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Letter to the editor

A rare case of nasopharyngeal adenoid cystic carcinoma treated with cetuximab-based induction therapy followed by concurrent chemoradiotherapy

Dear Editor-in-Chief,

In response to the treatment of adenoid cystic carcinoma, I'd like to describe a rare case of this type of tumor discovered in nasopharynx.

A 33-year-old female complained tinnitus in her left ear, then she received radical endoscopic surgery in January 2017. The postoperative pathology was classified as adenoid cystic carcinoma and Ki-67 was 20% positive. The patient did not receive further treatment after surgery. In May 2017, she accepted radical endoscopic surgery again because the tumor recurred in nasopharyngeal region. Histopathology confirmed locally recurrent adenoid cystic carcinoma with a solid portion exceeding 80%. Cell necrosis could be seen with microscope and EGFR was positive. In June 2017, the patient came to our Department of Radiation Oncology because she was suffering from a severe headache. The patient has a medical history of thalassemia, no smoking or drinking. Locally recurrent advanced nasopharyngeal adenoid cystic carcinoma was classified as T4bN0M0 by contrast-enhanced MRI, according to the American Joint Committee on Cancer staging (AJCC), 8th edition (Fig. 1).

The patient received a combined chemotherapy consisting of 3 cycles of docetaxel, cisplatin and 5-Fu couple with 9 cycles of cetuximab (docetaxel (75 mg/m^{-2}) (D1), cisplatin (75 mg/m^{-2}) (D1), 5-Fu (750 mg/m^{-2}) (D1-5), repeated every 3 weeks and cetuximab repeated every week). The dosage of cetuximab was 400 mg/m^{-2} on day 1 at the first week, then followed by 250 mg/m^{-2} on day 1 from the second to ninth week). Due to the serious nausea and vomiting caused by cisplatin, cisplatin was replaced with carboplatin (area under the curve 5 (D1)) from the second cycle and the patient was well tolerated with carboplatin. Contrast-enhanced MRI and CT of nasopharyngeal region were performed every 3 weeks, and the imaging evaluation was partial response (PR) which indicated that NACC significantly shrank. When three 3 cycles of induction chemotherapy finished, intensity Modulated Radiation Therapy was performed with concurrent chemotherapy which strengthened radiation sensibility. The concurrent chemotherapy regimen was comprised of carboplatin (area under the curve 5) (D1) and 5-fu (750 mg/m^{-2}) (D1-5). The radiation plan was divided into two phases. Phase 1: 95% of the planning target volume (PTV) receiving the prescription of 56 Gy/28 fractions containing the gross tumor and clinically node-negative neck as prophylactic area. Phase 2: The prescribed dose (12 Gy/6 fractions) to the 95% of the PTV which included residual tumor. The patient received Contrast-enhanced MRI of nasopharyngeal region every 3 months by follow-up and imaging evaluation had been sustained partial response which tumor volume decreased 90%, nearly achieving complete response (Fig. 2).

The patient had suffered from grade 2 dermatitis, grade 3 mucositis and myelosuppression, according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0, during the radiotherapy concurrent with chemotherapy. But the patient was well tolerated after receiving symptomatic therapy with acesodyne, gargle and recombinant human granulocyte colony-stimulating factor injection.

The incidence of Nasopharyngeal adenoid cystic carcinoma (NACC) is rare which represented about 0.29% of all Nasopharyngeal carcinomas. Over-expression Ki-67 and solid pattern of ACC may be associated with poor prognosis [1–3]. Efficacy of current treatment options, particularly for locally advanced NACC, is very restricted, that is why more aggressive treatment strategies should be developed [4]. Surgery followed by postoperative radiotherapy with or without chemotherapy is cornerstone of therapy [5–8].

The over-expression of EGFR in adenoid cystic carcinoma (ACC) makes it become a potential biological target [9–11]. Hitre et al. considered that the addition of cetuximab to cisplatin-based chemoradiotherapy improved the median PFS to 64 months in patients with locally advanced ACC which is better than other studies [12]. Some other opinions agreed that the addition of cetuximab to chemotherapy with carboplatin and paxlitaxel in locoregionally advanced head and neck cancer was tolerable and effective [13,14].

Platinum-based concurrent chemoradiotherapy in treating locally advanced ACC may receive satisfactory efficacy [15–17]. To achieve local control of ACC, radiation doses of more than 60 Gy or even 66 Gy are recommended [18]. In our case, the total dose of primary tumor area was 68 Gy which was accordant with the recommendation. In some reports, Concurrent chemoradiotherapy alone was applied to manage NACC of T4N0M0 and obtained objective response. But unfortunately, lung metastases appeared after 1 year and local recurrence after 3 years [19]. In our case, there was no local recurrence or distant metastasis found in this patient's follow-up.

