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Case Report

HER2-Positive Lacrimal Sac Squamous Cell Carcinoma in a 57-Year-Old Man

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Keywords
Epithelial lacrimal sac tumors · Squamous cell carcinoma · HER2 amplification · Molecular profile

Abstract
Introduction: Lacrimal sac squamous cell carcinoma (SCC) is a rare tumor. Only 241 cases of lacrimal sac SCC have been reported in the literature. However, the detailed molecular profile of this tumor is unknown. ***Case Presentation:*** Fifty-seven-year-old Caucasian male presented with a 6-month history of epiphora. Multimodal examination revealed a unilateral lacrimal sac SCC T4aN0M0. The patient underwent primary surgery with subsequent chemoradiotherapy. The patient was alive 18 months after the end of the treatment, with no signs of local or distant relapse. Complex molecular profiling revealed the FGFR p.G388R variant, HER2 amplification,

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and progression phenotype. ***Conclusion:*** Here, we describe a clinical case of a male patient with lacrimal sac SCC with a careful description of the disease history, treatment, and molecular-genetic patterns of the tumor. This is the first report of HER2-positive lacrimal sac SCC.

Introduction

Epithelial lacrimal sac tumors are rare, with squamous cell carcinoma (SCC) being the most common histological type [1]. These tumors are commonly affected in middle-aged patients, and unilateral epiphora and palpable masses are the most common clinical signs. Surgery, radiotherapy, and platinum-based chemotherapy as monotherapy or in combination are traditional treatment options for lacrimal sac SCC [2, 3]. Here, we present a case of a middle-aged male with lacrimal sac SCC with a careful description of the disease history, treatment plan, and molecular-genetic patterns of the tumor. 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/10.1159/000536061).

Case Presentation

Fifty-seven-year-old Caucasian male was admitted into hospital with a 6-month history of epiphora. Physical examination revealed a painful mass in the right orbital region. A complex examination was performed. Ultrasonography showed a tumor mass in the area of the right lacrimal sac with clear margins. Contrast-enhanced head and neck MRI revealed a soft tissue mass of 17 × 17 × 19 mm with moderate vascularization in the area of the right lacrimal sac and proximal part of the right nasolacrimal duct with destruction of the right orbital lamina of the ethmoid bone (Fig. 1). Fine needle aspiration biopsy revealed SCC.

Via PET/CT lymph node involvement and metastasis were excluded (Fig. 2). Thus, the diagnosis of the lacrimal sac SCC, T4aN0M0, stage IV Jones classification, stage III Song et al. [4] classification was confirmed (Table 1) [4–7].

The primary surgical procedure was indicated. Despite close contact of the tumor mass with the right eye and eye muscles and the risk of R1 resection, the patient did not provide consent for extended resection. Organ-sparing endoscopic-assisted lacrimal sac tumor resection extended via a part of the right orbital lamina, and nasolacrimal duct resection was performed. First, the lateral nasal wall mucosal flap was dissected via a nasal endoscopic approach. After anterior ethmoidectomy, a lacrimal sac tumor with a part of the orbital lamina was mobilized. A skin incision surrounding the tumor was made, and the lacrimal sac tumor resection en bloc with the right orbital lamina, the nasolacrimal duct, and the skin flap were completed. The skin defect was closed via a cheek flap, and the nasal endoscopic reconstruction of the lateral nasal mucosal wall was performed. Blood loss was 50 mL, and there were no intraoperative complications, Class-Intra 0 [8]. The postoperative course was uneventful, Clavien-Dindo 0 [9]. The patient was discharged on postoperative day 1 (POD 1), and sutures were removed on POD 10. Histological examination confirmed lacrimal sac keratinizing SCC grade 2 (Ki-67 98%) with invasion to the orbital plate periosteum and nasolacrimal duct and R1 resection at the level of the medial rectus and superior oblique muscles (Fig. 3).

