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OCULAR TUMORS (M MATERIN, SECTION EDITOR)

Malignant Orbital Tumors: Current Approach to Diagnosis and Management

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Abstract

Purpose of Review To review current approaches to the diagnosis and management of the most common primary and secondary malignant tumors of the orbit in children and adults.

Recent Findings Given the rarity of most malignant orbital tumors, randomized clinical trials are lacking, but small retrospective studies investigating multimodal treatment strategies show early promise in preserving the eye and improving survival outcomes.

Summary Malignant orbital masses may be due to a broad range of pathologies, including primary tumors of the lacrimal apparatus, tumors of mesenchymal origin involving the orbit, tumors of the optic nerve, lymphoproliferative disorders, and secondary tumors from adjacent structures or distant metastases. A good clinical knowledge of the most common characteristics and imaging findings is needed to make the correct diagnosis and provide appropriate treatment. Typically, a biopsy is required to confirm the diagnosis. Staging is also critical to determine the extent of disease. Prognosis generally depends on clinical stage and histological grade of the tumor. All patients with history of a malignant orbital tumor should undergo long-term surveillance for disease recurrence and progression.

Keywords Lacrimal tumor · Malignant optic nerve glioma · Malignant solitary fibrous tumor · Orbital lymphoma · Orbital tumor · Orbital rhabdomyosarcoma

Introduction

Malignant tumors account for approximately 32–36% of all space-occupying lesions in the orbit and may be due to a broad range of pathologies, including primary tumors of the lacrimal apparatus (e.g., adenoid cystic carcinoma, pleomorphic adenocarcinoma, squamous cell carcinoma), primary tumors of mesenchymal origin involving the orbit (e.g., rhabdomyosarcoma, malignant solitary fibrous tumor), primary tumors of the optic nerve (e.g., malignant optic nerve glioma), lymphoproliferative disorders, and secondary tumors from adjacent structures or distant metastases [1, 2]. Presenting symptoms typically include progressive upper eyelid swelling, proptosis, globe displacement, diplopia, decreased vision, ptosis, and/or periorbital pain, which may be unilateral or bilateral depending on the underlying disease process. Neuroimaging, specifically computed tomography (CT) and magnetic resonance imaging (MRI) of the brain and orbits with and without contrast, is particularly useful in localizing the lesion, assessing for malignant characteristics (e.g., adjacent bony changes, intralesional calcification), and determining the extent of local tumor spread [3, 4]. Typically, a biopsy is required to confirm the diagnosis, particularly when treatment is invasive and prognosis depends on histological grade. In general, the prognosis for disease-specific survival (DSS) and progression-free survival (PFS) depends on clinical stage and histological grade of the tumor. All patients with history of a malignant orbital tumor should undergo long-term surveillance for disease recurrence and progression.

This article is part of the Topical Collection on *Ocular Tumors*

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Primary Malignant Epithelial Tumors of the Lacrimal Gland

Adenoid Cystic Carcinoma

Adenoid cystic carcinoma (ACC) is the most common primary malignant epithelial tumor of the lacrimal gland and

typically presents with progressive upper eyelid swelling, proptosis, inferonasal globe displacement, diplopia, decreased vision, ptosis, and periorbital pain associated with paresthesias [1, 4–7]. Persistent pain with paresthesias is a classic feature of ACC and suggests perineural invasion [6]. Unlike benign neoplasms involving the lacrimal gland, symptoms are often present for less than 6 months prior to presentation [5, 8].

Both CT and MRI with and without contrast of the orbits can be useful for the diagnosis of ACC and determination of local tumor spread [4]. ACC is typically a heterogeneous, enhancing superotemporal orbital mass that may be either well-circumscribed or ill-defined with infiltration of adjacent tissues [9, 10]. Bony invasion, intralesional calcification, and/or a "tail" or "wedge" sign, showing posterior extension of lacrimal gland tissue between the lateral rectus and lateral orbital wall or between the superior rectus and orbital roof, can also be seen (Fig. 1) [10, 11]. Whereas CT imaging is best for visualizing bony changes in the lacrimal fossa, contrast-enhanced MRI is useful for detecting perineural invasion, intracranial extension, and bone marrow involvement [6, 9].

