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The Role of Immunotherapy and Radiation Therapy in Tumor Chemosensitivity in Advanced Head and Neck Cancer

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Data Interpretation D
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Conflict of interest: None declared

Patient: Male, 56
Final Diagnosis: Advanced stage squamous cell carcinoma of the head and neck
Symptoms: Rapidly enlarging mass in left neck
Medication: —
Clinical Procedure: —
Specialty: Oncology

Objective: Unusual clinical course

Background: Cancer is the second leading cause of death internationally, resulting in millions of deaths each year. While treatment in the past has heavily relied on surgery and radiotherapy, chemotherapy and immunotherapy are being increasingly utilized depending on disease presentation.

Case Report: A 56-year-old male presented to the Emergency Department with a 3-week history of a rapidly enlarging left supraclavicular neck mass. Computed tomography scan revealed a 12×13 cm mass extending from the angle of the mandible to the supraclavicular area. A biopsy confirmed advanced stage squamous cell carcinoma of the head and neck. The patient was started on a chemotherapy regimen of docetaxel, cisplatin, and 5-fluorouracil (TCF). The tumor progressed through chemotherapy, which was switched to cetuximab; however, this therapy was discontinued after an anaphylactic reaction. Palliative radiation treatment was begun along with pembrolizumab. Pembrolizumab was continued, and after 9 cycles, the patient's cancer was almost in complete remission. Three months later, disease progression was once again noted with pembrolizumab treatment, which was subsequently discontinued. The patient was started on paclitaxel and carboplatin chemotherapy regimen as a last resort, despite failure of prior TCF treatment, and the patient responded, this time with complete remission in 4 months.

Conclusions: This case demonstrates a unique outcome in which a patient who previously was resistant to chemotherapy, later responded to chemotherapy after a trial of radiation therapy and immunotherapy. Immunotherapy may have a synergistic effect with radiation therapy and play a role in tumor sensitivity to chemotherapy in head and neck cancer treatment.

MeSH Keywords: Chemoradiotherapy, Adjuvant • Head and Neck Neoplasms • Immunotherapy, Active

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/910224>



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Background

Cancer is the second leading cause of death internationally, resulting in millions of deaths each year [1]. Head and neck cancers account for approximately 6% of all cancers, with major risk factors including alcohol and tobacco use, sun exposure, human papilloma virus infection, and more. The risk of patients developing a secondary primary cancer is 4% per year. Five-year survival varies based on initial staging, with 91% in stage I disease, 77% in stage II, 61% in stage III, 32% in stage IVA, 25% in stage IVB, and <4% in stage IVC disease [2]. While treatment in the past has heavily relied on surgery and radiotherapy, chemotherapy and immunotherapy are being increasingly utilized depending on disease presentation [3]. This case demonstrates a unique outcome in which a patient who previously was resistant to chemotherapy, later responded to chemotherapy after a trial of radiation therapy and immunotherapy.

Case Report

A 56-year-old male presented to the Emergency Department with a 3-week history of a rapidly enlarging left supraclavicular neck mass suspicious of malignancy. Computed tomography (CT) scan revealed a 12×13 cm mass extending from the angle of the mandible to the supraclavicular area. A biopsy confirmed advanced stage squamous cell carcinoma of the head and neck. Due to the size and aggressive growth of the tumor

