



Letter to the editor

The interest of sequential treatment with immune check point inhibitors followed chemotherapy: A case report



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Introduction

Immune check point inhibitors (CPIs) have demonstrated efficacy in the treatment of squamous cell carcinomas of the head and neck (SCCHN) involving cases of recurrence or metastasis after failure of platinum-based chemotherapy.

Programmed death-1 or PD Ligand 1 inhibitors have been evaluated for first-line treatment and for locally advanced cancers. Past studies have reported that subsequent chemotherapy after platinum failure has shown low efficacy [1,2]. However recent studies have reported an increased objective response of salvage chemotherapy after disease progression, using CPI, which was especially effective for patients with

non-small cell lung cancer or SCCHN [3,4]. We described here the case of an unexpected response to salvage chemotherapy after a rechallenge using CPIs.

Case report

In April 2017, a 51-year-old male presented with squamous cell carcinoma (SCC) of the piriform sinus associated with bilateral lymph nodes and lung metastases (cT2N2cM1).

The first-line treatment, from June to October 2017, involved CPIs associated with anti-cytotoxic T-lymphocyte-associated protein 4. The patient presented with a stable disease as the best response according to

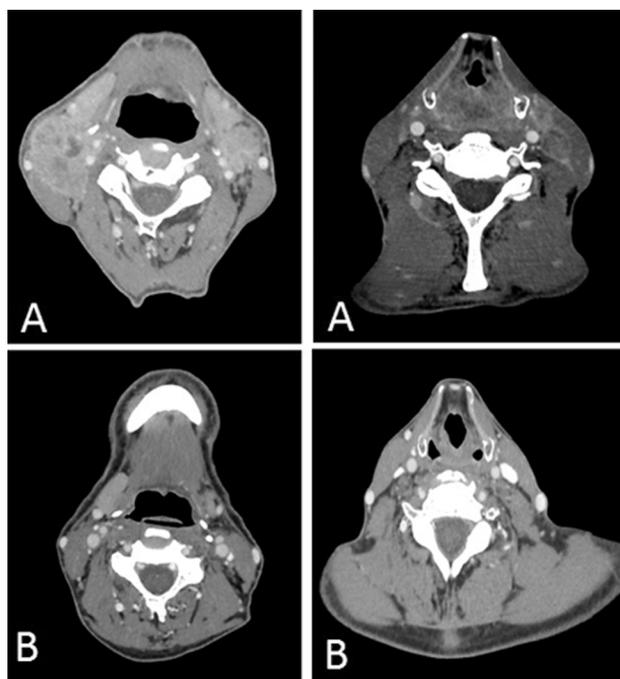


Fig. 1. Computed tomography scan of disease progression after the first treatment with immune check point inhibitors (A), and after six cycles of cisplatin and fluorouracil (B).

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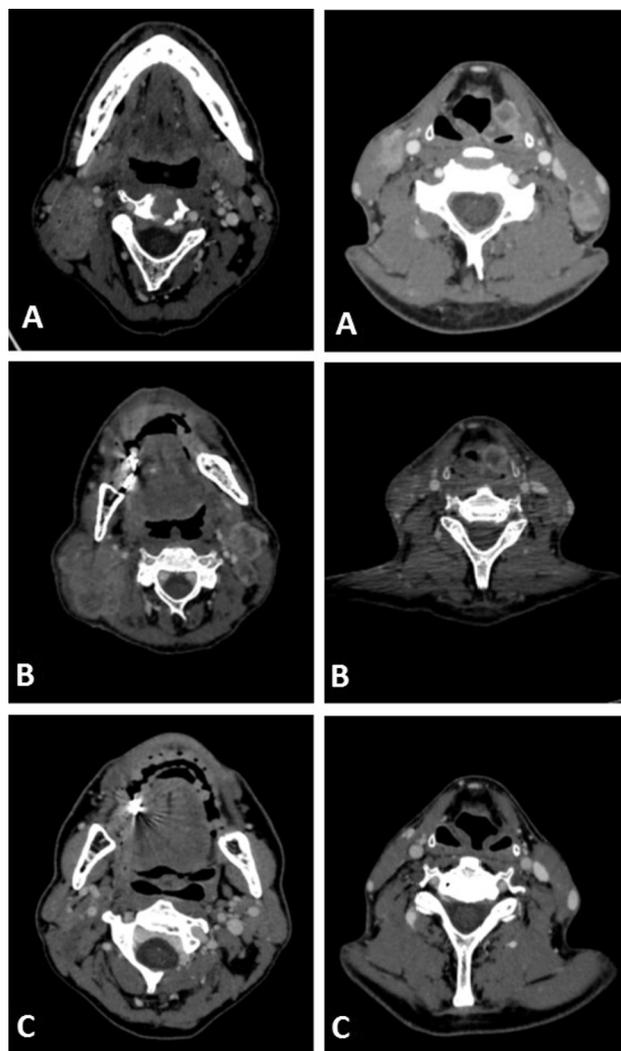