When there is strong clinical suspicion for lacrimal gland carcinoma, a direct transcutaneous biopsy should be performed [4]. After obtaining a histopathological diagnosis, staging by the American Joint Committee on Cancer (AJCC) classification system is recommended to determine treatment options [12, 13]. Despite earlier presentations due to rapid progression of symptoms, most patients have ≥ T3 tumors at the time of diagnosis [12, 14]. Thus, orbital exenteration with or without bony removal followed by adjuvant radiotherapy is typically the treatment of choice. However, recent studies show that globe-preserving surgery with or without bony removal followed by postoperative radiotherapy does not increase the risk of local recurrence in patients with < T3 disease [12, 15, 16]. Yet, because there is high risk of early perineural invasion, adjuvant radiotherapy is recommended for nearly all patients, even in those with T1 and T2 disease [12, 17]. Postoperative chemoradiotherapy may also be considered in certain patients with a predominantly non-basaloid pattern of ACC, but caution should be exercised given that only early outcomes data have been published at this time [18].

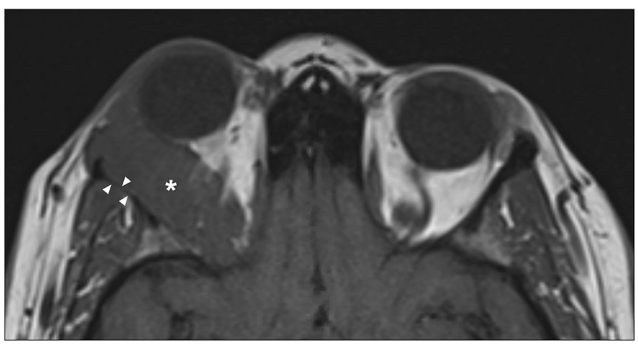

Fig. 1 An axial view on T1-weighted magnetic resonance imaging of the orbits with contrast, demonstrating a large right lacrimal gland mass (asterisk) with posterior extension and lateral orbital wall erosion (arrowheads) confirmed to be adenoid cystic carcinoma of the lacrimal gland

More recently, a treatment protocol comprising of neoadjuvant intra-arterial cytoreductive chemotherapy (IACC) followed by either orbital exenteration or globe-sparing resection in select cases, postoperative chemoradiation, and adjuvant chemotherapy has been studied in a small group of patients with ACC, but it requires an intact lacrimal artery, strict protocol adherence, and no prior surgical manipulation of lacrimal gland tissues aside from transcutaneous biopsy for histopathologic diagnosis [4, 19]. Although study findings show promise in achieving local-regional control and DSS in patients with ACC, prospective randomized multicenter clinical trials with long-term follow-up are needed to better assess treatment outcomes [20, 21].

Even with institution of aggressive multimodal therapy, prognosis is still very poor for patients with ACC, who have higher rates of local recurrence, regional nodal metastasis, distant metastasis, and tumor-related death than patients with other types of lacrimal gland tumors [12, 17, 22]. Tumors ≥ T3 by AJCC classification at the time of diagnosis, tumors with a predominantly basaloid pattern on histopathology, and tumors with evidence of perineural invasion are all associated with worse outcomes [5, 12]. All patients with ACC require long-term surveillance [4].