As we all know, cetuximab, platinum-based chemoradio- or chemotherapy also bring toxicity. Combination therapy may lead to more serious adverse events than the single one. In our case, grade 2 dermatitis, grade 3 mucositis and myelosuppression were observed. But the patient was well tolerated after receiving symptomatic therapy. Up to now, we have followed up the patient for 18 months, and no obvious long-term toxicity has been observed.

In summary, this combination treatment of cetuximab, induction chemotherapy, followed by concurrent chemoradiotherapy was tolerated well and yielded promising objective response and local control. However, current number of cases for this treatment is too rare to allow a more detailed assessment of this combination treatment. Hence, more prospective controlled trial is needed to investigate the potential significance of this combined treatment.

Conflict of interest

The author(s) indicated no potential conflicts of interest.

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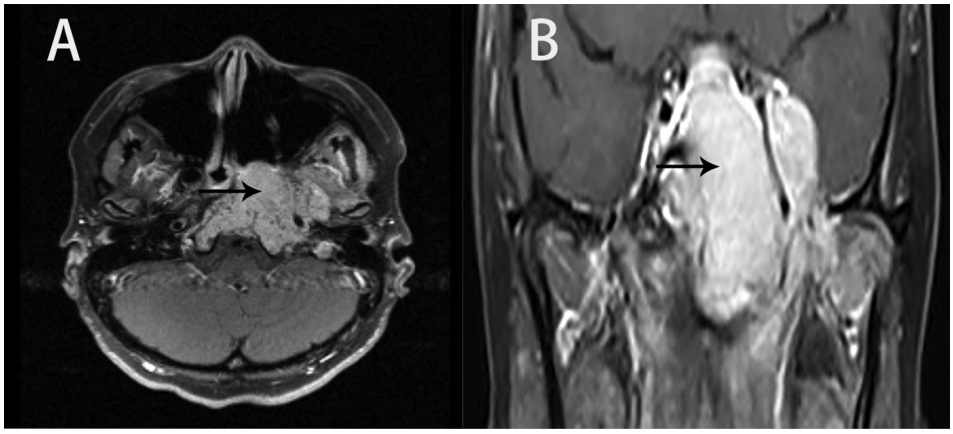

Fig. 1. 7.17 initial, contrast-enhanced MRI of adenoids cystic carcinoma extending the left pterygoid fossa, pterygoid muscle and sphenoid sinus (A) and oval foramen, cavernous sinus (B).

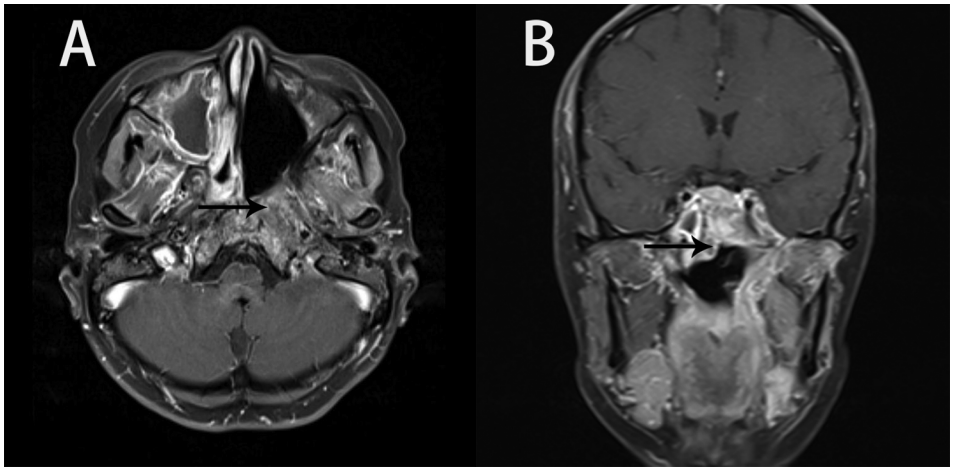

Fig. 2. 9.30 Follow-up contrast-enhanced MRI 14 months post radiotherapy: therapy-related changes: pterygoid fossa, pterygoid muscle and sphenoid sinus (A) and oval foramen, cavernous sinus (B).

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Shihai Wu*, Jingwen Liu[1], Rencui Quan[1]
Department of Radiation Oncology, Second Clinical Medicine College of Jinan University, Shenzhen People's Hospital, China
E-mail address: Jiangxiwu84@126.com (S. Wu).

Ling Han[1]
Department of E.N.T, Second Clinical Medicine College of Jinan University, Shenzhen People's Hospital, China

* Corresponding author.
[1] The three authors contributed equally to this research and shared the co-first author.