WITHDRAWN: Pembrolizumab combined with chemotherapy to treat parotid adenocarcinoma with pulmonary metastasis: a case report

YaDi Wu
First Affiliated Hospital of Xinxiang Medical University
HouYun Zhang
Xinxiang First People's Hospital
He Wang
First Affiliated Hospital of Xinxiang Medical University
LiFang Zhang
Xinxiang First People's Hospital
YanTing Liu
First Affiliated Hospital of Xinxiang Medical University
HongYan Zhou
Xinxiang First People's Hospital
Ping Lu
First Affiliated Hospital of Xinxiang Medical University
Min Zhang
zhangmin1982@xxmu.edu.cn

First Affiliated Hospital of Xinxiang Medical University

Research Article

Keywords: Parotid adenocarcinoma, pulmonary metastasis, immunotherapy, chemotherapy, pembrolizumab, curative

Posted Date: June 1st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1673582/v1

Additional Declarations: No competing interests reported.

EDITORIAL NOTE:

The full text of this preprint has been withdrawn by the authors while they make corrections to the work. Therefore, the authors do not wish this work to be cited as a reference. Questions should be directed to the corresponding author.

Abstract

Background: Our research for treating parotid adenocarcinoma was relatively slow due to its rare incidence. The consensus for treating pulmonary metastasis from parotid adenocarcinoma remains unclear as modern medicine is ineffective for patients with distant metastasis of primary parotid adenocarcinoma.

Case presentation: A male patient with pulmonary metastasis from primary parotid adenocarcinoma was presented and received three courses of pembrolizumab combined with chemotherapy as a first-line treatment. After which, there was an opportunity for surgery. No tumor cells were found in postoperative pathology. The patient achieved a complete response (CR) that continued on a follow-up of more than one year.

Conclusions: This case emphasizes a definitive multimodal approach, with immunotherapy being a promising treatment in patients with pulmonary metastasis from parotid adenocarcinoma.

Introduction:

Salivary gland tumors are classified into benign and malignant tumors. Cancer of the salivary gland is threatening to the human body. Malignant tumors of salivary glands are rare. The most common tumor site is the parotid gland. Tumors of the parotid gland account for 80% of salivary gland tumors [1]. Most parotid gland tumors present with no obvious symptoms in the early stage of onset. Clinically, parotid gland tumors are found inadvertently or during physical examination. Parotid adenocarcinoma is a malignant tumor of the parotid gland, comprising 10% of all parotid cancers. Still, compared to other types of malignant tumors, it does not frequently cause distant metastases. The most common site for metastases is the lung [2]. In modern medicine, surgical resection is the primary treatment for parotid adenocarcinoma. According to reports, the five-year survival rate of parotid adenocarcinoma is approximately 95%. Low-stage and low-grade tumors can generally be cured solely with surgery. Surgery is the mainstay therapy, while adjuvant radiation therapy plays a significant role in locoregional disease control [3, 4].

Pembrolizumab (Keytruda) is a humanized monoclonal anti-PD1 antibody that has been extensively studied in numerous malignancies. Currently, pembrolizumab has been approved for use in over 80 countries, covering more than 12 indications of nine tumor types, including melanoma, non-small cell lung cancer, head and neck cancer, Hodgkin lymphoma, bladder cancer, cervical cancer, gastric cancer, and B cell lymphoma. In refractory non-small cell lung cancer (NSCLC), pembrolizumab induced ORRs of 19–25% [5]. This provides an alternative treatment of parotid adenocarcinoma with pulmonary metastasis. However, there is little evidence as few studies reported pembrolizumab to treat parotid adenocarcinoma with pulmonary metastasis. Herein, we present a patient with pulmonary metastasis from primary parotid adenocarcinoma and a short review of the literature.