Pleomorphic Adenocarcinoma (Carcinoma ex Pleomorphic Adenoma or Malignant Mixed Tumor)

Pleomorphic adenocarcinoma, or carcinoma ex pleomorphic adenoma (CEPA), accounts for approximately 8% of all epithelial lacrimal gland tumors [1, 4, 7]. Patients classically have known history of pleomorphic adenoma, which was either biopsied or incompletely excised years or even decades ago, but adenocarcinoma of the lacrimal gland can also arise de novo in patients with no prior diagnosis or surgical history [4, 23, 24]. As with other malignant epithelial lacrimal gland tumors, patients with CEPA typically present with rapid progression of symptoms, including lateral upper eyelid swelling, proptosis, diplopia, decreased vision, and/or pain [5]. Malignant mixed tumors also characteristically have ill-defined margins and are more likely to be heterogeneous, have calcifications, and demonstrate bony invasion on CT compared to pleomorphic adenomas [4, 10]. Radiographic evidence of orbital spread is not uncommon.

A transcutaneous biopsy is generally recommended to confirm the diagnosis of CEPA [4]. Histopathology typically shows poorly differentiated adenocarcinoma, but ACC, mucoepidermoid carcinoma, carcinosarcoma, squamous cell carcinoma, and sebaceous cell carcinoma have all been previously described as histologic subtypes of CEPA despite the term "pleomorphic adenocarcinoma" [25–29]. Once

histopathologic diagnosis and operability are determined, eyelid-sparing orbital exenteration with or without bony removal should be performed, if possible [26, 30]. Regional and cervical lymph node dissection should also be performed at the time of surgery because lymphatic dissemination can occur early in the disease process [4, 26]. Adjuvant radiotherapy may also be considered but does not improve outcomes if surgical resection is incomplete [4, 31]. Occasionally, CEPA may be well-circumscribed and noninvasive; in these cases, local resection may be sufficient [4, 6, 26, 29, 32].

Despite aggressive treatment, prognosis is dismal when there is evidence of poorly differentiated or undifferentiated invasive carcinoma, which can be associated with intracranial spread and metastasis to the lung, chest, and bones [4, 25, 26, 32]. Patients with CEPA who have known history of pleomorphic adenoma may live longer (median: 12.0 years) than those whose tumor arose de novo (median: 3.5 years) [4, 33].

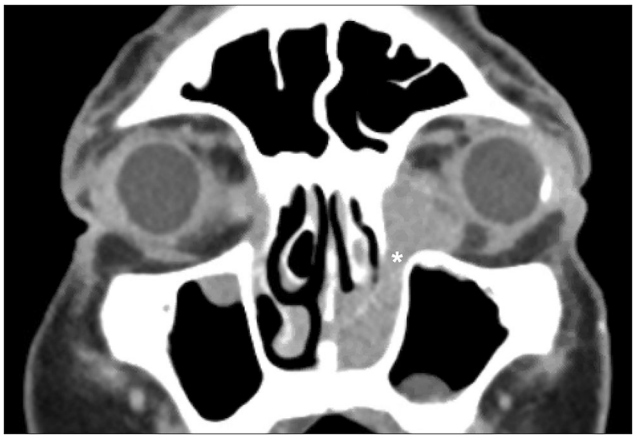

Fig. 2 A coronal view on computed tomography of the face, demonstrating squamous cell carcinoma originating in the left nasolacrimal duct (asterisk) and extending into the ipsilateral medial orbit and ipsilateral nasal cavity

Malignant Epithelial Tumors of the Lacrimal Sac and Nasolacrimal Duct

Primary Squamous Cell Carcinoma of the Lacrimal Sac and Nasolacrimal Duct

Squamous cell carcinoma (SCC) is the most common primary epithelial malignancy of the lacrimal sac and nasolacrimal duct [34]. Although malignant transformation of incompletely excised benign papillomas can occur, SCC typically arises de novo in the epithelium of the lacrimal sac and/or nasolacrimal duct [35]. Presenting symptoms can include unilateral epiphora, recurrent dacryocystitis, medial canthal mass, pain, and/or punctal discharge; blood-tinged tears rarely occur and are seen in only 4% of cases [34]. Approximately 7% of patients are also incidentally diagnosed during dacryocystorhinostomy for acquired nasolacrimal duct obstruction [34].

