criteria were selected for further analysis.

Eligibility criteria

To be included for detailed analysis, only peer-reviewed case studies and case series were included that documented OA (conjunctiva, eyelid, orbital fat, extraocular muscle, lacrimal gland, and orbital bone) biopsy-confirmed metastases from RCC. If an OA biopsy was not performed, documentation of response to systemic therapy for metastatic RCC was required for inclusion in this study. Isolated intraocular RCC metastases were excluded.

Data collection

All articles that met the inclusion criteria were reviewed for the following data: patient demographics (age at diagnosis of OA metastases, sex, and ethnicity), presenting ocular symptoms, eye laterality, duration of symptoms, distribution of OA involvement by metastasis, history of RCC, histopathological type of RCC, presence of other synchronous metastases, American Joint Committee on Cancer (AJCC) tumor-node-metastasis system staging at the time of RCC diagnosis,[12] diagnostic modalities, management of OA and systemic disease, ophthalmic and systemic outcomes, and follow-up period.

Statistical analysis

All analysis was performed using RStudio Desktop 1.2.5033 (RStudio Inc., Boston, MA, USA). Significance testing was performed on Kaplan–Meier survival distributions using the log-rank test. $P \leq 0.05$ was considered statistically significant.

Results

Patient demographics and presenting features

Review of the literature identified 44 patients[8,13-51] who met the inclusion criteria for this study. Table 1 summarizes the demographics and presenting characteristics. Patients with OA metastases from RCC presented at an average age of 60 years (median: 60, range: 22–87). Thirty-four (77%)

Table 1: Ocular adnexal metastases from renal cell carcinoma: Demographics and presenting characteristics

Variables	*n* (%)
Age (years)	
Mean	60
Median	60
Range	22-87
Sex	
Male	34/44 (77)
Female	10/44 (23)
Ethnicity	
Caucasian	8/12 (67)
African American	1/12 (8)
Hispanic	1/12 (8)
Asian	1/12 (8)
Other	1/12 (8)
Presenting ocular symptoms	
Proptosis	19/44 (43)
Mass	14/44 (32)
Diplopia	12/44 (27)
Pain/discomfort	8/44 (18)
Vision change	8/44 (18)
Swelling/chemosis	4/44 (9)
Other*	16/44 (36)
Laterality	
Right eye	22/44 (50)
Left eye	19/44 (43)
Bilateral	3/44 (7)
Tissue primarily involved	
Conjunctiva	8/44 (18)
Orbital space not otherwise specified	7/44 (16)
Muscle	6/44 (14)
Orbital bone†	10/44 (23)
Intraconal orbital fat	3/44 (7)
Extraconal orbital fat	3/44 (7)
Lacrimal gland	1/44 (2)
OA focality	
Unifocal	33/40 (83)
Multifocal	7/40 (18)
History of RCC at the time of diagnosis	
Yes	26/44 (59)
No	18/44 (41)

*Epistaxis, nasal obstruction/congestion, redness, photophobia, epiphora, ptosis, headache, †In 7 patients, orbital involvement occurred as a result of extension from the sinonasal tract. RCC: Renal cell carcinoma, OA: Ocular adnexal

patients were male. Of the 12 patients with documented ethnicity, most were Caucasian (8/12, 67%). The most common presenting ocular symptoms were proptosis (19/44, 43%), an OA mass (14/44, 32%), and diplopia (12/44, 27%). The average duration of ocular symptoms was 3 months (median: 3, range: 0.3–8). In most patients, the OA metastases were unilateral (41/44, 93%) and unifocal (33/40, 83%). Most OA metastases were centered in the orbital bone with extension into the adjacent orbital fat, accounting for 10 of 44 (23%) cases. Bony orbital involvement generally occurred as a result of extension of metastasis from the sinonasal tract in 7 of these 10 (70%) patients. Other frequently involved OA tissues were conjunctiva (8/44, 18%), muscle (6/44, 14%), intraconal orbital fat (3/44, 7%), extraconal orbital fat (3/44, 7%), lacrimal gland (1/44, 2%), or orbital space not otherwise specified (7/44, 16%).

