



Letter to the editor

Trastuzumab-based therapy is effective for salivary duct carcinoma: Case report and review of the literature



Dear Editor-in-Chief,

In response to the article published in the journal of *Oncology Letters* entitled, “Salivary duct carcinoma of the parotid gland: A case report and review of the literature,” I would like to describe the patient’s follow-up therapy and survival status.

A 54-year-old man with a chief complain of a painless mass in the right parotid gland for almost two weeks presented to the Peking University Shenzhen Hospital. A physical examination revealed a firm and mobile lump that was not attached to the overlying skin. Magnetic resonance imaging (Fig. 1) of the head and neck showed a neoplasm measuring 26 × 22 mm in the deep lobe of the right parotid gland, for which he underwent radical surgery in August 2013. The postoperative pathology confirmed that six out of eight lymph node metastases at cervical levels III and IV on the right side of the neck showed vessel carcinoma embolus and perineural invasion. Histopathological analysis confirmed positive expressions of human epidermal growth factor 2 (Her-2), cytokeratin (CK)-7, p63, and calponin. Immunostaining for estrogen and progesterone receptors were negative. The final pathological staging was pT4N2M0 according to the World Health Organization International Classification of Tumors [1].

Fifteen days after surgery, the patient underwent a PET/CT scan that showed several small swollen lymph nodes in the lower right neck; the maximum diameter of the lymph nodes was 13 × 10 × 11 mm, with a standardized uptake value of 5.4. The other organs appeared negative for distant metastatic lesions. Results of the carcinoembryonic antigen test showed a value of 11.42 ng/ml. Contrast-enhanced MRI

also confirmed the presence of swollen lymph nodes, measuring 16 × 9 × 10 mm, in the lower right neck, which indicated tumor recurrence after surgery. Genetic analysis showed that exons 18, 19, 20, and 21 of the *EGFR* gene carried the wildtype allele. Subsequently, two cycles of adjuvant chemotherapy were administered 20 and 41 days after surgery, respectively. The regimen consisted of trastuzumab on day 1, abraxane 260 mg/m² and cisplatin 80 mg/m² on day 2. The dosage of trastuzumab was 8 mg/kg in the first cycle, followed by 6 mg/kg in subsequent cycles. Concurrent chemoradiation was performed using intensity modulated radiation therapy (IMRT) 20 days after the first two cycles of chemotherapy were completed. This concurrent regimen comprised of trastuzumab (6 mg/kg, D1) and cisplatin (80 mg/m², D2). The cumulative radiation doses were 66 Gy to the primary tumor and 60 Gy to the involved neck area. The patient tolerated the treatment well and had only grade 2 mucositis according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, during concurrent chemoradiotherapy.

The patient underwent contrast-enhanced MRI of the nasopharyngeal region every three months during the follow-up assessment, and imaging evaluation showed sustained complete response for already 5 years.

Salivary duct carcinoma (SDC) was first described by Kleinsasser et al. in 1968. It resembles in situ infiltrative ductal adenocarcinoma of the breast and is the most aggressive salivary gland tumor in that most patients die within four years from diagnosis [2]. The tumor usually presents as a rapidly growing painless mass with facial nerve palsy, whose most characteristic feature is the formation of multiple large

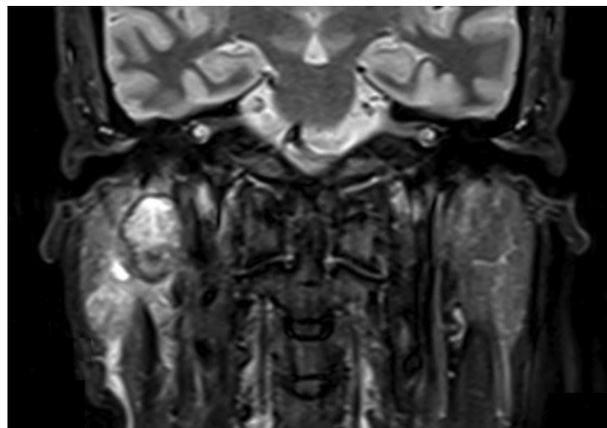


Fig. 1. Contrast-enhanced MRI revealing neoplasm in the deep lobe of the parotid gland (2013-8-11).

ducts with cribriform configurations [3,4]. The treatment usually includes total parotidectomy with a neck dissection followed by adjuvant radiotherapy. About one-third of SDC cases show overexpression of the HER-2 protein. Alotaibi et al. identified 12 studies that correlated the existence of HER2/neu and reported that it was associated with poor prognosis and aggressive behavior [5]. Nicole et al. systematically reviewed the clinical characteristics and effects of treatment, including targeted therapy and androgen deprivation therapy and demonstrated the superior efficacy of trastuzumab-based therapy [6].