Orbital imaging can show variable enhancement of a medial canthal mass, but there is often radiographic evidence of medial canthal involvement, nasolacrimal canal expansion, nasolacrimal duct erosion, and/or adjacent sinonasal spread, all of which strongly suggest malignant disease (Fig. 2) [34]. CT dacryocystography can be normal or may show filling defects [34, 36]. A tissue biopsy should be performed to obtain a histopathologic diagnosis. Given the rarity of disease, there are currently no consensus guidelines on staging, although some groups have adopted either the tumor, node, metastasis (TNM) staging system for head and neck SCCs [37] or "clinical stages" based solely on clinical signs [38].

En bloc resection with partial anterior ethmoidectomy and medial maxillectomy is typically the treatment of choice, with orbital exenteration and/or additional bony removal if there is evidence of orbital involvement and/or more extensive bony involvement [34, 38, 39]. However, if combined with concurrent chemoradiation or adjuvant radiotherapy, globe-sparing surgery may be performed to preserve the ipsilateral eye and maintain relatively good visual function, without adversely affecting long-term survival outcomes [40]. High-grade tumors still require orbital exenteration due to the rapid growth of tumor, but prognosis is quite dismal due to the aggressive nature of disease [40].

Malignant Lymphoproliferative Disorders Involving the Orbit

Orbital lymphomas account for 9–12% of all space-occupying lesions in the orbit [1, 2]. In fact, B cell non-Hodgkin's lymphomas and in particular extranodal marginal zone lymphomas (EMZL) or mucosa-associated lymphoid tissue (MALT) lymphomas are the most common malignant orbital tumors and have a predilection for older patients [1, 2]. A large majority of patients have the EMZL/MALT lymphoma subtype, which is considered to be histologically a low-grade tumor generally with an indolent clinical course, but intermediate- or high-grade lymphomas, such as follicular lymphoma, diffuse large B cell lymphoma (DLBCL), mantle cell lymphoma, and lymphoplasmacytic lymphoma, have also been reported [41]. Presenting symptoms can include eyelid swelling, palpable mass, proptosis, ptosis, diplopia, decreased vision, and/or mild pain or discomfort, but patients may occasionally be asymptomatic [42, 43]. Orbital imaging classically demonstrates a well-circumscribed, round or oblong orbital mass that conforms to the globe and orbital bones, without bony invasion (Fig. 3); however, a diffuse, ill-defined orbital mass may be seen in up to 52% of patients, and bony erosion can be seen in cases of DLBCL [41, 43]. Lesions can be unifocal, multifocal, or bilateral.

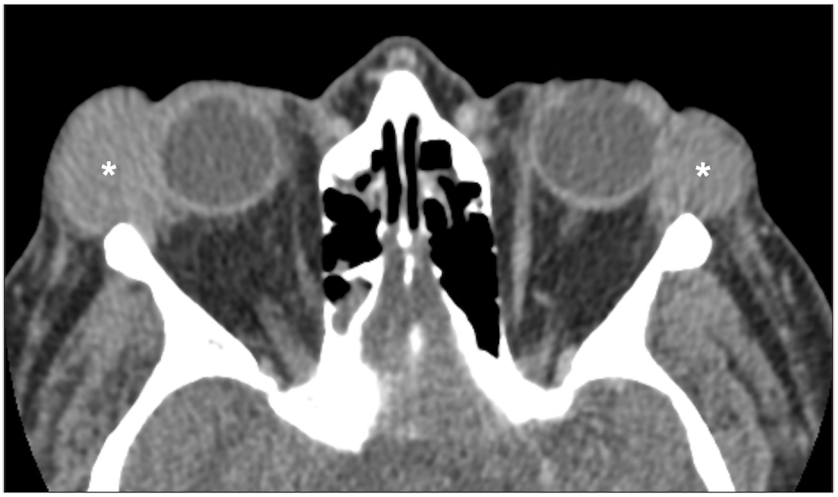

Fig. 3 An axial view on computed tomography of the orbits, demonstrating bilateral superotemporal orbital masses (asterisks) conforming to the globe and adjacent bony structures, with histopathology confirming follicular lymphoma of the lacrimal glands