Imaging

The detailed information on diagnostic work-up is documented in Table 2. Orbital imaging was performed in 34 of 44 (77%) patients. The most common diagnostic study for evaluation of orbital disease was computed tomography (CT) scan (17/34, 50%). Multimodal imaging was performed in 10 of 34 (29%) patients, which included a combination of plain X-ray, ultrasound, CT/CT angiography (CTA), and magnetic resonance imaging (MRI). CT of the abdomen was the most common systemic imaging study performed (15/24, 63%) followed by multimodal imaging (5/24, 21%), which included a combination of plain X-ray/pyelogram, ultrasound, CT/CTA, or MRI.

Table 2: Ocular adnexal metastases from renal cell carcinoma: Diagnostic work-up

Variables	*n* (%)
OA metastasis work-up	
OA biopsy	
Incisional/fine-needle aspiration*	26/41 (63)
Excisional	15/41 (37)
Ancillary studies on biopsied tissue	
Immunohistochemical stains**	18/25 (72)
None	7/25 (28)
Orbital imaging	
CT	17/34 (50)
Multimodal†	10/34 (29)
MRI	3/34 (9)
X-ray	2/34 (6)
Ultrasound	2/34 (6)
Systemic work-up	
RCC biopsy, primary site	
Incisional biopsy	5/14 (36)
Nephrectomy	9/14 (64)
Systemic imaging	
CT	15/24 (63)
Multimodal‡	5/24 (21)
Other§	3/24 (13)
MRI	1/24 (4)

*Immunohistochemical stains including positive for any of the following: CD10, vimentin, cytokeratin (CK7/18/20), CAM 5.2, AE1/AE3, EMA, Ki67, CAIX, PAX8, CD34, CD68, bh11, CEA, anti-AFP, smarcb1/ini1, cyclin D1, RCC antigen, †Combination of imaging with plain X-ray, CT/CT angiogram, MRI or ultrasound, ‡Combination of imaging with CT/CT angiogram, MRI or ultrasound, §Pyelogram. RCC: Renal cell carcinoma, OA: Ocular adnexal, CT: Computed tomography, MRI: Magnetic resonance imaging, CEA: Carcinoembryonic antigen, AFP: Alpha-fetoprotein, EMA: Epithelial membrane antigen, CAIX: Carbonic anhydrase IX, PAX8: Paired-box gene 8, CK8: cytokeratin 8

Pathologic diagnosis and histopathologic characteristics of renal cell carcinoma

OA biopsy documenting metastatic RCC was performed in 41 of 44 (93%) patients, which was incisional in 26/41 (63%) and excisional in 15/41 (37%) [Table 2]. Three of 41 (7%) patients were empirically diagnosed with metastatic OA RCC based on clinical and imaging findings and had a documented response to systemic therapy for metastatic RCC. Ancillary immunohistochemical studies on tissue were performed in 18/25 (72%) cases and included cytokeratins (6/25, 24%), CD10 (8/25, 32%), vimentin (7/25, 28%), epithelial membrane antigen (EMA) (3/25, 12%), carbonic anhydrase IX (CAIX) (2/25, 8%), paired-box gene 8 (PAX8) (2/25, 8%), and RCC antigen (RCC) (1/25, 4%). In 14 patients with documented pathology data on primary RCC, the diagnosis was established by incisional biopsy in 5/14 (36%) and by nephrectomy in 9/14 (64%). Of 22 patients with available information, the most common RCC type was clear cell (18/22, 82%), followed by papillary (2/22, 9%) and medullary (2/22, 9%) [Table 3].