Case Presentation:

In April 2020, a 69-year-old man presented with a swelling of the right parotid and developed 11 years ago without known etiology. The swelling in the front of the right ear has increased rapidly with pain from the past four months. On April 22, 2020, an ultrasound of the parotid gland showed solid space with multiple swollen lymph nodes of the right parotid gland. On April 27, 2020, the patient underwent a percutaneous core biopsy for the swelling of his parotid gland. On April 29, 2020, pathological examination of the right parotid gland revealed a malignant tumor (right parotid gland), and a further diagnosis was made by immunohistochemistry. Results of immunohistochemistry (Fig. 1) were as followed: P63 (+), CK5/6 (+), CK7 (+), Cam5.2 (+), Vimentin (+), Ki67 (+, 70%), S-100 (-), CEA (-), and EMA (+). These results were consistent with the diagnosis of adenocarcinoma. Physical examination showed an inflamed anterior mass of the right ear and multiple swollen lymph nodes of the right parotid gland. On April 23, 2020, chest computed tomography (CT) scan displayed the following results (Fig. 2) : 1. multiple nodules of both lungs and considering the possibility of transfer, 2. bilateral emphysema: mild bronchiectasis of both lower lungs, 3. double lung hypostatic effect, 4. bilateral pleural local thickening, 5. multiple lymph nodes in mediastinum and bilateral hilar with no obvious swelling, 6. aortic and coronary atherosclerosis, and 7. low-density nodule on the left lobe of the thyroid. On April 23, 2020, computed tomography (CT) of parotid gland scan (Fig. 3) showed a space-occupying the right parotid gland and multiple peripheral swollen lymph nodes with malignant signs. The results suggested stage IV parotid gland adenocarcinoma cancer with lung metastases, and there was no opportunity for surgery. As first-line treatment, he received three courses of immunotherapy combined with chemotherapy. The medication regimen was as follows: The 1th cycle was initiated on May 1, 2020, pembrolizumab (venous 60 min) 200 mg Day 1; paclitaxel 400 mg (twice) Day 1, 7. And repeated every 3 weeks. The main adverse reaction during treatment was rash, for which dexamethasone was administered. After three treatment cycles, the condition of the patient improved, and surgery was considered. The patient underwent parotidectomy in October 2020. In postoperative pathology, no tumor cells were discovered. Regular outpatient re-examinations have been performed following surgery.

Discussion:

Cancer of the salivary gland is uncommon. Therefore, the research progress for treating salivary gland cancer has a slow pace. At present, the mainstay treatment is surgery and radiotherapy. However, as salivary gland cancer develops, the degree of malignancy will become higher with recurrences and metastasis. We can only provide comprehensive palliative care in this situation [6]. Chemotherapy currently has an insignificant curative effect on salivary gland cancer, and patient survival is difficult to predict [7]. Immunotherapy has advanced rapidly in recent years, particularly for tumors that lack therapeutic targets. The advent of immunotherapy has given patients hope [8]. Simultaneously, clinical studies have demonstrated that once patients respond to immunotherapy, it often results in long-term benefits, including complete remission of the disease.

A total of 26 patients with advanced PD-L1-positive SGC was enrolled in the trial of pembrolizumab in patients with PD-L1-positive advanced solid tumors (KEYNOTE-028; NCT02054806). All patients received ≥ one dose of pembrolizumab (safety population). Three patients achieved PR for an ORR of 12%. An additional 12 (46%) patients experienced stable disease (SD) for a disease control rate (CR + PR + SD) of 58% [9].

This report presents the case of stage IV parotid gland adenocarcinoma cancer with lung metastases and right facioplegia. After three courses of treatment with immunotherapy combined with chemotherapy, the tumor shrunk significantly, allowing for surgery. Following surgery, no tumor cells were found in pathology, and postoperative outpatient re-examination was carried out for nearly two months.

Tumors can be divided into "cold tumors" and "hot tumors." "Cold tumors" are tumors without immunogenicity; however, this is variable. Changes in the immune microenvironment of the patient could turn "cold tumor" into "hot tumor." In this report, the patient with salivary gland cancer benefited from immunotherapy. Furthermore, the following queries required attention and more research. How can "cold tumors" such as salivary gland cancer accumulate immune cells in tumor tissues and improve the immune microenvironment of salivary gland cancer? [10]. How to screen patients who would respond to immunotherapy? How can patients with salivary gland cancer benefit from immunotherapy in the future?

Declarations:

Acknowledgments: We gratefully acknowledge the patient reported here for allowing us to publish her case details and images.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Author contributions: The first draft of the manuscript was written by YaDi Wu.HouYun Zhang is the patient's attending physician.Medical records are mainly provided by HouYun Zhang, He Wang and YaDi Wu.The patients were followed-up by LiFang Zhang and YanTing Liu.The pathological results of the patient were provided by HongYan Zhou.Min Zhang and Ping Lu gave guidance on clinical problems.All authors reviewed the manuscript.