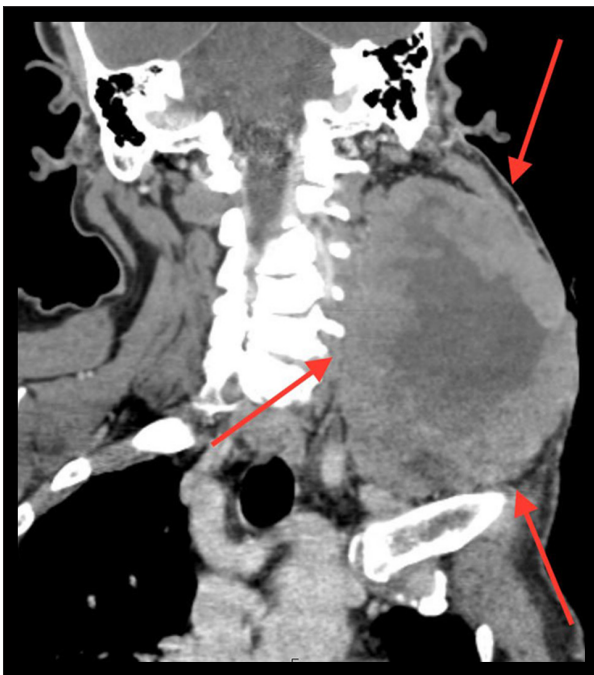


Figure 1. Computed tomography image demonstrating progression with chemotherapy. Arrows denoting tumor borders.

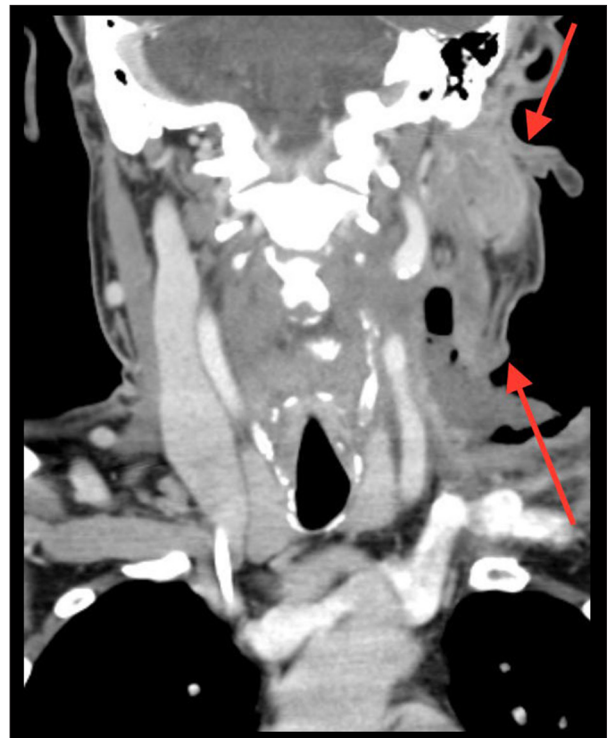


Figure 2. Computed tomography image demonstrating remission after immunotherapy/radiation. Arrows denoting remaining tumor.

at the time of diagnosis, resection was not an option. The patient was started on a chemotherapy regimen of docetaxel, cisplatin, and 5-fluorouracil (TCF). He was also referred to Radiation Oncology. A single session of 2000 cGy high dose radiation was performed for de-bulking. The tumor progressed through chemotherapy (Figure 1) and the regimen was switched to cetuximab; however, the patient had an anaphylactic reaction, and cetuximab was discontinued. Palliative radiation treatment was begun along with pembrolizumab. Radiation therapy was administered at 4750 cGy in 20 fractions over a 1-month period. Pembrolizumab was continued, and after 9 cycles (one infusion every 3 weeks), the patient's cancer was almost in complete remission (Figure 2). Three months later, disease progression was once again noted with pembrolizumab treatment (Figure 3), which was subsequently discontinued. The patient was in good health otherwise, and therefore, he was started on paclitaxel and carboplatin chemotherapy regimen as a last resort, despite failure of prior TCF treatment. The patient responded to chemotherapy this time with complete remission in 4 months (Figure 4).

Discussion

Cancer incidence is expected to rise by 70% over the next 2 decades [1]. Approximately 644 000 cases of head and



Figure 3. Computed tomography image demonstrating disease recurrence. Arrows denoting growing tumor.