Systemic disease characteristics

Table 3 summarizes the systemic characteristics of RCC. The AJCC 8th edition staging system for kidney tumors

Table 3: Ocular adnexal metastases from renal cell carcinoma: Systemic disease characteristics

Variable	*n* (%)
Type of renal cell carcinoma	
Clear cell	18/22 (82)
Papillary	2/22 (9)
Medullary	2/22 (9)
AJCC staging at the time of primary tumor diagnosis*	
Stage I (T1, N0, M0)	3/30 (10)
Stage II (T2, N0, M0)	2/30 (7)
Stage III (T1/T2/T3, N1, M0) or (T3, N0, M0)	3/30 (10)
Stage IV (T4, any N, M0) or (any T, any N, M1)	22/30 (73)
Time (months) to ocular metastases from diagnosis or nephrectomy of RCC	
Mean, median, range	79.5 (78, 1-180)
Other synchronous metastases sites	
Multifocal†	13/23 (57)
Lung	5/23 (22)
Adrenal gland	1/23 (4)
Vertebrae	1/23 (4)
Pelvic bones	1/23 (4)
Mediastinum	1/23 (4)
Other‡	1/23 (4)

*RCC TNM staging, AJCC 8th edition.[12] †Two or more sites from brain, adrenal gland, lung, vertebrae, pelvic bones, mediastinum, liver, skin, breast, diaphragm, oral cavity, ‡Perihilar region. RCC: Renal cell carcinoma, AJCC: American Joint Committee on Cancer, TNM: Tumor-node-metastasis

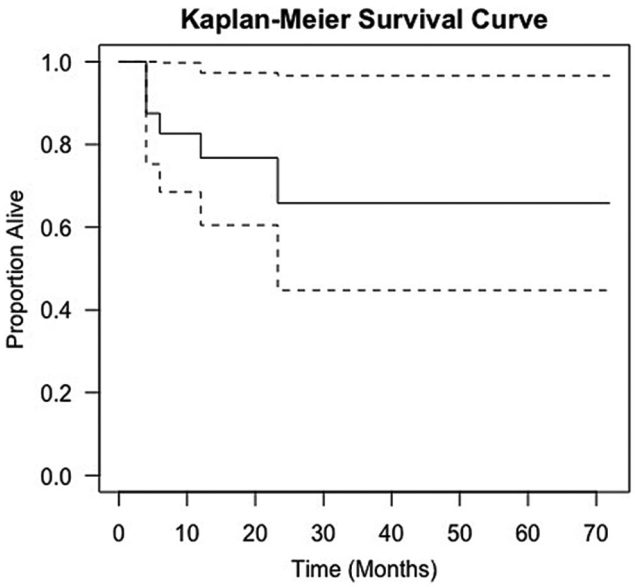

Figure 1: Overall survival analysis using Kaplan–Meier curve. Dotted lines represent 95% confidence intervals. Final death occurred at the last follow-up point at 23 months ($n = 27$). Overall, the 5-year survival rate is 66%

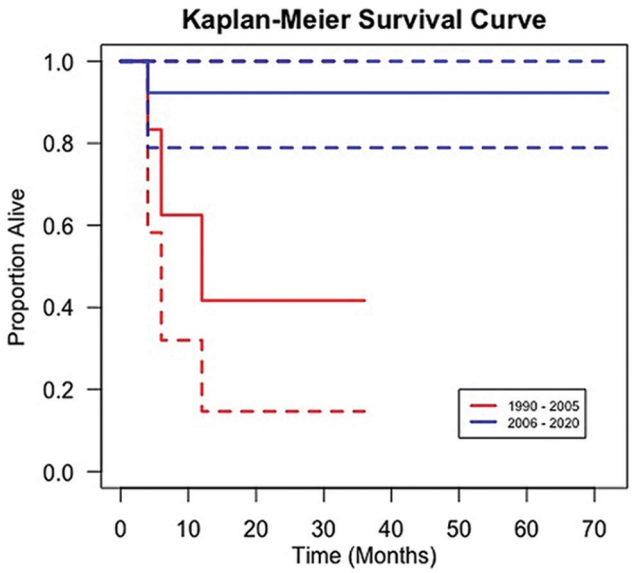

Figure 2: Kaplan–Meier curve stratified by study date, between 1990 and 2005 versus 2006 and 2020. Dotted lines represent 95% confidence intervals. The 5-year survival rate at the 30-month mark from 1990 to 2005 was 42% and from 2006 to 2020 was 92%. A log-rank test comparing the two survival curves revealed a test statistic of 4.2 (degree of freedom: 1), $P = 0.04$ ($n = 22$)