A tissue biopsy is recommended to obtain a histologic diagnosis. The surgical approach depends on the location of the lesion(s). Sufficient tissue should be sent, with half in formalin for histopathology and the other half in transport media for cytology, lymphocyte immunophenotyping, and molecular genetics [4, 41].

Systemic evaluation with a hematologist-oncologist, including a thorough physical examination, bone marrow aspiration biopsy (as clinically appropriate), and whole-body imaging is required for staging, prognostication, and treatment [4, 41]. At the time of diagnosis, approximately 50–75% of patients have primary orbital lymphoma, whereas approximately 5–28% have prior history of lymphoma, and approximately 13–28% are newly diagnosed with systemic lymphoma [42, 44]. For patients with lymphoma localized to the orbit, but with lacrimal gland involvement or bilateral disease on presentation, there is higher risk of subsequently developing disseminated disease [42, 43].

Treatment options may include surgical excision, radiation, chemotherapy, and/or immunotherapy and largely depend on the size, location, and histologic grade of lymphoma [4, 41]. Orbital radiation is typically the treatment of choice, even for low-grade lymphomas because they are highly radiosensitive [41, 45]. Even with radiotherapy, high-grade tumors, such as DLBCL, also usually require chemotherapy [41, 46]. If there is any evidence of systemic involvement, bilateral disease, and/or aggressive histologic subtype, systemic treatment with chemotherapy and/or immunotherapy (i.e., rituximab) should also be considered [4, 41].

Prognosis for orbital lymphomas is generally good, with DSS of 81% at 5 years and 63% at 10 years [42]. Compared to patients with lymphoma localized to the orbit without systemic involvement at the time of diagnosis, patients with prior or concurrent systemic disease at the time of diagnosis, bilateral disease, and/or more aggressive lymphoma subtypes, such as DLBCL, have significantly lower rates of DSS and PFS [42, 44]. All patients, regardless of histologic grade, require long-term surveillance for disease recurrence and progression.

Malignant Tumors of Mesenchymal Origin Involving the Orbit

Primary Orbital Rhabdomyosarcoma

Orbital rhabdomyosarcoma accounts for 2–3% of all space-occupying lesions in the orbit and can be classified into 4 main histologic subtypes [1, 2]. Pleomorphic is the most common subtype in adults, followed by alveolar, embryonal, and botryoid [47, 48]. Although more frequently seen in children less than 10 years old, orbital rhabdomyosarcomas can be seen in adults, with a slight predilection for males [47, 49]. Because it can occur in any quadrant of the orbit, symptoms depend on tumor location and may include proptosis, globe displacement, ptosis, eyelid swelling, chemosis, palpable mass, and/or pain [47]. Rhabdomyosarcomas may also arise from mesenchymal tissues of the paranasal sinuses, nasopharynx, or the eye itself and then secondarily invade the orbit; patients may present with other symptoms and signs as related to the primary origin of tumor (e.g., epistaxis, vision loss) [47, 50].

Orbital imaging is critical for diagnosis and management. In the early stages of disease, primary orbital rhabdomyosarcoma is typically a round, homogeneous, well-circumscribed orbital mass that is isotense to extraocular muscles on T1 and enhances moderately to markedly with contrast (Fig. 4), but in more advanced disease, a diffuse, infiltrative mass can be seen, with evidence of bony invasion and even intracranial extension [47].

