CASE REPORT

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The Efficacy of Combination of Pembrolizumab plus Chemotherapy in Locally Advanced Squamous Cell Carcinoma of Mandible: A Case Report

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ABSTRACT

Introduction: Pembrolizumab as a humanized monoclonal antibody blocks the interaction between programmed death ligand 1(PD-1) and its ligands that has been used for head and neck squamous cell carcinomas (HNSCCs). This study aimed to evaluate the efficacy of combination therapy of pembrolizumab plus chemotherapy in the treatment of locally advanced HNSCC patient. **Case report**: A 55-year-old male referred to the Oncology Clinic. The histopathological report revealed moderately differentiated SCC of the mandible. Magnetic resonance imaging (MRI) of the neck showed abnormality enhanced nodular mass located in the left submandibular space. He received three courses of docetaxel, carboplatin and 5-fluorouracil (TCF) plus Erbitux chemotherapy regimen after that he received radiation therapy plus Xeloda. After two months, mandibular mass re-growth and this time checked PD-L1 marker was positive. He treated with previously chemotherapy protocol combined with pembrolizumab 200 mg every two weeks. After three months, lesions grossly resolved and treatment continued with pembrolizumab 200 mg and Erbitux 400 mg every two weeks for three months. **Conclusions**: Immunotherapy with pembrolizumab plus chemotherapy after radiotherapy had a good effect on locally advanced SCC of the mandible. Therefore, we can suggest using combination therapy after radiotherapy as a new treatment in the patients with locally advanced HNSCC patients.

Keywords: Immunotherapy, squamous cell carcinoma, head and neck cancer, PD-L1

1. INTRODUCTION

Head and neck squamous cell carcinomas (HNSCCs) are aggressive cancers that surgery or radiation plus chemotherapy are traditionally treatment options for these carcinomas [1]. Nowadays, the success rate of treatments despite developments in treatment options and efforts at organ preservation has not improved significantly and has typically resulted in weak effects with decreased quality of life [2]. Immunotherapy has demonstrated efficacy in several types of the tumor including HNSCC, where an increase in median overall survival (OS) has been seen [3]. Anti-cancer immunotherapies are finally becoming clinically efficacious after many decades of intense research and development. Antibody mediated disruption of programmed death ligand 1 (PD-L1)/programmed death receptor 1 (PD-1) interactions are one of the most efficacious with milder adverse effects than chemo (radio) therapy [4]. Pembrolizumab is a humanized monoclonal antibody that prevents the interaction between PD-1 and its ligands (PD-L1 and PD-L2). Food and Drug Administration (FDA) for the first time had approved it for the treatment of melanoma and then non-small cell lung cancer (NSCLC) and was recently for the treatment of recurrent or metastatic HNSCC in patients with disease progression during or after platinum-containing chemotherapy [5]. The aim of this study was to assess the efficacy of combination of pembrolizumab plus chemotherapy in the treatment of locally advanced HNSCC patient.

2. CASE REPORT

A 55-year-old male referred to the Oncology Clinic in September 2016. The histopathological report revealed moderately differentiated SCC with lymph node involvement and all lateral and deep surgical margins were free of tumor. Three tesla magnetic resonance imaging (MRI) of the neck showed abnormality enhanced nodular mass located in the left submandibular space with necrotic center suggesting infected infiltration lymph node (Figure 1). He had debulking surgery and received three courses docetaxel, carboplatin and 5-fluorouracil (TCF) plus erbitux chemotherapy regimen after that received radiation therapy plus Xeloda. Deep venous thrombosis was one of the adverse events. Multi-slice spiral computerized tomography (CT) scan of the abdomen with oral with intravenous contrast showed that axial views were abnormal (Figure 2). After two months from the previous treatment protocol, mandibular mass re-growth (Figure 3) and in this time, PD-L1 has checked that the marker was positive more than 40% with Immunohistochemistry method. In this time white blood cell (WBC), hemoglobin (Hb) and platelet were 9400 cells/mm^3, 10.6 g/dl and 201000/mm^3.He was treated with previously chemotherapy protocol (TCF plus Erbitux) combined with pembrolizumab 200 mg every two weeks in April 2017. After this protocol, white blood cell (WBC) was 3700; hemoglobin (Hb), and platelet count became normal. Brain CT showed edema and increased the thickness of skin in the left side of the face with multiple small fluid collections that could suggest cellulite and abscess formation (Figure 4). After three months, lesions grossly were resolved (Figure 5) and treatment continued with pembrolizumab 200 mg and erbitux 400 mg every two weeks for three months. In October 2017, he was alive without any other complaints. A written informed consent was obtained from the patient to report the case.