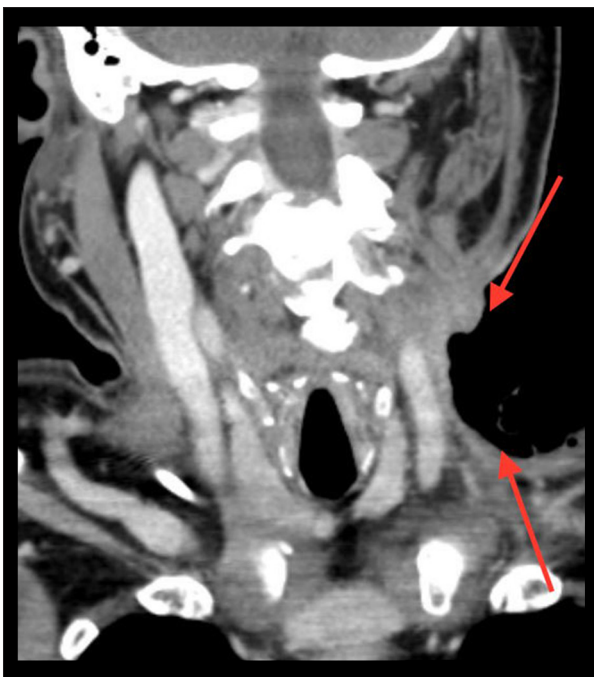


Figure 4. Computed tomography image demonstrating complete remission with chemotherapy. Arrows denoting area previously occupied by tumor.

neck cancer are diagnosed each year, with greater than 90% being of squamous cell origin [4]. Mainstays of cancer treatment are surgical resection, radiotherapy, chemotherapy, and

immunotherapy. Treatment is tailored depending on the patient's disease presentation and response. For advanced stage head and neck cancer that cannot be resected, chemoradiotherapy is the first-line treatment. The platinum-based chemotherapy regimen used is a combination of docetaxel, cisplatin, and 5-fluorouracil [4]. Second-line treatment is with radiation and the epidermal growth factor receptor (EGFR) monoclonal antibody cetuximab [5]. For cases that show progression after these treatments, the FDA-approved nivolumab and pembrolizumab, anti-PD-1 antibodies [6].

Many head and neck cancers were found to express high levels of PD-L1. This was shown to be a negative prognostic indicator, with these patients showing reduced overall survival time [7]. However, PD-L1 expression was found to be variable over time and to display intratumor heterogeneity, which limits the efficacy of measuring these levels in head and neck cancer patients [8]. Additionally, both patients with and without PD-L1 expression in their tumors have been shown to benefit from anti-PD-1 antibody treatment, further demonstrating the value of immunotherapy in head and neck cancer patients [9].

Anti-PD-1/PD-L1 antibody has been shown to enhance the effect of EGFR antibodies such as cetuximab [10]. Likewise, cetuximab has been shown to improve the efficacy of treatment in patients receiving radiotherapy for head and neck cancers [11]. Less studied, however, are the effects of immunotherapy on tumor sensitivity to chemotherapy regimens, and the possibility of radiosensitization with immunotherapy. Concomitant administration of immunotherapy and radiotherapy in mice showed superior antitumor immunity than either treatment alone [12]. The concurrent treatment in humans has not been well-documented. The previously presented patient did not initially respond to chemotherapy; however, following a trial of immunotherapy with pembrolizumab and concurrent palliative radiation therapy, the patient's disease did respond to treatment with chemotherapy. As demonstrated in this case, immunotherapy may have a synergistic effect with radiation therapy and play a role in tumor sensitivity to chemotherapy in head and neck cancer treatment. Further studies would need to be undertaken with respect to this possible synergism.

Conclusions

This case demonstrates a unique outcome in which a patient who previously was resistant to chemotherapy, later responded to chemotherapy after a trial of radiation therapy and immunotherapy. Immunotherapy may have a synergistic effect with radiation therapy and play a role in tumor sensitivity to chemotherapy in head and neck cancer treatment.

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