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Case report

Lacrimal sac adenocarcinoma managed with androgen deprivation

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ABSTRACT

Purpose: To describe a case of primary lacrimal sac adenocarcinoma treated primarily with androgen deprivation therapy (ADT) with good clinic response.

Observations: An 82-year-old male presented with a painless right orbital mass. Pathology following partial resection was consistent with primary lacrimal sac adenocarcinoma positive for androgen receptors (AR). Magnetic resonance imaging (MRI) scan showed an orbital mass with extension into the nasolacrimal apparatus and intraconally between the medial and inferior recti. Staging positron emission tomography/computed tomography (PET/CT) showed one hypermetabolic right sided lymph node in addition to the known orbital mass. Orbital exenteration and external beam radiation therapy were offered as the primary treatment modality however the patient refused. He subsequently received four years of androgen deprivation monotherapy, before stopping due to sexual side effects, with no progression of local or metastatic disease and some local regression documented on MRI at 5 years.

Conclusions and Importance: Lacrimal sac adenocarcinoma is commonly found to be AR positive on pathology. Our case shows that ADT can serve as an effective treatment modality for those patients that defer primary surgical management.

1. Introduction

Although tumors of the lacrimal gland are not rare, tumors of the lacrimal sac are, with approximately 775 cases reported in the literature since the 1930s[1]. Within the malignant subset of lacrimal sac tumors, adenocarcinoma ranks as one of the least common histologies.[1,2] Cases of lacrimal sac adenocarcinomas have been previously presented in the literature, mainly through isolated case reports.[3–6] Surgery and radiation therapy are the primary treatment modalities and orbital exenteration is often required.[3–7] In this case, our patient was hesitant to proceed with exenteration given its high morbidity, permanence and life-changing nature and thus ultimately deferred for a less invasive option. We present the first case of biopsy proven lacrimal sac adenocarcinoma treated solely with androgen deprivation therapy (ADT).

2. Case report

An 82-year old man with a history of localized prostate cancer developed excessive lacrimation and one year later presented with a painless, palpable mass in the anterior right orbit. At presentation, the patient had fullness of the right lower lid, with mild epiphora on the medial aspect of the eye (Fig. 1). Extraocular movements were intact and visual acuity was 20/25 in the right eye and 20/20 in the left eye. Pupils were equal, round and reactive to light with a normal fundus exam in both eyes. Magnetic resonance imaging (MRI) scan showed a transcompartmental orbital mass extending into the nasolacrimal apparatus with inferior pre and postseptal extension with extension intraconally in between the medial and inferior recti (Fig. 2).

This lesion was subsequently partially resected, and pathology revealed poorly-differentiated adenocarcinoma of the lacrimal sac composed of cells with round, large nucleoli, with an oncocytic cytoplasm and vacuoles. Immunostains were focally positive for

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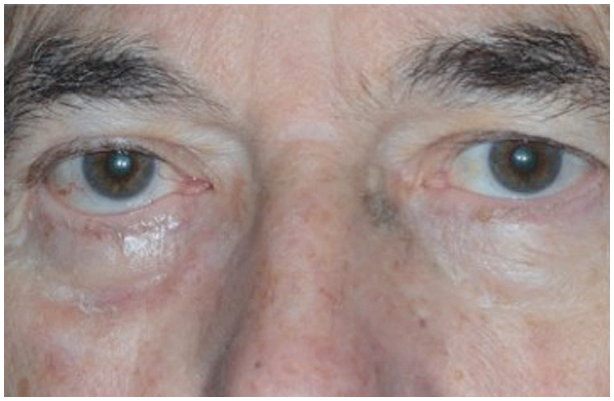

Fig. 1. Photograph of patient at presentation showing prominent fullness of right lower lid.