Informed consent: Written informed consent was obtained from the patient for the publication of his case details and images.

References:

1. Guzzo M, Locati LD, Prott FJ, Gatta G, McGurk M, Licitra L. Major and minor salivary gland tumors. Crit Rev Oncol Hematol. 2010 May;74(2):134-48. doi: 10.1016/j.critrevonc.2009.10.004. Epub 2009

Nov 24.

2. Dhaliwal J, Calafiore R, Bulsara KR, Onyiuke H. Vertebral Metastasis from Primary Parotid Adenocarcinoma. World Neurosurg. 2019 Jun;126:472-474. doi: 10.1016/j.wneu.2019.02.229. Epub 2019 Mar 15.
3. Lewis AG, Tong T, Maghami E. Diagnosis and Management of Malignant Salivary Gland Tumors of the Parotid Gland. Otolaryngol Clin North Am. 2016 Apr;49(2):343-80. doi: 10.1016/j.otc.2015.11.001.
4. Vander Poorten V, Bradley PJ, Takes RP, Rinaldo A, Woolgar JA, Ferlito A. Diagnosis and management of parotid carcinoma with a special focus on recent advances in molecular biology. Head Neck. 2012 Mar;34(3):429-40. doi: 10.1002/hed.21706. Epub 2011 May 25.
5. Kwok G, Yau TC, Chiu JW, Tse E, Kwong YL. Pembrolizumab (Keytruda). Hum Vaccin Immunother. 2016 Nov;12(11):2777-2789. doi: 10.1080/21645515.2016.1199310. Epub 2016 Jul 11.
6. Rodriguez CP, Parvathaneni U, Méndez E, Martins RG. Salivary Gland Malignancies. Hematol Oncol Clin North Am. 2015 Dec;29(6):1145-57. doi: 10.1016/j.hoc.2015.08.002. Epub 2015 Oct 17.
7. Even C, Baste N, Classe M. New approaches in salivary gland carcinoma. Curr Opin Oncol. 2019 May;31(3):169-174. doi: 10.1097/CCO.0000000000000527.
8. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al. Pembrolizumab plus Chemotherapy in Metastatic Non-Small-Cell Lung Cancer. N Engl J Med. 2018;378(22):2078-2092. doi:10.1056/NEJMoa1801005.
9. Cohen RB, Delord JP, Doi T, et al. Pembrolizumab for the Treatment of Advanced Salivary Gland Carcinoma: Findings of the Phase 1b KEYNOTE-028 Study. Am J Clin Oncol. 2018;41(11):1083-1088. doi:10.1097/COC.0000000000000429.
10. Theocharis S, Tasoulas J, Masaoutis C, Kokkali S, Klijanienko J. Salivary gland cancer in the era of immunotherapy: can we exploit tumor microenvironment?. Expert Opin Ther Targets. 2020;24(10):1047-1059. doi:10.1080/14728222.2020.1804863.