According to ad hoc analyses from the Intergroup Rhabdomyosarcoma Study Group (IRSG), an attempt should be made to excise the entire tumor, if possible, because clinical staging, treatment, and subsequent prognostication for orbital rhabdomyosarcoma are largely determined by

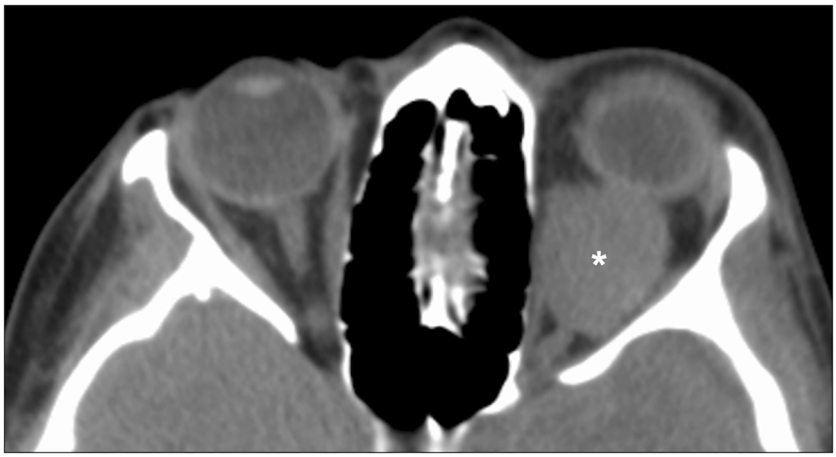

Fig. 4 An axial view on computed tomography of the orbits, demonstrating a well-circumscribed intraconal mass encasing the optic nerve on the left (asterisk), which was found to be primary orbital rhabdomyosarcoma after orbital biopsy and systemic imaging

histologic subtype and the presence of residual tumor post-biopsy [47, 50, 51].

Because rhabdomyosarcoma is chemo- and radiosensitive, adjuvant chemoradiation is recommended for nearly all patients due to improved survival outcomes with institution of adjuvant therapy [47, 52, 53]. Although external beam radiation has traditionally been the treatment modality of choice, limited-margin conformal radiotherapy and brachytherapy have been shown to be effective in achieving local-regional control in children [54, 55]. A survival benefit has also been shown with additional maintenance chemotherapy in children and young adults with localized high-risk rhabdomyosarcoma, but no such studies have been performed in older adults [56]. Additional surgical resection may also be required if there is incomplete remission or disease recurrence following chemoradiation [53, 57]. Targeted molecular therapies and immunotherapies are currently being investigated for rhabdomyosarcomas [58].

Prognosis of orbital rhabdomyosarcomas is largely dependent on age, histologic subtype, anatomic location, stage, and local control of disease after treatment [57]. Compared with pleomorphic and embryonal subtypes, the alveolar subtype has the worst prognosis [48, 57]. When accounting for tumor subtype, adults still fare worse than children [48, 57]. Fortunately, patients with primary orbital rhabdomyosarcomas have a better prognosis than those with rhabdomyosarcomas that originate elsewhere in the body due to the earlier onset of symptoms from mass effect within the orbit [47]. Patients with tumors located anteriorly within the orbit also have a better prognosis, as complete resection is more likely to be possible for these tumors. Because there are few, if any, lymphatic channels within the orbit, early lymphatic invasion is rare, but if there is local invasion into adjacent conjunctiva and/or eyelids, lymphatic spread can occur. Metastatic disease in the brain, lung, and bone from hematogenous spread has been previously reported and is associated with dismal prognosis [47, 48, 57]. All patients require long-term surveillance for disease recurrence and secondary effects from radiotherapy [47].