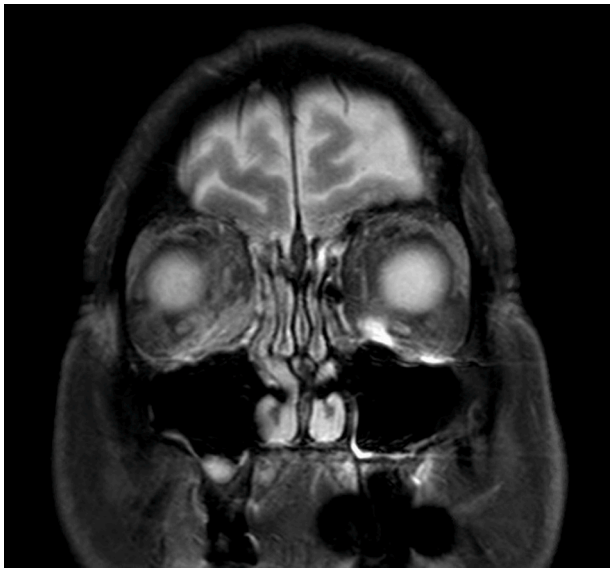

Fig. 2. Coronal T2 Weighted MRI on presentation showing right inferior orbital mass.

mucicarmine, pan-keratin, cytokeratin 7, androgen receptors (AR), and cytoplasmic HER-2-neu and negative for prostate-specific antigen, prostatic specific acid phosphatase, thyroid transcription factor 1, S100, estrogen and progesterone receptors, consistent with a primary tumor of the lacrimal sac. Follow-up staging positron emission tomography/computed tomography (PET/CT) showed a hypermetabolic right cervical lymph node, the known orbital mass and no other evidence of disease.

Primary orbital exenteration with external beam radiation therapy was recommended, however the patient preferred to take a more conservative approach. Given the pathology revealed androgen receptors and the well-known use of ADT in both salivary gland and prostate cancer, ADT therapy was offered as a treatment modality. The patient decided to proceed with ADT with close follow up. He subsequently received a loading dose of 250 mg of degarelix, a gonadotropin releasing hormone (GnRH) antagonist, followed by 80 mg monthly. Degarelix works by binding to the GnRH receptors on pituitary cells, therein blocking luteinizing hormone (LH) and follicle stimulating hormone (FSH) release which ultimately suppresses testosterone release. Six-month re-staging MRI of the orbit showed stable disease and PET/CT showed stable uptake in the primary tumor but a 0.1 cm increase in size and uptake in the ipsilateral cervical lymph node. A non-steroidal androgen antagonist, bicalutamide, was initiated to induce a further response and was subsequently increased from 50 to 150 mg orally daily. Bicalutamide works by blocking testosterone and dihydrotestosterone (DHT) from binding to the androgen receptor. His excessive lacrimation and lower lid fullness improved (Fig. 3). Follow-up PET/CT two months following this showed resolution of FDG avidity of the right cervical lymph node. The patient subsequently underwent 4 years of the aforementioned regimen without any progression of disease on surveillance imaging, before deciding to stop treatment due to side effects. The patient experienced hot flashes and sexual dysfunction, including loss of libido and erectile dysfunction which ultimately led him to discontinue therapy. Upon discontinuation, the patient was able to regain some sexual function. Presently, 60 months following initial treatment with ADT, he remains with stable disease (Fig. 4).

3. Discussion

Surgical resection of lacrimal sac tumors is the mainstay of treatment.[2–7] In the few case reports of lacrimal sac adenocarcinomas, it has been described that these malignancies are commonly positive for androgen receptors.[3,4] The decision to proceed with ADT stemmed from the experiences published in the literature about use of androgen blockade in patients with salivary gland carcinoma. In 2003, Locati et al. published a case of locally recurrent parotid gland adenocarcinoma that achieved complete remission at two months with ADT.[9] This patient was treated with triptorelin, a GnRH agonist, and bicalutamide. Further studies were conducted investigating the use of ADT in salivary gland cancer, including a recent case series[10] and prospective phase II trial.[11] In 2018, Boon et al. published a retrospective case series detailing 35 cases of locally recurrent or metastatic salivary treated with ADT, with either bicalutamide monotherapy or bicalutamide plus a luteinizing hormone-releasing hormone (LHRH) analog.[10] Of these 35 patients, 50% showed clinical benefit, defined as complete response, partial response or stable disease, with a median follow-up of 10 months. Fushimi et al. published results of a phase II clinical trial evaluating leuprorelin, a GnRH agonist, in conjunction with bicalutamide in patients with locally recurrent or metastatic salivary gland cancer showing a clinical benefit in 75% of patients with a median follow up of 15 months.[11] In our case, we utilized a GnRH antagonist, degarelix, a newer medication which avoids the immediate and transient increase in testosterone seen with GnRH agonists due to their initial temporary stimulation of LH and FSH release.