was used to record the stage at the time of diagnosis of the primary tumor.[12] Most patients (22/30, 73%) had Stage IV (any T, any N, M1) disease at the time of diagnosis, presenting with distant metastasis [Table 3]. OA metastases presented following detection of primary RCC in 26/44 (59%) and were initial manifestation of RCC in 18/44 (41%) patients [Table 1]. The average time from diagnosis of primary RCC to OA metastases was 80 months (median: 78, range: 1–180) [Table 3]. OA was the only metastatic site in 8 of 31 (26%) patients who had documented systemic evaluation data. Concurrent extra-OA metastases were identified in 23 on 31 (74%) patients, which most commonly involved lung (5/23, 22%) and were multifocal (two or more sites) in 13/23 (57%) patients [Table 3].

Management

Table 4 summarizes the management and outcomes of patients with OA metastasis from RCC. Information on management of OA RCC metastases was available on 42 of 44 (95%) patients. Of patients with OA metastases who underwent local therapy only (17/42, 40%), the most common intervention was resection with margin control in 10/17 (59%) patients and biopsy or resection followed by radiotherapy to the orbit in 6/17 (35%) patients. Two patients with a locally advanced disease involving sinuses and skull base underwent orbital exenteration, either as a monotherapy (reported in 2012)[38] or followed by radiotherapy (reported in 1957).[13] Twenty-five of 42 (60%) patients had systemic treatment in addition to any local OA therapy, which included biologic agents only (11/42, 26%), chemotherapy only (3/42, 7%), radiotherapy only (1/42, 2%), surgical resection of extra-OA metastases (1/42, 2%), palliative therapy (1/42, 2%), and combination therapy in 8 out of 42 (19%). The combination therapy included radiotherapy with surgery (2/8, 25%), chemotherapy with biologic agents (2/8, 25%), radiotherapy with biologic agents (2/8, 25%), chemotherapy with radiotherapy and biologic agents (1/8, 13%), and chemotherapy with radiosurgery (1/8, 13%). Treatment of primary RCC included nephrectomy in 30/33 (91%) with neoadjuvant biologic agents in 2/33 (6%) and surgery with radiotherapy in 1/33 (3%). Two patients (2/33, 6%) refused treatment. Biologic agents used included receptor protein-tyrosine kinase inhibitors (sunitinib, sorafenib, and pazopanib) and immunomodulatory agents (immune checkpoint inhibitors, interferon-alpha, and interleukin-2).

Outcome

The average follow-up was 18 months (median: 12, range: 0.3–72 months) [Table 4]. Of the 37 patients with available follow-up, 10/37 (27%) were alive with no evidence of disease, 18/37 (49%) alive with disease, 8/37 (22%) deceased due to disease, and 1/37 (3%) deceased due to another cause. The overall 5-year Kaplan–Meier survival rate for 27 patients with available information was 66% [Figure 1]. A subgroup analysis of 22 patients with complete information on OA RCC metastasis reported between 2006 and 2020 (15/22, 68%) demonstrated a significantly improved survival at 30-month mark when compared to those reported between 1990 and 2005 (92% vs. 42% vs. $P = 0.04$) [Figure 2]. In addition, in a subgroup analysis of 21 patients with complete information, patients who presented with metastases to OA only (8/21, 38%) versus those who had metastases to additional sites (13/21,