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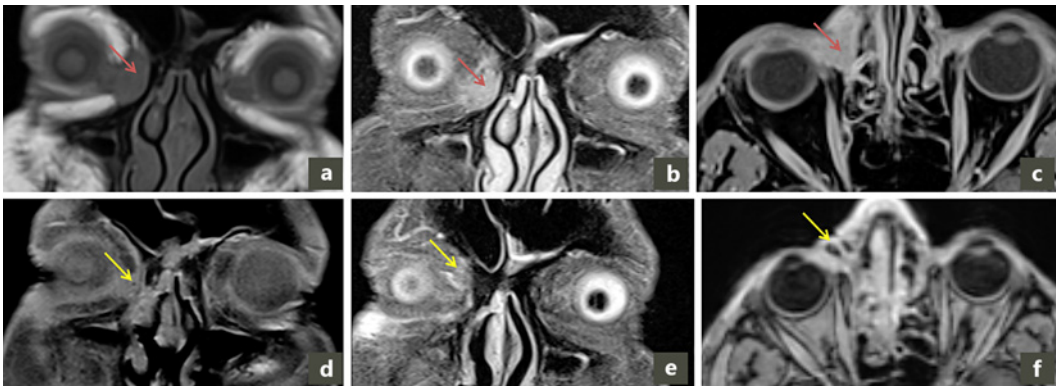

Fig. 1. Baseline MRI scans (**a–c**) and postoperative follow-up (**d–f**). The vascularized soft tissue mass (red arrows) and postoperative scar tissue (yellow arrows) can be seen in the right orbit. Precontrast coronal T1 (**a**, **d**), STIR (**b**, **e**), and postcontrast axial (**c**, **f**) slices.

Chemoradiotherapy (CRT) was initiated on POD 27. Additive radiotherapy 60 Gy (fraction 5 × 2 Gy/every week) was combined with weekly cisplatin (40 mg/m^2, 240 mg/m^2). No significant side effects were observed during the treatment. At the time of this study, the follow-up period was 18 months, and no signs of local or distant relapse or side effects were observed.

Complex molecular-genetic testing was performed, considering the rarity of the disease. Immunohistochemistry (IHC) revealed a stable MSI status, positive PD-L1 status (SP263 and 22c3), CPS = 38, TPS = 3%, positive HER2/Neu (3+), and panNTRK-negative expression. Additionally, PD-L1 was overexpressed, as determined by qPCR. Using FISH, c-erbB2 (HER2) amplification was identified (HER2:CEN17 = 2, 5) (Fig. 3).

We examined the gene expression activity of all human genes (approximately 21,000) in the tumor tissue using >34 K gene expression markers and hybridization techniques: PD-1, TIGIT, CTLA4, IDO1, LAG3 and epidermal growth factor receptor overexpression and wild-type TP53 were found. In addition, elevated expression of the A2b receptor, TGFb1, and COX-2 was observed.

Finally, next-generation sequencing target oncological panel (500 genes, Oncomine Comprehensive Assay v4.4, an Ion S5 System) identified the FGFR p.G388R variant, BAP1, MLH1, and RB1 deletions. Low tumor mutation burden was identified (4, 76 mutations/megabases).

Discussion

Primary tumors of the lacrimal drainage system are rare. According to Krishna and Coupland [1], approximately 775 cases were described in the literature. All lacrimal sac lesions can be subdivided into three groups: primary epithelial neoplasm, primary non-epithelial neoplasm, and inflammatory lesions [10–12]. Malignant epithelial neoplasms constitute the majority of lacrimal sac tumors [13, 14]. In 2021, Singh and Ali [15] performed a review of available literature about primary malignant epithelial tumors of the lacrimal sac: authors identified a total of 431 patients, and clinical symptoms and treatment details were available in 331 cases. SCC is the most common histological type of SCC (approximately 60%) [16, 17]. Singh and Ali [15] identified 241 patients with lacrimal sac SCC in the literature.

