Lacrimal sac adenocarcinoma managed with androgen deprivation

David H. Abramson a,*, Julia Fallon b, Noa Biran c, Jasmine H. Francis a, Korey Jaben a, William K. Oh d

a Department of Surgery, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY, 10065, USA
b Department of Medicine, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY, 10065, USA
c John Theurer Cancer Center, Hackensack University Medical Center, 30 Prospect Avenue, Hackensack, NJ, 07601, USA
d Division of Hematology and Medical Oncology, Icahn School of Medicine at Mount Sinai, 1 Gustave L. Levy Place, New York, NY, 10029, USA

ARTICLE INFO

Keywords:
Lacrimal sac adenocarcinoma
Androgen deprivation therapy
Androgen receptor

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 intracranially 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. Within the malignant subset of lacrimal sac tumors, adenocarcinoma ranks as one of the least common histologies. Cases of lacrimal sac adenocarcinomas have been previously presented in the literature, mainly through isolated case reports. Surgery and radiation therapy are the primary treatment modalities and orbital exenteration is often required. 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 left eye. Magnetic resonance imaging (MRI) scan showed an orbital mass with extension into the nasolacrimal apparatus and intracranially between the medial and inferior recti (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 trans-compartmental orbital mass extending into the nasolacrimal apparatus with inferior pre and postseptal extension with extension intracranially 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 nucleioli, with an oncocytic cytoplasm and vacuoles. Immunostains were focally positive for...
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 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. 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 and prospective phase II trial. 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. 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. 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.

3. Discussion

Surgical resection of lacrimal sac tumors is the mainstay of treatment. In the few case reports of lacrimal sac adenocarcinomas, it has been described that these malignancies are commonly positive for androgen receptors. 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. 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 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).
progressed and responded well to ADT as a salvage treatment. 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. 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. 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 sequelae 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.

Acknowledgements and disclosures

The Fund for Ophthalmic Knowledge, Inc. and Cancer Center Support Grant (P30 CA008748).

The following authors have no financial disclosures: DHA, JF, NB, JHF, KJ, WO.

All authors attest that they meet the current ICMJE criteria for Authorship.

Funding

No funding was received for this work.

Declaration of competing interest

No conflict of interest exists.

Acknowledgements

None.

References

1. Krishna Y, Coupland SE. Lacrimal sac tumors—A review. Asia Pac J Ophthalmol (Phila). 2017 Mar-Apr;6(2):173–178.
2. Kim HJ, Shields CL, Langer PD. Lacrimal sac tumors: diagnosis and treatment. In: Black EH, Nesi FA, Cavanaugh CJ, et al., eds. Smith and Nesi’s Ophthalmic Plastic and Reconstructive Surgery. New York: Springer; 2012:609–614.
3. Vagia E, Economopoulos P, Oikonomopoulos N, et al. Androgen-Receptor positive lacrimal sac adenocarcinoma demonstrating long-lasting response to LHRH analog plus abiraterone treatment. Front Oncol. 2015 Feb 2;5:10.
4. Ishida M, Iwai M, Yoshida K, et al. Primary ductal adenocarcinoma of the lacrimal sac: the first reported case. Int J Clin Exp Pathol. 2013 Aug;6(6):1929–1934.
5. Baredes S, Ludwin D, Troubleshoot Y, et al. Adenocarcinoma ex-pleomorphic adenoma of the lacrimal sac and nasolacrimal duct: a case report. Laryngoscope. 2003 Jun;113(6):940–942.
6. Brennan PA, Kersten RC, Schneider S, et al. A case of primary adenocarcinoma of the lacrimal sac. Orbit. 2005 Dec;24(4):291–293.
7. Alahbadi CR, Weed UT, Walker TJ, et al. En bloc resection of lacrimal sac tumors and simultaneous orbital reconstruction: surgical and functional outcomes. Ophthalmic Plast Reconstr Surg. 2014 Nov-Dec;30(6):459–467.
8. Nguyen PL, Aliabhai SM, Basaria S, et al. Adverse effects of androgen deprivation therapy and strategies to mitigate them. Eur Urol. 2015 May;67(5):825–836.
9. Locati LD, Quattrone P, Bosi P, et al. A complete remission with androgen-deprivation therapy in a recurrent androgen receptor-expressing adenocarcinoma of the parotid gland. Ann Oncol. 2003 Aug;14(8):1327–1328.
10. Boman E, van Boxtel W, Bouter J, et al. Androgen deprivation therapy for androgen receptor-positive advanced salivary duct carcinoma: a nationwide case series of 35 patients in The Netherlands. Head Neck. 2018 Mar;40(3):605–613.
11. Fushimi C, Tada Y, Takahashi H, et al. A prospective phase II study of combined androgen blockade in patients with androgen receptor-positive metastatic or locally advanced unresectable salivary gland carcinoma. Ann Oncol. 2018 Apr;29(4):979–984.
12. Dalin MG, Watson PA, Ho AL, et al. Androgen receptor signaling in salivary gland cancer. Cancers (Basel). 2017 Feb 6;9(2).
13. Denham JW, Steigler A, Lamb DS, et al. Short-term neoadjuvant androgen deprivation and radiotherapy for locally advanced prostate cancer: 10-year data from the TROG 96.01 randomised trial. Lancet Oncol. 2011 May;12(5):451–459.
14. Roach M, Bae K, Speight J, et al. Short-term neoadjuvant androgen deprivation therapy and external-beam radiotherapy for locally advanced prostate cancer: long-term results of RTOG 8610. J Clin Oncol. 2008 Feb 1;26(4):585–591.
15. Shelley MD, Kumar S, Wilk T, et al. A systematic review and meta-analysis of randomised trials of neo-adjuvant hormone therapy for localised and locally advanced prostate carcinoma. Curr Treat Rev. 2009 Feb;3(1):9–17.