Figures

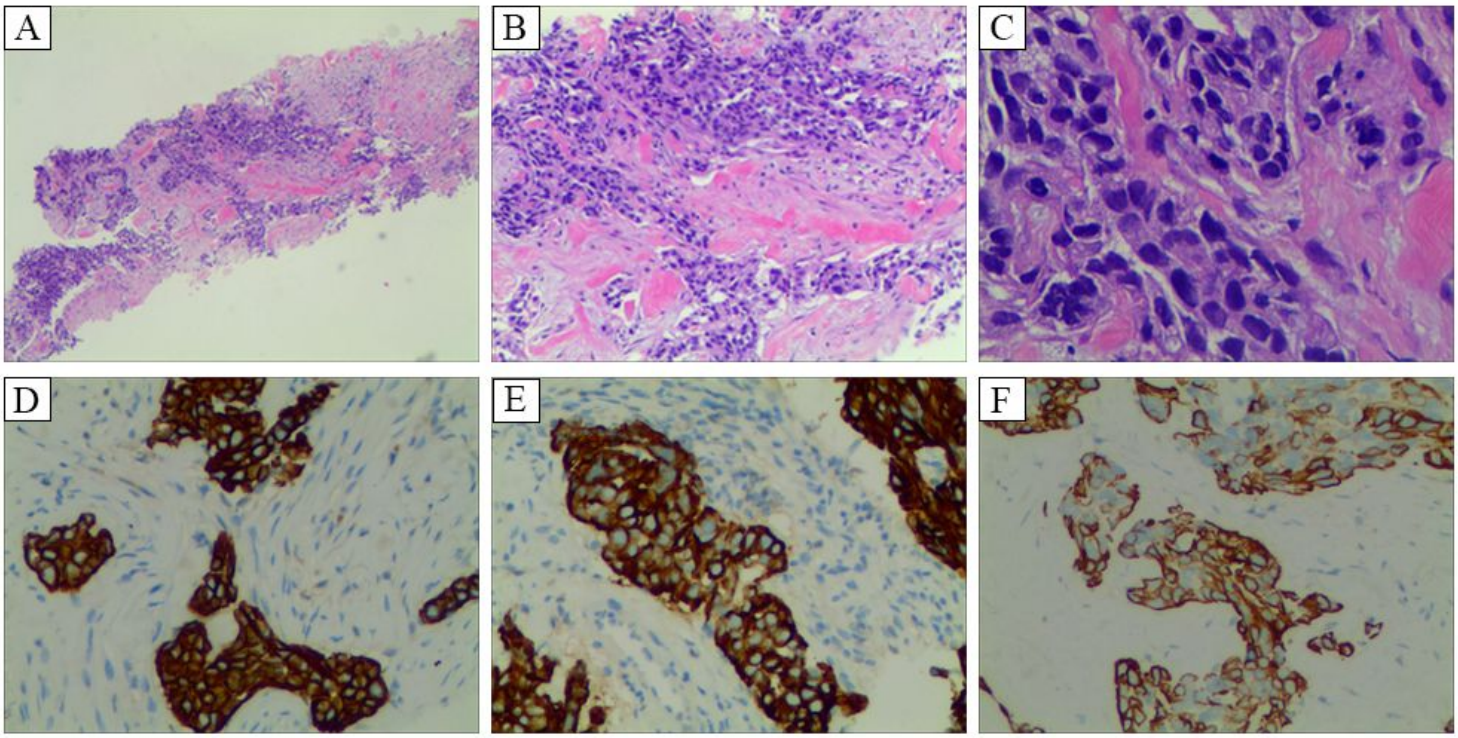

Figure 1

Representative images of hematoxylin & eosin (H&E) and immunohistochemistry (IHC) results. (A):H&E stain shows tumor cells (H&E ×4). (B):H&E stain shows tumor cells (H&E ×10).(C):H&E stain shows tumor cells (H&E ×20).(D):IHC stain indicates CK7 positivity (IHC ×20).(E):IHC stain indicates Cam5.2 positivity (IHC ×20).(F):IHC stain indicates CK5/6 positivity (IHC ×20).