Commonly, epithelial tumors of the lacrimal sac are unilateral and affect middle-aged adult patients (median age 50–60 years) [15]. Meel et al. [18] described the clinical case of a 6-

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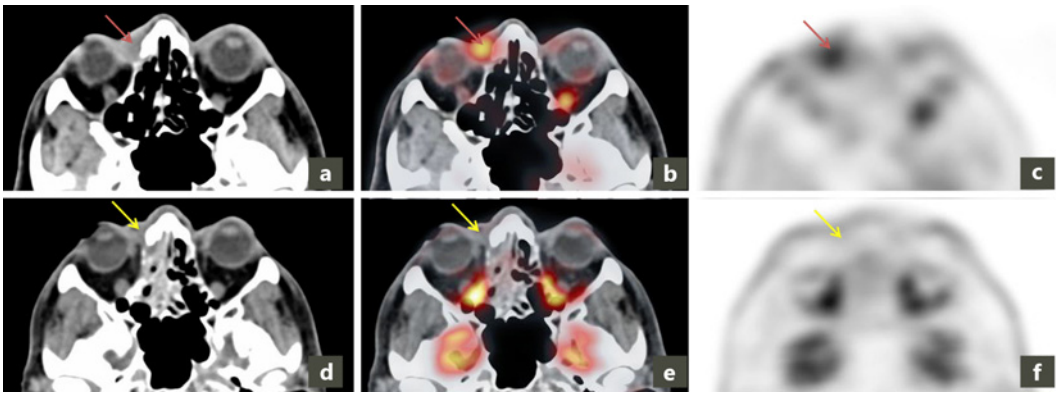

Fig. 2. Baseline PET-CT (**a–c**) and postoperative follow-up (**d–f**). Pathological metabolic activity up to SUVmax = 8.1 was detected in the right orbit soft tissue mass (red arrows). No metabolic activity was found in the postoperative scar tissue (yellow arrows). CT scans (**a**, **d**), fusion (**b**, **e**), and corresponding PET (**c**, **f**) images.

Table 1. Disease staging

	Stage	Description	Confirmation
TNM [5]	T4aN0M0	The tumor has invaded the periosteum	Orbital plate of the right part of the ethmoidal bone destruction
Jones [6]	IV	Extension beyond sac	MRI sign of the nasolacrimal duct invasion with the ethmoidal bone destruction
Song et al. [4]	III	Tumor invades the nasolacrimal canal	MRI sign of the nasolacrimal duct invasion with the ethmoidal bone destruction

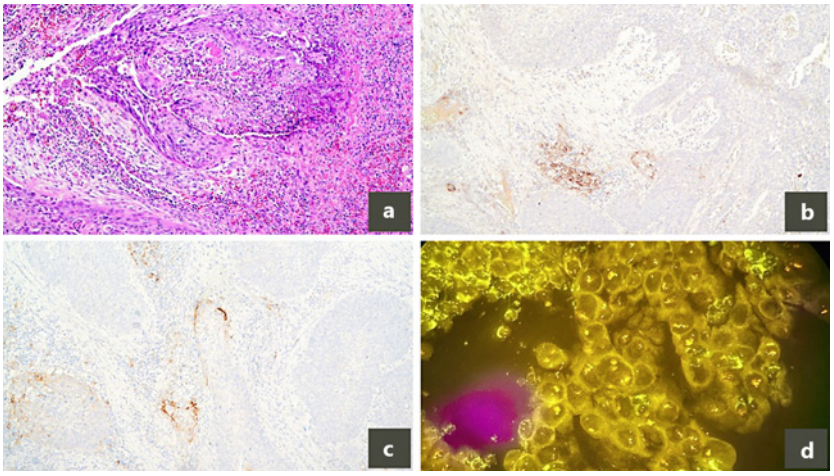

Fig. 3. **a** Hematoxylin staining. ×40, complex of SCC with keratinizing signs. **b** PD-L1 (22c3) staining. ×100, CPS = 38, TPS = 3%. **c** PD-L1 (SP263) staining. ×100, CPS = 38, TPS = 3%. **d** FISH HER2/neu, strong increase in the HER2:CEN17 ratio over 2.5.

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year-old boy with lacrimal sac SCC. The patient had tumor progression after neoadjuvant chemotherapy [18]. Cases of metachronous tumors involving the contralateral lacrimal sac have been described in adults [19, 20]. Lin et al. [21] described a rare case of lacrimal sac primary SCC with synchronous tonsillar primary SCC. The authors emphasize the significance of additional examinations, including nasoendoscopy and PET-CT, in rare head and neck cancers.