Malignant Solitary Fibrous Tumor

Orbital solitary fibrous tumors (OSFTs) are rare spindle cell tumors of mesenchymal origin that can originate from any location within the orbit and account for < 1% of all orbital lesions [1, 2, 59]. OSFTs present most commonly in the fifth decade of life, with gradual onset of symptoms, including unilateral proptosis, globe displacement, diplopia, facial disfigurement, and/or decreased vision [59]. Although most OSFTs are benign, up to a quarter can be clinically aggressive and may demonstrate invasion of adjacent tissues, recurrent disease, and/or systemic metastasis [60]. CT orbital imaging of malignant OSFTs often shows a large, well-circumscribed, enhancing, extraconal or intraconal mass, with radiographic evidence of bony infiltration [60]. Systemic imaging is also required; orbital metastasis from another primary source (e.g., pleura) and recurrence after incomplete excision have been reported [60–62].

Complete en bloc resection is recommended for OSFTs, as recurrent disease is often associated with incomplete resection [59]. Stereotactic radiosurgery has also been described for OSFTs and can achieve local control and tumor regression, but these studies are limited by the few number of cases and short follow-up times [63]. Although tyrosine kinase inhibitors have been used to reduce tumor burden and improve operability of advanced extraorbital SFTs, it has not yet been used in patients with OSFTs [64]. All patients require long-term surveillance due to risk of late recurrence [59].

Primary Malignant Tumors of the Optic Nerve

Malignant Optic Nerve Glioma

Malignant optic nerve gliomas include anaplastic astrocytoma (World Health Organization (WHO) grade III) and glioblastoma multiforme (WHO grade IV) and account for < 1% of all orbital lesions [1, 2, 65, 66]. Whereas optic nerve gliomas are typically benign, low-grade tumors in children, malignant

optic nerve gliomas are aggressive, high-grade neoplasms that primarily occur in the sixth decade of life [66]. Patients usually present with unilateral vision loss within weeks, followed by rapid progression of vision loss in the contralateral eye. Pain, proptosis, ophthalmoplegia, visual field defects, papilledema, disc and retinal hemorrhages, optic atrophy, and even other focal neurologic deficits (e.g., hemiparesis) may also be seen on presentation [66]. In some cases, malignant optic nerve glioma may clinically resemble optic neuritis or nonarteritic anterior ischemic optic neuropathy, delaying the true diagnosis [67, 68]. Findings on contrast-enhanced orbital MRI are indistinguishable from those of a benign optic nerve glioma or other causes of an enlarged optic nerve; thus, rapid progression of symptoms with clinical and/or radiographic evidence of chiasmal spread should prompt tissue biopsy to obtain a histopathologic diagnosis [69, 70].

Given the rarity of this disease, its rapid progression, and very poor prognosis, there are no established treatment protocols for malignant optic nerve gliomas. If one eye is primarily affected, surgical resection of the tumor can be attempted to preserve the contralateral eye, but it is often not possible due to chiasmal and/or bilateral involvement. Furthermore, contralateral spread may still occur, regardless of surgical resection [66]. Orbital radiation is typically performed in an attempt to prolong survival, but retrospective studies have not shown a significant survival benefit, although patients treated with radiotherapy do survive a few months longer on average [66, 71]. Additional treatment with temozolomide has also been tried for WHO grade IV tumors, but without improvement in outcomes [66, 68]. Based on a phase I/II study that showed prolonged survival in patients with high-grade gliomas treated with chemically induced hypothyroidism in combination with high-dose tamoxifen therapy [72], one patient with malignant optic nerve glioma was treated with propylthiouracil-induced hypothyroidism in conjunction with carboplatin chemotherapy and demonstrated rapid response to therapy on two separate occasions with a remission period of 2.5 years and overall survival of 4.5 years [73]. Despite being a single case report, this is in stark contrast to the dismal mean survival of 5.9 months in untreated patients with malignant optic nerve gliomas and 9.7 months in patients treated with radiotherapy [66]. Due to rapid progression of blindness, intracranial invasion, and death, prognosis is grim for patients with malignant optic nerve gliomas even with treatment.