There is less published information available in the literature describing ADT in lacrimal sac malignancies. To our knowledge, there are no published prospective trials looking at ADT in lacrimal sac malignancies. The literature is limited to case reports. Vagia et al. describe a case of recurrent metastatic lacrimal sac adenocarcinoma, primarily treated with surgery, radiation and systemic chemotherapy, which

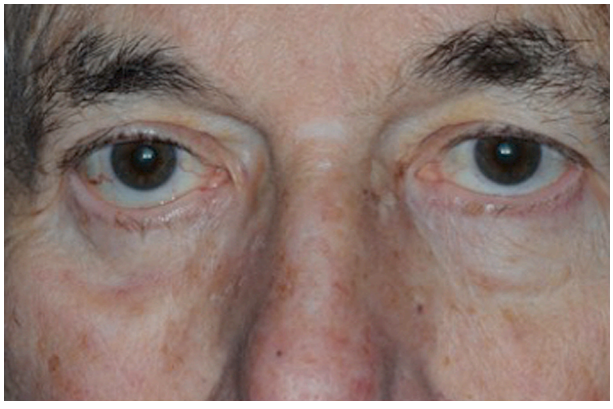

Fig. 3. Photograph of patient following 7 months of ADT showing improvement in right lower lid fullness.

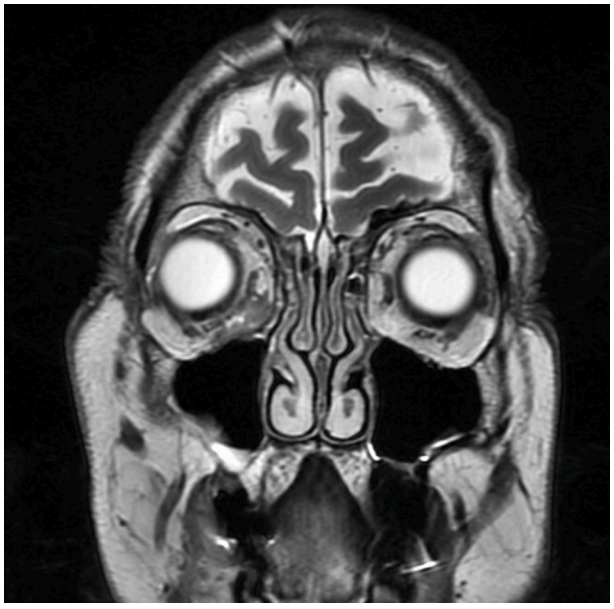

Fig. 4. Coronal T2 Weighted MRI on 5 year follow up showing decreased size of right inferior orbital mass.

progressed and responded well to ADT as a salvage treatment.[3] In this report, following primary treatment, the patient was started on bicalutamide and a LHRH analog after which the patient showed partial response but ultimately progressed two months later. At this stage, abiraterone, which blocks androgen synthesis, with prednisolone was substituted for bicalutamide, and the patient showed complete response at one year.

ADT has side effects including sexual dysfunction as experienced by our patient. Other commonly described side effects include loss of bone mineral density, weight gain, fatigue, and anemia.[8] This case highlights the importance of immunostaining for AR in all patients with this malignancy, as signaling via AR may be a critical pathway in lacrimal sac adenocarcinoma, as it is in prostate cancer and salivary gland cancer, in which ADT is a mainstay of therapy.[9–15] Prospective studies are needed to further evaluate the use of ADT in AR-positive lacrimal sac adenocarcinoma.

4. Conclusions

We present a case where ADT treatment served as an effective monotherapy for a surgically unresectable lacrimal sac adenocarcinoma, with minimal side effects. Although resultant sexual dysfunction led our patient to stop treatment, upon termination, he was able to regain some sexual function. Other treatment options including orbital exenteration and radiation therapy carry long-term sequela and morbidity. Our case suggests that primary therapy with ADT may serve as an effective treatment modality for those patients that defer primary surgical management. Our findings suggest further consideration be given to prospectively evaluate the use of ADT in patients with AR-expressing primary adenocarcinoma of the lacrimal sac.

Patient consent

The patient consented to the publication of this case report orally.

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Declaration of competing interest

No conflict of interest exists.

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