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Case Report

Complete Clinical Regression of Orocutaneous Fistula in Contralateral Relpased Oral Cavity Squamous Cell Carcinoma Patient Following Surgery and Adjuvant Radiotherapy

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Abstract

Prior to beginning treatment, it is essential that a multidisciplinary tumour board discuss each patient's situation and devise a treatment plan for oral cavity squamous cell carcinoma (OSCC), a heterogeneous illness. One of the common postoperative consequences following oral cancer surgery is an orocutaneous fistula (OCF). This incident broadens the amount of knowledge on OCF regression after adjuvant therapy. It is also important not to give up on a relpased oncology case, just on the basis of age of the patient.

Keywords: Oral Cavity Squamous Cell Carcinoma; Orocutaneous Fistula; Hemi Mandibulectomy; Radiation; Adjuvant Therapy; Afatinib; Metronomic Targeted Frug

Introduction

Oral Cavity Squamous Cell Carcinoma (OSCC) is a heterogenous disease with respect to risk factors, geographic predelictions, treatment response and outcome [1]. Although non-surgical treatment is used in other head and neck sub-sites, surgery is the primary treatment option for oral malignancies. Surgery is then followed by adjuvant radiotherapy or chemoradiation therapy according on the risk factors identified by the final histopathology [2]. Prior to starting treatment, it is crucial that a multidisciplinary tumour board discuss each patient's case and develop a treatment strategy. It should be highlighted, though, that surgical treatment for oral cancer is insufficient on its own. Chemotherapy is sometimes used as induction therapy and sometimes it is administered together with radiation. To increase the effectiveness of the primary therapy and stop the emergence of second-primary malignancies, the primary cancer treatment and risk factor reduction are of the utmost importance [3]. Orocutaneous fistula (OCF) is one of the frequently encountered postoperative complications following surgery for oral cancer, leading to prolonged hospital stay and delay in the initiation of adjuvant therapy [4]. This instance adds to the body of research on contralateral OCF developed due to metastasis, regressed completely with treatment albeit the setting remain as palliative.

Case Report

A hemi mandibulectomy was performed on the right side of a 64-year-old elderly woman with a diagnosis of oral squamous cell carcinoma. After receiving radiation and surgery, she experienced a contralateral oro-cutaneous fistula on the LEFT side within 6 months figure 1.

Since the OCF formed out of the radiation field, it was suspected too due to non-oncological reason. However, it was proven otherwise by a biopsy from the periphery of the lesion. This biopsy confirmed it to be squamous cell carcinoma. As it was a non-regional recurrence, the treatment intent changed to palliative.

In 2019, a three-cycle palliative chemotherapy treatment of 5-fluorouracil, cisplatin, and paclitaxel was started (TPF regimen). After three cycles, she showed no improvement in her condition, and cachexia related to cancer, sets in.

Paclitaxel + cisplatin+ infusional 5-FU[27, d]	Day 1: Paclitaxel 175mg/m^2 over 3 hours Day 2: Cisplatin 100mg/m^2; plus Day 2–6: 5-FU 500mg/m^2/day continuous IV infusion for 5 days. Repeat every 3 weeks for 3 cycles.

Table 1: TPF regimen.

Nivolumab immunotherapy (3 mg/kg) was given to the patient every 15 days for three months. The patient made a partial recovery during this time, and his symptoms and lesion only slightly improved figure 2.

Due to budgetary limitations, the patient was switched to Afatinib 30 mg as a metronomic targeted therapy. Over the course of six months, the patient responded well, and the lesion completely healed figure 3.

With a slight cachexia CSE category 1 side effect, the patient's tolerance to the medication was satisfactory. She did, however, developed viral infection during the COVID pandemic, which was not recorded as a COVID case, and she passed away from septic shock, which was unrelated to the medication.

Figure 1: Contralateral Oro-cutaneous fistula.

Figure 2: lesion only slightly improved in follow up pf 3months.

Figure 3: Over the course of six months, the lesion completely healed.