Epiphora and mass lesion are the most common clinical features, also features similar to dacryocystitis are often observed [11, 15]. In addition, the latent clinical course is typical for lacrimal sac malignant tumors. Matos et al. [22] reported the clinical case of a 63-year-old male patient with an 8-year history of unilateral epiphora in the right eye. The patient was not examined during this period. During dacryocystorhinostomy, tumor mass was found, and a biopsy revealed SCC. In the described case, the most common clinical signs were observed: the patient complained of unilateral epiphora, and physical examination revealed a painful mass in the right orbital area.

In 1956, Jones proposed a classification of lacrimal sac tumors based on clinical signs: epiphora only (I), simulated dacryocystitis (II), painless nonreducible swelling (III), and extension beyond the sac (IV). This classification considers the clinical signs of the disease and is helpful for the primary understanding of tumor process spread [6]. As an alternative to the TNM classification, Song et al. [4] proposed the following staging method:

- Stage I: the tumor is confined to the lacrimal sac fossa without a palpable mass or invasion of the surrounding tissues.
- Stage II: tumor invades the globe, nasolacrimal duct, lacrimal canaliculi, caruncula lacrimalis, or palpebral conjunctiva.
- Stage III: tumor invades the nasal cavity/nasolacrimal canal/ethmoid sinus/sphenoid sinus/maxillary sinus/frontal sinus, peripheral bone, or skin.
- Stage IV: the tumor invades the orbital apex, meninges, brain, lymph node, or distant metastasis.

Authors reported a series of 69 patients with lacrimal sac SCC and demonstrated that lymph node involvement and staging were associated with negative outcomes [4]. Surgery, radiotherapy, and platinum-based chemotherapy as monotherapy or in combination are traditional treatment options for lacrimal sac SCC [2, 3]. Zhang et al. [23] recommended concurrent CRT with cisplatin, fluorouracil, and docetaxel and subsequent surgery in patients with lacrimal sac carcinomas. In 2020, Song et al. [24] showed that radiotherapy alone could achieve excellent outcomes without severe complications in patients with lacrimal sac SCC. In the study, 17 patients were included (none of them had distant metastasis, and 8 had stage IV disease). The 5-year overall survival, progression-free survival, locoregional control, and disease metastasis-free survival rates were 84.7%, 73.5%, 93.8%, and 78.4%, respectively [24]. Chemotherapy (induction or concurrent) can help preserve organs in locally advanced cases. Song et al. [16] proposed to use chemotherapy in addition to radiotherapy in cases of lymph node involvement and advanced stages. Ogawa et al. [25] suggested that positive p16 IHC can be used as biomarker of tumor chemosensitivity. Authors used neoadjuvant CRT in 2 patients with positive p16 IHC and positive human papillomavirus (HPV) RNA in situ hybridization locally advanced squamous cell lacrimal sac carcinoma. In 1 case, complete response was confirmed via PET-CT, and in second case, tumor shrinked and R0 endoscopic tumor resection was performed [25]. In our case, primary surgery and adjuvant concurrent CRT with cisplatin were chosen, considering the absence of lymph node involvement and distant metastasis.

In 2022, Sun et al. [26] reported the first experience of transcatheter arterial infusion chemotherapy and embolization in a 34-year-old male with locally advanced lacrimal sac SCC with bone destruction who received two transcatheter arterial infusion chemotherapies (lobaplatin and docetaxel). After two procedures, the tumor size was reduced, but the bone destruction was stable. The patient also received concurrent radiochemotherapy and targeted therapy (anlotinib). The follow-up period was 10 months, and there was no evidence of recurrence.

Lacrimal sac SCC is associated with HPV infection. In a study by Hongo et al. [27], a series of 6/7 lacrimal sac SCC were positive for high-risk HPV (via in situ hybridization). HPV positivity was associated with young age, non-keratinizing histology, p16-positivity, and loss of Rb expression. For head and neck SCC epidermal growth factor receptor overexpression, alterations of the TP53, phosphatidylinositol 3-kinase (PIK3CA), and phosphatase and tensin homolog are frequent events [28]. In KEYNOTE-012 study, efficacy of pembrolizumab in patients with PD-L1-positive metastatic head and neck cancer has been demonstrated [29]. According to last meta-analysis, patients with PD-L1-positive head and neck SCC, who received PD-1/L1 inhibitors, have a better tumor response and overall survival [30]. The Food and Drug Administration (FDA) has approved anti-PD[L]-1 drugs for tumor site-agnostic solid tumor indication [31].