Secondary Orbital Tumors from Adjacent Structures

Malignant tumors of the sinuses and periocular skin may secondarily invade the orbit and account for 1–2% and 3–7% of all orbital lesions, respectively [1, 2]. Sinonasal malignancies typically arise from within the ethmoid or maxillary sinuses, followed by the nasopharynx and oropharynx [74]. Symptoms may include nasal obstruction, epistaxis, and/or epiphora. Maxillofacial imaging is helpful in assessing the extent of tumor spread. If there is evidence of orbital invasion of the tumor, orbital exenteration followed by adjuvant radiotherapy is typically recommended, although globe-sparing surgery may be considered to preserve vision without increasing the risk of recurrence or death in some cases [74]. Cutaneous malignancies of the eyelid and periocular skin, such as sebaceous gland carcinoma, basal cell carcinoma, and SCC (Fig. 5), may also invade the orbit. Orbital imaging is recommended, especially when perineural invasion is strongly suspected. Treatment largely depends on the primary malignancy and the extent of disease and may involve multimodal therapy, including chemotherapy, radiation, and/or surgery [75].

Metastatic Tumors to the Orbit

Metastatic tumors account for approximately 3–10% of all orbital lesions [1, 2, 76]. Breast carcinoma is the most common neoplasm that metastasizes to the orbit; other carcinomas include prostate carcinoma, lung carcinoma, renal cell carcinoma, and gastrointestional carcinoma, among others [1, 2, 76]. Signs and symptoms typically include proptosis or enophthalmos (with scirrhous breast carcinoma), diplopia, decreased or blurred vision, ptosis, and/or pain [76]. A thorough clinical assessment, including history, physical examination, ophthalmic examination, and imaging, is required to assess the extent of involvement and to guide treatment. Most patients have prior history of malignancy, with evidence of widespread systemic involvement at the time of orbital metastasis, but in up to a quarter of cases, there may be no known history of cancer [76]. If there is no prior history of malignancy, a tissue biopsy is warranted, with systemic evaluation for staging. Treatment depends on the type of tumor, histologic grade, and clinical stage.

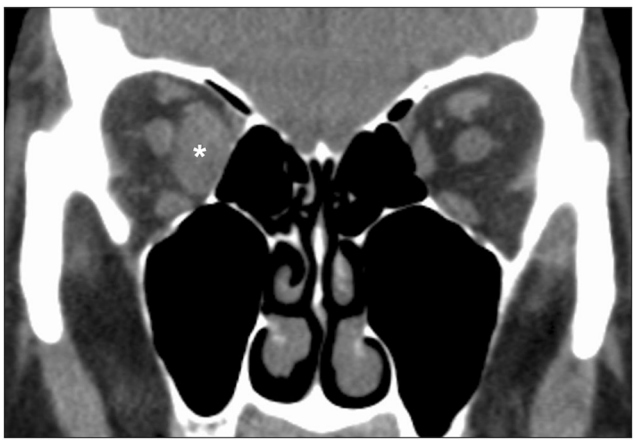

Fig. 5 A coronal view on computed tomography of the face, demonstrating enlargement of the right medial rectus muscle (asterisk) secondary to invasion of cutaneous squamous cell carcinoma of the eyelid

Conclusion

Orbital malignancies can be primary or secondary tumors of a broad range of pathologies, and systematic assessment with detailed clinical history, examination, and imaging studies is required for diagnosis and management. For malignant orbital tumors, symptoms are typically related to mass effect and/or tissue infiltration, such as progressive upper eyelid swelling, proptosis, globe displacement, diplopia, decreased vision, and/or ptosis, but they also may be indicative of perineural invasion, such as periorbital pain, hypoesthesia, and/or paresthesias. These symptoms typically rapidly progress within less than a year, prompting patients to be seen by their primary care physician or eye care provider. Orbital imaging and tissue biopsy are often critical for diagnosis of orbital malignancies, while prognostication largely depends on histologic grade and clinical stage. All patients with history of a malignant orbital tumor should undergo long-term surveillance for disease recurrence and progression.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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