Figure 1 Abnormality enhanced nodular mass located in the left submandibular space

Figure 2 Multiple small fluid collections are seen with edema

Figure 3 Mandibular mass regrowth after chemotherapy and chemo-irradiation therapy

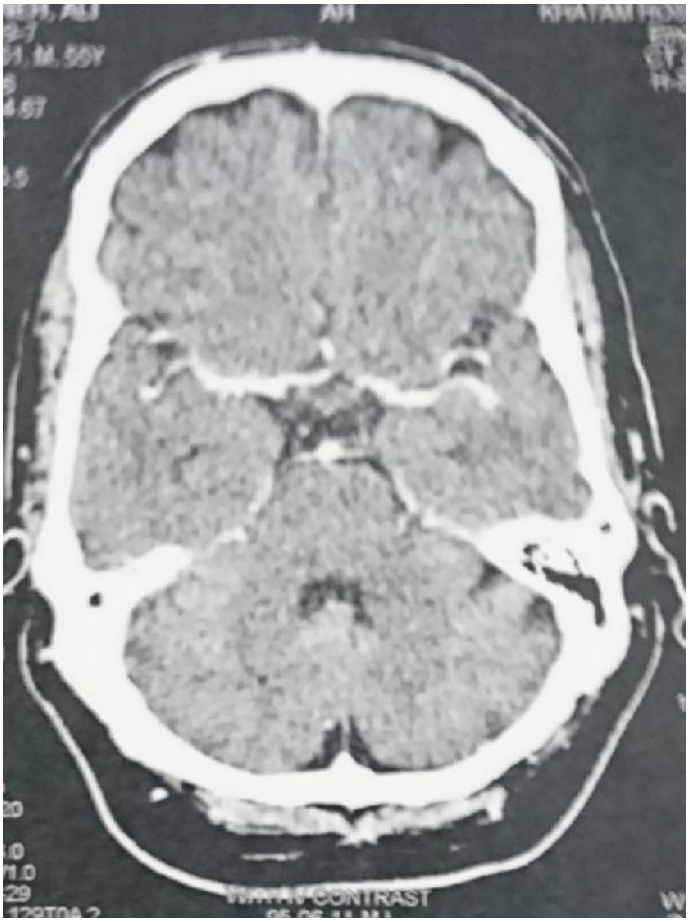

Figure 4 Spiral CT scan with IV contrast, axial views

Figure 5 Three months after treatment with pembrolizumab

3. DISCUSSION

Several trials are doing the efficacy of pembrolizumab on metastatic HNSCC patients [6,7]. PD-1 plays a critical role in tumor immune evasion [8]. Pembrolizumab has been tested clinically in a series of KEYNOTE studies and is testing in twelve categories of neoplasm including head and neck cancers to determine its clinical efficacy [9]. One study [10] checked PD-L1 for 60 patients with HNSCC that the results showed pembrolizumab therapy led to an objective response rate (ORR) of 20% and for denser PD-L1 expressing tumors demonstrated higher ORR of 50%. Chang et al. [11] reported unresectable cutaneous SCC case that had a good response to pembrolizumab and Degache et al. [12] showed a major response to pembrolizumab in two patients with locally advanced cutaneous SCC.

There are a number of trials underway using novel combinations with chemotherapy, radiation and other checkpoint inhibitors or DNA-modulating agents to help improve responses and outcomes in HNSCC [13]. Argiris et al. [14] reported that in the first-line treatment of recurrent/metastatic HNSCC, combination therapy with cetuximab plus cisplatin/carboplatin plus 5-fluorouracil (5-FU) followed by maintenance cetuximab has shown the best results so far in terms of ORR, progression-free survival, and OS. The combination of immunotherapeutic strategies represents a challenging approach, with a view to enhance antitumor immunity by targeting several aspects of immune response [15]. Nowadays, the new treatments for HNSCC go to an immunotherapy combination with radio(chemo) therapy for better response [16]. The most beneficial timing for the combination of radiotherapy with immunotherapy has remained as a challenge that priority of radiotherapy or at the same time with immunotherapy may conclude in more effective of immunotherapy. On the other hand, if radiotherapy is done after immunotherapy, the active immune microenvironment may maximize radiation efficacy [17]. The present case with SCC of mandible received combination of immunotherapy plus chemotherapy after radiotherapy that resulted in disease stable phase.

4. CONCLUSION

Immunotherapy with pembrolizumab plus chemotherapy after radiotherapy had a good result in locally advanced SCC of the mandible. Therefore, we can suggest using combination therapy after radiotherapy as the new therapy in the patients with locally advanced HNSCC patients.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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