Controversially, hyperprogression of sinonasal SCC after PD-L1 inhibitors has been already described [32]. In this case, the molecular landscape of the tumor was distinctly altered after pembrolizumab treatment [32]. It makes sense to analyze the molecular-genetic profile of rare tumors when the efficiency of anti-PD[L]-1 drugs is low or absent.

In our case, the molecular-genetic analysis of the tumor showed controversial data: stable MSS status and low tumor mutation burden, but positive PD-L1 IHC and qPCR, overexpression of PD-1, TIGIT, CTLA4, IDO1, and LAG3 were identified. Using next-generation sequencing, FGFR p.G388R was found, and this variant was earlier identified in cancer patients with a high risk of recurrence and poor outcome [33, 34]. In addition, expression analysis showed the progression phenotype of this tumor: adenosine A2b receptor was found to be a driver of progression in oral SCC cancer, and TGF-beta can undergo a conversion from tumor suppressor to tumor promoter in squamous cell cancer [35, 36].

Importantly, positive HER2/Neu IHC status and HER2 c-erbB2 (HER2) amplification were identified using FISH. Two cases of extremely rare lacrimal sac HER2 (IHC)-positive ductal adenocarcinoma have been described in the literature [37, 38]. According to recent data, trastuzumab deruxtecan is effective in different tumor types with positive HER2 status [39]. Nevertheless, we did not identify cases of HER2-positive lacrimal sac SCC, and the potential effectiveness of antiHER2 drugs is also unknown.

Conclusion

In this article, we describe the clinical case of a 57-year-old patient with lacrimal sac SCC with careful description of disease history, treatments, and molecular-genetic patterns of the tumor. From our point of view, it is important to provide a detailed description of the experience of treating patients with lacrimal sac SCC to improve our knowledge of this disease.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. Ethical approval is not required for this study (clinical case) in accordance with national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Nikolay Grachev: article design development, text writing, and responsibility for the surgical procedure explanation; Gavriil Rabaev: article design development, text writing, and responsibility for the integrity of all parts of the work; Ashot Avdalyan: data collection for publication and responsibility for the pathomorphology part of the work explanation; Igor Znamenskiy: text editing and responsibility for the figure preparation; Dmitry Mosin: participation in data collection and responsibility for the figure preparation; Dmitry Ustyuzhanin: writing the article's body and responsibility for the figure preparation; Gennady Rabaev: development of article design, data collection, article's text editing, and approval of the final version of the manuscript; and Martin Lužbeták: responsibility for the molecular-genetic part description, development of article, and approval of the final version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

1 Krishna Y, Coupland SE. Lacrimal sac tumors: a review. Asia Pac J Ophthalmol. 2017;6(2):173–8.
2 Valenzuela AA, Selva D, McNab AA, Simon GB, Sullivan TJ. En bloc excision in malignant tumors of the lacrimal drainage apparatus. Ophthalmic Plast Reconstr Surg. 2006;22(5):356–60.
3 Alabiad CR, Weed DT, Walker TJ, Vivero R, Hobeika GA, Hatoum GF, et al. En bloc resection of lacrimal sac tumors and simultaneous orbital reconstruction: surgical and functional outcomes. Ophthalmic Plast Reconstr Surg. 2014;30(6):459–67.
4 Song X, Wang S, Wang J, Wang W, Wang S, Yang G, et al. Clinical management and outcomes of lacrimal sac squamous cell carcinoma. Head Neck. 2019;41(4):974–81.
5 Rootman J, White VA. Changes in the 7th edition of the AJCC TNM classification and recommendations for pathologic analysis of lacrimal gland tumors. Arch Pathol Lab Med. 2009;133(8):1268–71.
6 Jones SI. Tumors of the lacrimal sac. Am J Ophthalmol. 1956;42(4 Part 1):561–6.
7 Stephen BE, David RB, Carolyn CC, et al. Head and neck. In: Edge SE, Byrd DR, Compton CC, editors. AJCC cancer staging manual. 7th ed. New York (NY): Springer; 2010. p. 69–73.
8 Dell-Kuster S, Gomes NV, Gawria L, Aghlmandi S, Aduse-Poku M, Bissett I, et al. Prospective validation of classification of intraoperative adverse events (ClassIntra): international, multicentre cohort study. BMJ. 2020;370:m2917.
9 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6,336 patients and results of a survey. Ann Surg. 2004;240(2):205–13.
10 Stefanyszyn MA, Hidayat AA, Pe'er JJ, Flanagan JC. Lacrimal sac tumors. Ophthalmic Plast Reconstr Surg. 1994;10(3):169–84.
11 von Goscinski C, Koch KR, Cursiefen C, Heindl LM. Tumoren der ableitenden Tränenwege [Tumors of the lacrimal drainage system]. HNO. 2016;64(6):386–93.