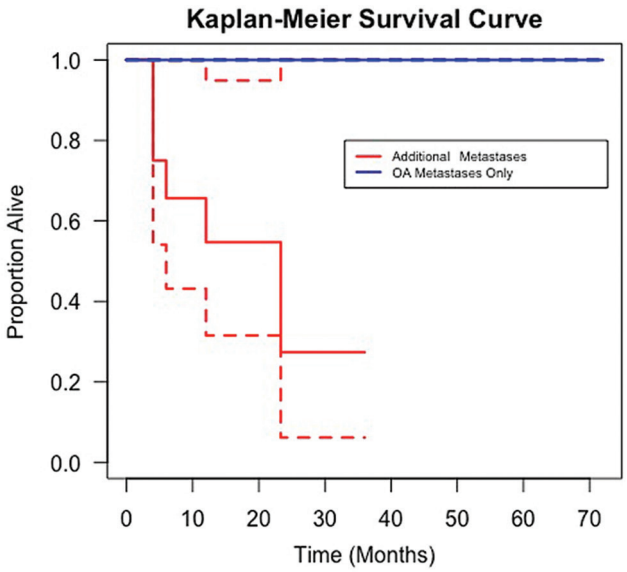

Figure 3: Kaplan–Meier curve: isolated ocular adnexal metastases versus additional metastases to other sites. Dotted lines represent 95% confidence intervals. The survival rate at the 30-month mark was 100% in patients who presented with metastases to OA only versus 27% in patients with metastases to additional sites. A log-rank test comparing the two survival curves revealed a test statistic of 5.9 (degree of freedom: 1), $P = 0.02$ ($n = 21$)

62%) showed an improved survival at the 30-month mark (100% vs. 27%, $P = 0.02$) [Figure 3].

Discussion

Orbital metastases are uncommon, with the incidence ranging between 1% and 13%.[52-54] RCC accounts for 5%–11% of orbital metastases.[53,55] In this review of 44 patients, OA metastases from RCC were more common in males (77%), with an average age of 60 years. These demographic data are similar to the distribution of RCC in general population[56] and are concurrent with the previously published studies on OA metastases from RCC.[8]

OA metastases from RCC present with symptoms related to mass effect, such as proptosis, mass, swelling, and diplopia. Notably, RCC is the most common malignant tumor that metastasizes to the nasal cavity and paranasal sinus[57] and can extend into the orbit from the sinonasal tract, presenting with symptoms of nasal obstruction and epistaxis. It is, therefore, crucial that detailed eye examination is performed along with thorough review of symptoms.

Orbital imaging plays a valuable role in the diagnostic work-up of OA metastases. The most common imaging modality is CT scan, performed in up to 80% of cases as a single imaging modality or in combination with other imaging studies [Figure 4]. However, definitive diagnosis requires tissue biopsy. In this review, clear cell RCC accounted for 82% of all RCC metastases, which is in keeping with the overall frequency of clear cell RCC [Figure 5a].[58] Ancillary