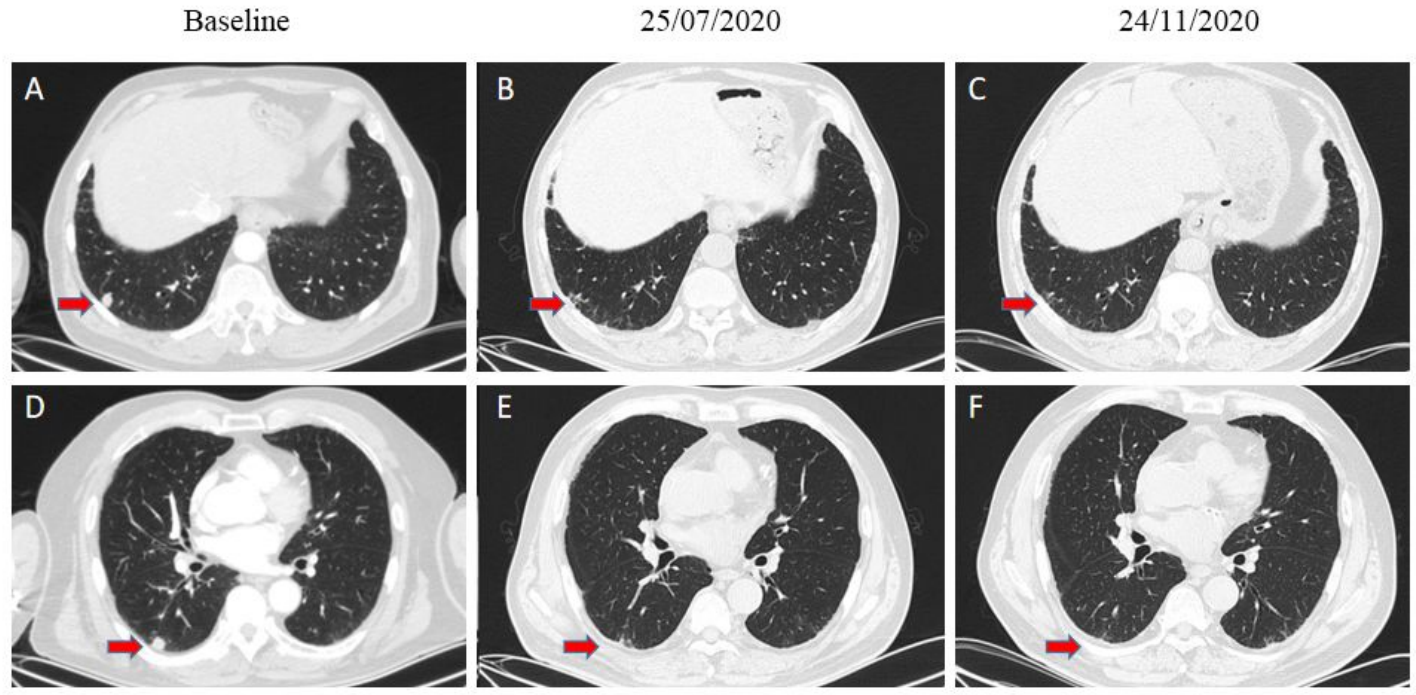

Figure 2

Chest CT scans. (A and D): Before medical treatment, two measurable tumor lesions were shown. (B and E) After medical treatment, a Partial response was observed. (C and F) After operation treatment , a continued partial response was observed.

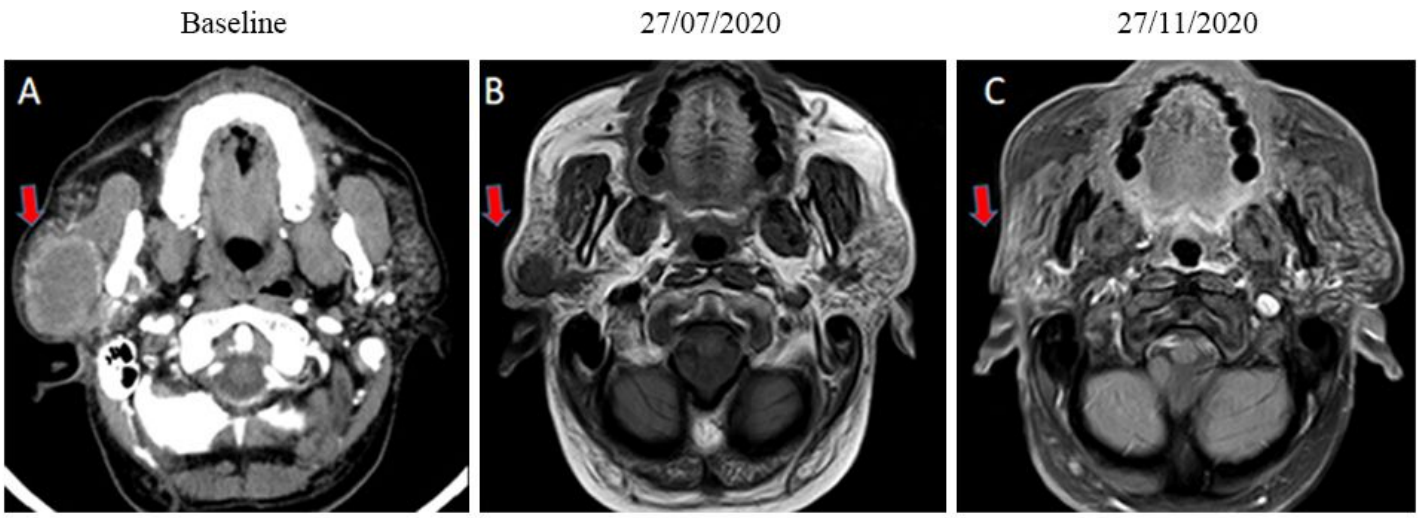

Figure 3

Head and Neck CT scans. (A): Before medical treatment. (B) After medical treatment. (C) After operation treatment.