12 Heindl LM, Jünemann AG, Kruse FE, Holbach LM. Tumors of the lacrimal drainage system. Orbit. 2010;29(5):298–306.
13 Montalban A, Liétin B, Louvrier C, Russier M, Kemeny J-L, Mom T, et al. Malignant lacrimal sac tumors. Eur Ann Otorhinolaryngol Head Neck Dis. 2010;127(5):165–72.
14 Parmar DN, Rose GE. Management of lacrimal sac tumours. Eye. 2003;17(5):599–606.
15 Singh S, Ali MJ. Primary malignant epithelial tumors of the lacrimal drainage system: a major review. Orbit. 2021;40(3):179–92.
16 Song X, Wang J, Wang S, Wang W, Wang S, Zhu W. Clinical analysis of 90 cases of malignant lacrimal sac tumor. Graefes Arch Clin Exp Ophthalmol. 2018;256(7):1333–8.
17 Zhang R, Qian J, Meng F, Yuan Y, Bai M, Bi Y, et al. A staged procedure in the treatment of primary lacrimal sac epithelial malignancy: a retrospective cases analysis. Ophthalmic Plast Reconstr Surg. 2019;35(2):187–92.
18 Meel R, Surve A, Bakhski S, Kashyap S, Gupta B, Sharma S. A rare case of pediatric lacrimal sac: squamous cell carcinoma. J Pediatr Ophthalmol Strabismus. 2019;56:e8–11.
19 Hodgson N, Whipple K, Lin JH, Brumund KT, Kikkawa DO, Korn BS. Bilateral squamous cell carcinoma of the lacrimal sac. Ophthalmic Plast Reconstr Surg. 2013;29(6):e149–51.
20 Islam S, Eisenberg RL, Hoffman GR. Malignant transformation of metachronous bilateral Schneiderian inverted papilloma of the lacrimal sac: management considerations and the contentious issue of orbital exenteration. Eur Arch Otorhinolaryngol. 2014;271(7):1857–60.
21 Lin Z, Philpott C, Sisson K, Hemmant B. Lacrimal sac primary squamous cell carcinoma with synchronous tonsillar primary squamous cell carcinoma. Orbit. 2020;39(5):374–8.
22 Matos AMF, Brega DR, Gollner AM, Gonçalves ACP. Chronic unilateral tearing as a sign of lacrimal sac squamous cell carcinoma. Arq Bras Oftalmol. 2021;84(6):602–5.
23 Zhang R, Qian J, Meng F, Yuan Y, Bai M, Bi Y, et al. A staged procedure in the treatment of primary lacrimal sac epithelial malignancy: a retrospective cases analysis. Ophthalmic Plast Reconstr Surg. 2019;35(2):187–92.
24 Song X, He H, Zhu Y, Wang S, Wang J, Wang W, et al. Treatment outcomes after definitive radio(chemo)therapy for 17 lacrimal sac squamous cell carcinoma. Br J Radiol. 2020;93(1115):20190633.
25 Ogawa T, Yo K, Okamoto H, Inukai D, Yamanaka S, Sano R, et al. A novel treatment strategy for advanced lacrimal sac carcinomas confirmed by p16 immunostaining. Semin Ophthalmol. 2022;37(3):307–12.
26 Sun MH, Yi WD, Shen L, Zhou L, Lu JX. Transcatheter arterial infusion chemotherapy and embolization for primary lacrimal sac squamous cell carcinoma: a case report. World J Clin Cases. 2022;10(21):7467–73.