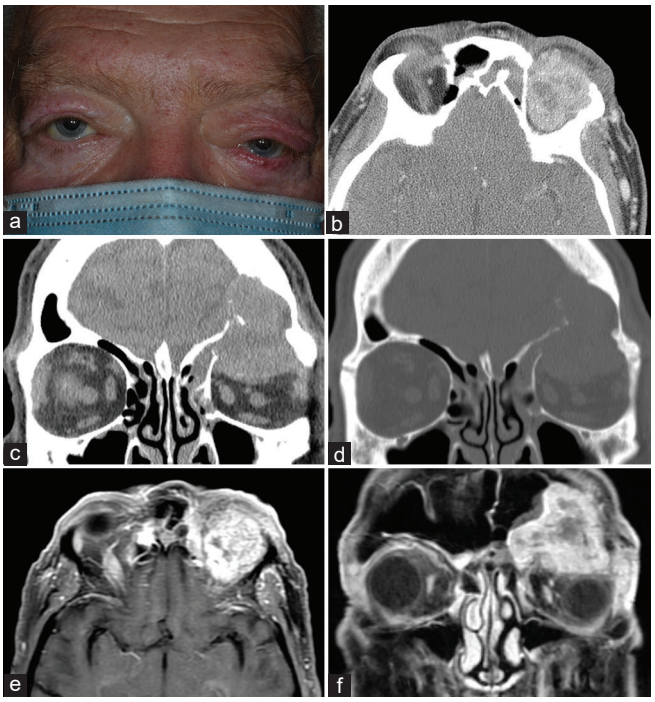

Figure 4: Renal cell carcinoma metastases to the ocular adnexa: clinical findings and imaging studies in a 67-year-old male with an 8-month history of slowly progressive left exophthalmos. There was no history of renal cell carcinoma. (a) Left exophthalmos and hypoglobus. (b) Axial and (c) coronal computed tomography (soft-tissue window) shows a left superior orbital mass extending into the frontal sinus and anterior cranial fossa. (d) Coronal computed tomography (bone window) with obvious bone erosion along the skull base. (e) Axial and (f) coronal magnetic resonance imaging, T1-weighted image with contrast and fat suppression. Note the inferior displacement of the left globe by the mass on the coronal image

immunohistochemical studies are frequently performed to support the morphologic diagnosis. Clear cell RCC expresses PAX8, CD10, CAIX, RCC, epithelial markers (cytokeratins AE1/AE3 and CAM5.2 and EMA), and vimentin [Figure 5b-d]. Thus, this immunohistochemical panel is frequently used in evaluation of suspected metastatic RCC.[42,59,60]

OA involvement by RCC occurs on average 6–7 years following the diagnosis of primary tumor in 59% of patients. However, metastases as late as 15 years following the diagnosis of primary RCC can occur, highlighting the importance of careful medical and surgical history.[16,19,39] Importantly, our review demonstrated that OA RCC can also occur as an initial manifestation of metastatic disease in 41% of patients. Thus, RCC should be an important consideration in a patient with orbital metastasis from an unknown primary, prompting appropriate systemic evaluation. Systemic imaging such as CT, positron emission tomography/CT, MRI, and ultrasound are useful screening modalities for RCC with multimodal imaging employed in 21% of patients in this review.

Approximately 15%–30% of patients with RCC have metastases at the time of diagnosis[56,61,62] and 20%–50% will progress to metastatic cancer,[63] with distant metastases most

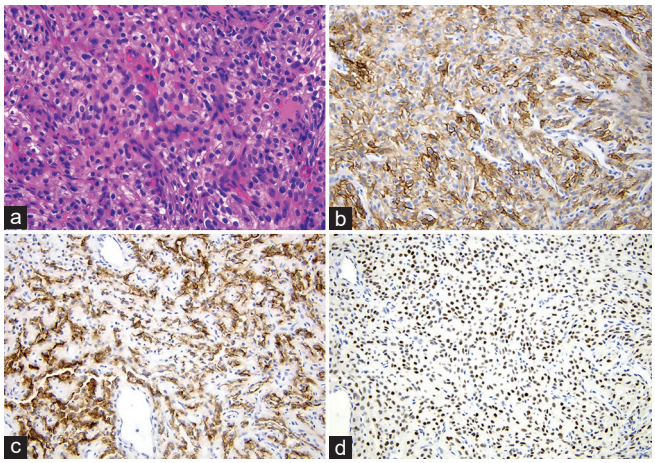

Figure 5: Renal cell carcinoma metastases to the ocular adnexa: pathology. Biopsy of the mass documented in Figure 4 demonstrates (a) nests and sheets of cells with clear cytoplasm and distinct cell membranes separated by capillaries, characteristic of clear cell renal cell carcinoma. Immunohistochemical studies show that the neoplastic cells demonstrate membranous staining for carbonic anhydrase IX (b), cytoplasmic and membranous staining for renal cell carcinoma antigen (c), and nuclear staining for paired-box gene 8 (d) supporting the diagnosis of clear cell renal cell carcinoma. (stains: h and E [a], carbonic anhydrase IX [b], renal cell carcinoma [c], paired-box gene 8 [d]; original magnification × 400 [a], 250 [b-d])