Discussion

One of the most typical forms of cancer in the head and neck region is oral squamous cell carcinoma (OSCC), which develops from the lips and oral cavity [5]. According to data from the Global Cancer Observatory (GCO), there were 377,713 OSCC cases annually in 2020, with Asia recording the largest number (248,360), followed by Europe (65,279), and North America (27,469) [6]. The five-year prevalence of OSCC was close to one million (959,248)

and exhibited the same trends, with Asia having the highest rates [6]. An uncommon extraoral channel of infection between the oral cavity and the skin is known as a mouth cutaneous fistula (OCF). The most frequent causes of oral cutaneous fistulas include chronic dental infections, trauma, dental implant problems, diseases of the salivary glands, and neoplasms. Instead of dentists, affected patients typically turn to dermatologists or surgeons for assistance [7]. In present case, OCF developed in post operative time period after radiation and chemotherapy, albeit on the contralateral side. Advanced head and neck cancer is often treated with a combination of various methods. When advanced characteristics are identified in surgical patients, adjuvant radiation (RT) can lower the chance of tumors recurrence [8]. The recommended therapeutic method is surgery, and abnormalities brought about by surgical excision are typically fixed using free flaps. Free flap reconstruction frequently results in complications. An illustration is an orocutaneous fistula (OCF) [9]. It can greatly prolong the time before adjuvant therapies begin, lengthen the patient's stay and treatment expenditures, put off oral feeding and voice therapy, and raise the risk of carotid blowout [10]. Based on 587 eligible oral SCC patients, Girkar., *et al*. (2019) reported a rate of 9%, and they found that conducting bilateral neck dissection and having surgical site infection increased the likelihood of OCF the most [11]. Treatment for OCF often takes 4 weeks or longer and is time-consuming. The three types of management for OCF at the moment are surgical intervention, traditional wound care, and negative pressure wound therapy [12]. In present case when palliative chemo response was not appreciable, the patient was given immunotherapy-Nivolumab. Oral squamous cell carcinoma has been approved for treatment with immune checkpoint inhibitors (ICIs) (OSCC). However, not all patients would benefit from ICIs. Therefore, the effectiveness and safety of combination immunotherapy are still being examined in order to increase the response rate. Nivolumab, a human monoclonal IgG4 antibody that targets PD-1 on T cells, has been used to treat head and neck cancer that is platinum-resistant, recurrent, and/or metastatic [13]. Limited information is available regarding the long-term sustainable response to nivolumab in metastatic oral cancer, despite the fact that nivolumab has been clinically successful in extending the overall life of patients with recurrent and/or metastatic head and neck cancer. Financial constraints forced the changeover to Afatinib metronomic targeted therapy. Drugs are administered in a low-dose, repetitive, and regular manner during metronomic therapy, without a lengthy drug-free period. Antiangiogenesis and immunomodulation are the two primary anticancer mechanisms of metronomic treatment. Metronomic therapy has comparable efficacy to the conventional maximum tolerated dose (MTD) dosing of chemotherapy, but significantly lower incidence and severity of adverse effects [14]. Clinical trials employing metronomic anticancer therapy have shown encouraging outcomes in a range of cancer types and certain patient demographics, such as elderly patients and children with malignancies. The class of drugs known as tyrosine kinase inhibitors includes afatinib [15]. According to our experience, afatinib focused metronomic therapy produced a satisfactory response and the healing of the lesion (OCF) with no too few adverse effects. This is all the more appreciable because the patient developed contralateral relapse, with no response to chemo and partial response to Immunotherapy

Conclusion

Here, we disclose the first instance of a patient with contralateral relapsed oral squamous cell carcinoma who presented with Orocutaneous fistula and experienced a lasting full response following nivolumab and afatinib metronomic targeted therapy. The learning point of this case is not to give up on a relapsed case if there is initially no response with chemotherapy and novel agents may give unexpected results.

Q - discussion part not include - the case focuses on effectiveness of immunotherapy and targeted therapy traditional treatment of oral malignancy is combination of surgery plus radiation and chemotherapy. there is no question of radiotherapy and chemotherapy being better than surgery.

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