27 Hongo T, Yamamoto H, Tanabe M, Yasumatsu R, Kuga R, Miyazaki Y, et al. High-risk HPV-related squamous cell carcinoma in the conjunctiva and lacrimal sac: clinicopathologic characteristics and diagnostic utility of p16 and Rb immunohistochemistry. Am J Surg Pathol. 2022;46(7):977–87.
28 Feldman R, Gatalica Z, Knezetic J, Reddy S, Nathan CA, Javadi N, et al. Molecular profiling of head and neck squamous cell carcinoma. Head Neck. 2016;38(Suppl 1):E1625–38. Epub 2015 Nov 28.
29 Seiwert TY, Burtness B, Mehra R, Weiss J, Berger R, Eder JP, et al. Safety and clinical activity of pembrolizumab for treatment of recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-012): an open-label, multicentre, phase 1b trial. Lancet Oncol. 2016;17(7):956–65.
30 Patel JJ, Levy DA, Nguyen SA, Knochelmann HM, Day TA. Impact of PD-L1 expression and human papillomavirus status in anti-PD1/PDL1 immunotherapy for head and neck squamous cell carcinoma-Systematic review and meta-analysis. Head Neck. 2020;42(4):774–86.
31 Marcus L, Lemery SJ, Keegan P, Pazdur R. FDA approval summary: pembrolizumab for the treatment of microsatellite instability-high solid tumors. Clin Cancer Res. 2019;25(13):3753–8.
32 Izreig S, Alzahrani F, Earles J, Mehra S, Judson BL, Pan Z, et al. Hyperprogression of a sinonasal squamous cell carcinoma following programmed cell death protein-1 checkpoint blockade. JAMA Otolaryngol Head Neck Surg. 2020;146(12):1176–8.
33 Kim JH, Jeong SY, Jang HJ, Park ST, Kim HS. FGFR4 Gly388Arg polymorphism reveals a poor prognosis, especially in asian cancer patients: a meta-analysis. Front Oncol. 2021;11:762528.
34 Peng T, Sun Y, Lv Z, Zhang Z, Su Q, Wu H, et al. Effects of FGFR4 G388R, V10I polymorphisms on the likelihood of cancer. Sci Rep. 2021;11(1):1373.
35 Kasama H, Sakamoto Y, Kasamatsu A, Okamoto A, Koyama T, Minakawa Y, et al. Adenosine A2b receptor promotes progression of human oral cancer. BMC Cancer. 2015;15:563.
36 Pang X, Tang YL, Liang XH. Transforming growth factor-β signaling in head and neck squamous cell carcinoma: insights into cellular responses. Oncol Lett. 2018;16(4):4799–806. Epub 2018 Aug 17.
37 Ueda H, Hirao M, Tsukada Y, Kikuchi T, Sugiyama K, Kato Y, et al. Primary HER2-positive lacrimal SAC cancer. Ann Oncol. 2013;24(Suppl 9):ix84, ix66–ix99.
38 Vagia E, Economopoulou P, Oikonomopoulos N, Athanasiadis I, Dimitriadis G, Psyrri A. Androgen-receptor positive lacrimal sac adenocarcinoma demonstrating long-lasting response to LHRH analog plus abiraterone treatment. Front Oncol. 2015;5:10.
39 Meric-Bernstam F, Makker V, Oaknin A, Oh D, Banerjee SN, Martin AG, et al. Efficacy and safety of trastuzumab deruxtecan (T-DXd) in patients (pts) with HER2-expressing solid tumors: DESTINY-PanTumor02 (DP-02) interim results. J Clin Oncol. 2023;41(17 suppl):LBA3000.