Table 4: Ocular adnexal metastases from renal cell carcinoma: Management and outcomes

Variables	*n* (%)
OA metastases local intervention only	
Excision/exenteration with margin control only	10/17 (59)
Biopsy or excision followed by regional radiotherapy	6/17 (35)
Other*	1/17 (6)
RCC primary treatment	
Nephrectomy	30/33 (91)
Other*	2/33 (6)
Surgery + radiotherapy	1/3 (33)
Systemic treatment	
No treatment	17/42 (40)
Biologic agents only†	11/42 (26)
Combination‡	8/42 (19)
Chemotherapy only	3/42 (7)
Palliative only	1/42 (2)
Surgical resection of extra-OA metastases	1/42 (2)
Radiotherapy only	1/42 (2)
Time (months) from diagnosis of OA metastases to final follow up	
Mean, median, range	18 (12, 0.3-72)
Outcome	
Alive with no evidence of disease	10/37 (27)
Alive with disease	18/37 (49)
Deceased due to disease	8/37 (22)
Deceased due to other causes§	1/37 (3)

*Refused treatment, †Biologic/biologic response modifier drugs; sunitinib, sorafenib, pazopanib, interferon, interleukin-2, ‡Combination includes radiation + surgery in 2/8, chemotherapy + biologic in 2/8, radiotherapy + biologic in 2/8, chemotherapy + radiotherapy + biologic in 1/8, chemotherapy + radiosurgery in 1/8, §Dead from other causes (pulmonary embolism). RCC: Renal cell carcinoma, OA: Ocular adnexal

commonly involving the lungs, liver, and bone.[5] Interestingly, in this review, 73% of patients with OA metastases had Stage IV metastatic disease at the time of primary tumor diagnosis. Thus, most OA metastases from RCC occur either in a setting of previously known metastatic disease or as an initial manifestation of RCC.

Because OA metastases from RCC present in a setting of advanced disease, systemic therapy plays an important role and was employed in 57% of patients in this review. Biologic therapy has become increasingly important in management of RCC, evolving from nontargeted immune-based therapies, such as interferon-alpha and interleukin-2 in the 1990s[56] to targeted therapies, such as receptor protein-tyrosine kinase inhibitors from 2006 and on, and immune checkpoint inhibitor therapies in recent years.[63] This trend is also seen in our review of reports from 2006, which documented the use of mammalian target of rapamycin inhibitors, checkpoint inhibitors, and receptor tyrosine kinase inhibitors.[43,48]

Survival for RCC is highly dependent on the stage at diagnosis, with only 10%–12% 5-year survival for Stage IV metastatic disease documented in prior studies.[63,64] However, the recent SEER database review found that mortality rate for metastatic RCC decreased significantly since 2012.[2] This improvement in survival has been attributed to the more rigorous imaging guidelines to detect RCC and the use of novel immunotherapy and targeted therapy agents. In our review for OA RCC metastases, we found that the absolute 5-year survival rate was 66%. Patients with isolated OA RCC metastases had improved survival when compared to those with additional metastases to other sites. In line with the observations from SEER database,[2] we noted a significantly improved 5-year survival in patients who had OA RCC metastases reported in the last 15 years (2006–2020).

Limitations

The inherent limitations of this study are the small sample size, which reflects rarity of RCC metastases to OA and heterogeneity in pathology reporting, diagnostic studies, oncologic staging, and therapeutic options, which reflects the evolution in our diagnostic approach, risk stratification, and management of RCC over the course of 5 decades.

Conclusion

OA metastasis from RCC can occur as an initial manifestation of RCC in 41% of patients. In patients with previously diagnosed RCC, OA metastases tend to occur in a setting of previously known metastatic disease on average 6–7 years after diagnosis and as late as 15 years following diagnosis. Advances in diagnostic modalities and targeted therapies over the last 15 years have allowed significant improvement in survival of patients with metastatic RCC, including those with OA metastasis.

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Conflicts of interest

There are no conflicts of interest.

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