Fig. 2. Computed tomography scan of the progression of the disease after treatment with afatinib (A), after three treatments with nivolumab (B), and after six cycles of salvage chemotherapy (C).

RECIST with a size increase of less than 20%. With progression of the disease (PD), a platinum regimen of chemotherapy (cisplatin, fluorouracil, and cetuximab) was used as a second-line treatment. The patient achieved an impressive partial response (PR) after three treatments, which was confirmed after six treatments (Fig. 1). Cetuximab was maintained until July 2018, then stopped because of PD. The patient started afatinib as part of the EORTC 1559, but PD occurred in October 2018.

Because of the potential efficacy of chemotherapy following CPI, after discussion on the part of the multidisciplinary team, it was decided to use CPIs again when PD occurred after platinum chemotherapy. Three nivolumab injections of 240 mg were conducted, but were stopped due to a clinical PD with dyspnea and dysphonia, which was confirmed by a computed tomography (CT) scan in November 2018 (Fig. 2). Chemotherapy with carboplatin-paclitaxel was started and the patient presented within 2 weeks with an unexpected clinical response involving the disappearance of the dysphonia and dyspnea. A CT scan performed after three treatments showed a PR, which was confirmed with subsequent CT scans after six treatments (Fig. 2).

Discussion

Our observations were similar to previous case reports or retrospective data, indicating an unexpected response after sequential

treatment by CPIs, followed by chemotherapy. To our knowledge it is the first case report of the interest of sequential treatment. Saleh et al. reported 30% objective response rates (ORRs) in cases of salvage chemotherapy after treatment with CPIs for SCCHN patients, which was better than the best ORRs previously reported [1–3]. The results suggested an increased ORR using chemotherapy after pretreatment with CPIs for some patients, when compared to what was expected using chemotherapy alone after PD. In our case report, the patient was treated with carboplatin, which was less effective than cisplatin; however, the patient showed a major response after chemotherapy. The scientific rationale for explaining the positive response to chemotherapy after rechallenge of immunotherapy may involve modification of the tumor microenvironment. Different studies have reported that chemotherapy has many immunomodulatory effects, such as a decrease of myeloid-derived suppressor cells and regulatory T cells, which results in a modified balance among cytokines. All these changes eventually enhanced the antitumor immune response [5]. We hypothesize that the use of CPIs improved the chemosensitivity of the tumor, although other explanations are still possible.

In our case report, we also hypothesize that this unexpected response was due to the combined treatment with CPIs and chemotherapy, with a long half-life (approximately 1 month) for the CPIs and a possible synergistic effect between nivolumab and paclitaxel.

Conclusion

We report here the case of an unexpected response to salvage chemotherapy after rechallenge with immunotherapy.

This case supports the potential efficacy of a sequential treatment of chemotherapy and immunotherapy for SCCHN patients, based on modifications of the tumor microenvironment.

Prospective trials are needed to confirm the different case reports, as well as retrospective studies of unexpected responses to salvage chemotherapy.

Declaration of Competing Interest

The authors declare no conflict of interest.

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