Trastuzumab (Herceptin), an inhibitor of HER-2, has been used for systemic therapy in patients with advanced SDC with promising responses. The patient in our report suffered from a rapid recurrence in the neck region within a mere two weeks after radical surgery. However, he received two cycles of a combination of trastuzumab with abraxane and cisplatin, a frequent regimen in breast cancer, as well as concurrent chemoradiation. Furthermore, the patient sustained complete response for already 5 years since radiation. Thorpe et al. reported two similar cases: one patient with lung metastasis who achieved a partial response after receiving paclitaxel/trastuzumab combination for six months in total, and the other patient who achieved complete response after three months of trastuzumab-based therapy and had already been on maintenance trastuzumab-based therapy for seven months [7]. Other studies have also claimed the efficacy of maintenance trastuzumab-based therapy [8–10]. Our case shows prominent efficacy with only three cycles of trastuzumab-based therapy that significantly shortened the mean hospitalization days and eased the patient's economic burden. In summary, trastuzumab-based therapy followed by concurrent radiochemotherapy is well tolerated and yields promising objective response and local control, which merits further exploration.

Conflict of interest statement

The authors declared that there is no conflict of interest.

References

- [1] Seifert G, Brocheriou C, Cardesa A, Eveson JW. WHO international histological classification of tumours. Tentative histological classification of salivary gland tumours. *Pathol Res Pract* 1990;186:555–81.
- [2] Kleinsasser O, Klein HJ, Hubner G. Salivary duct carcinoma. A group of salivary gland tumors analogous to mammary duct carcinoma. *Arch Klin Exp Ohren Nasen Kehlkopfheilkd* 1968;192:100–5.
- [3] AL-Qahtani KH, Tunio MA, Bayoumi Y, Gurusamy VM, Bahamdain FAA, Fatani H. Clinicopathological features and treatment outcomes of the rare, salivary duct carcinoma of parotid gland. *J Otolaryngol - Head Neck Surg* 2016;45.
- [4] Luk PP, Weston JD, Yu B, Selinger CI, Ekmejian R, Eviston TJ, et al. Salivary duct carcinoma: clinicopathologic features, morphologic spectrum, and somatic mutations. *Head Neck* 2016;38(Suppl. 1):E1838–47.
- [5] Alotaibi AM. Human epidermal growth factor receptor 2 (HER2/neu) in salivary gland carcinomas: a review of literature. *J Clin Diagnost Res* 2015.
- [6] Schmitt NC, Kang H, Sharma A. Salivary duct carcinoma: an aggressive salivary gland malignancy with opportunities for targeted therapy. *Oral Oncol* 2017;74:40–8.
- [7] Thorpe LM, Schrock AB, Erlich RL, Miller VA, Knost J, Le-Lindqwister N, et al. Significant and durable clinical benefit from trastuzumab in 2 patients with HER2-amplified salivary gland cancer and a review of the literature. *Head Neck* 2017;39:E40–4.
- [8] Krishnamurthy J, Krishnamurthy DM, Baker JJ, Zhen W, Lydiatt D, Ganti AK. Salivary duct carcinoma responding to trastuzumab-based therapy: case report and review of the literature. *Head Neck* 2013;35:E372–5.
- [9] Limaye SA, Posner MR, Krane JF, Fonfria M, Lorch JH, Dillon DA, et al. Trastuzumab for the treatment of salivary duct carcinoma. *Oncologist* 2013;18:294–300.
- [10] Kaidar-Person O, Billan S, Kuten A. Targeted therapy with trastuzumab for advanced salivary ductal carcinoma: case report and literature review. *Med Oncol* 2012;29:704–6.

Shihai Wu*

Department of Radiation Oncology, Second Clinical Medicine College of Jinan University, Shenzhen People's Hospital, China
E-mail address: Jiangxiwu84@126.com.

Rencui Quan¹

Department of Radiation Oncology, Second Clinical Medicine College of Jinan University, Shenzhen People's Hospital, China

Ling Han²

Department of Otorhinolaryngology, Second Clinical Medicine College of Jinan University, Shenzhen People's Hospital, China

* Corresponding author.

¹ Contributed equally to this research and shared the co-first author.

² Contributed equally to this research and shared the co-first author.