

## Case Report

# Metabolic recurrence of oropharyngeal squamous carcinoma surviving with cancer after second-line chemotherapy with paclitaxel, platinum, and S-1 (PPS) and follow-up PET/CT: a case report and review of literature

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**Abstract:** The efficiency of second-line triplet chemotherapy with paclitaxel, platinum, and S-1 (PPS) after in the management of metabolic recurrent local advanced oropharyngeal squamous carcinoma has not been reported. The role of follow-up positron emission tomography/computed tomography (PET/CT) in the strategy of surviving with cancer has not been discussed. We report a case of local advanced oropharyngeal squamous carcinoma received concomitant radiochemotherapy followed by consolidation chemotherapy. The follow-up PET/CT revealed the dynamic change in metabolism of malignant lesions and identified the metabolism recurrence missed by conventional examinations. Then chemotherapy consisting of PPS was planned as the second-line therapy. PET/CT was routinely included in follow-up. Without the use of salvage surgery, the patient is still alive longer than 2 years since the metabolism recurrence. In conclusion, our combined therapy regimen including triplet PPS chemotherapy may be effective for metabolic recurrent local advanced oropharyngeal cancer. In addition, the value of follow-up PET/CT requires further exploration.

**Keywords:** Oropharyngeal cancer, recurrence, chemotherapy, PET/CT

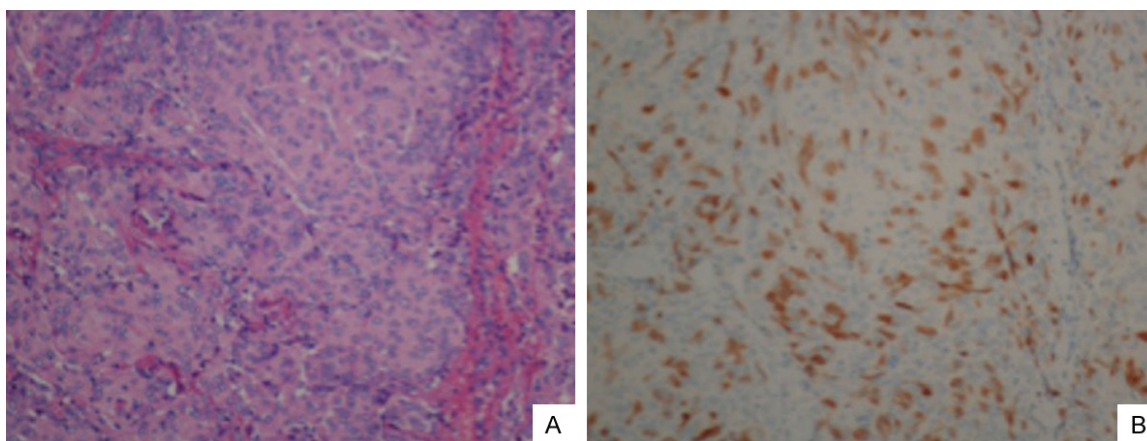
## Introduction

Head and neck squamous cell cancer (HNSCC) is considered a homogeneous disease involving multiple anatomic sites. The first-line treatments for local advanced HNSCC include concurrent chemoradiotherapy (CRT) and induction chemotherapy (IC) followed by CRT or radiotherapy [1, 2]. The best combinations of radiotherapy and the most comprehensive chemotherapy regimen have not been defined. Considering the risk of local failure, early radiotherapy may lead to better local control and, therefore, better survival. Besides, these patients are known to be at the greatest risk of recurrence within the first 2 years after treatment [3]. Many researches have focused on therapy and follow-up of these cases of recurrent HNSCC. Salvage surgery, secondary radiotherapy, and chemotherapy are all accepted treatment strategies. Surviving with cancer could be considered since it allows patients to avoid operative trauma and conserve function. Triplet combination chemotherapy of paclitaxel,

platinum, and S-1 (PPS) is a feasible option for patients with a compromised performance status and can be considered a modified regimen of docetaxel, cisplatin and 5-FU (TPF) [1, 2]. The effectiveness of the continued application of triplet chemotherapy as second-line therapy is unknown.

It is worth noting that active monitoring is necessary for patients surviving with cancer. Here we explore the use of follow-up positron emission tomography/computed tomography (PET/CT), which can reflect the effectiveness of therapy, enable early detection of metabolic recurrence, and lead to early management [4].

The case is a patient with local advanced oropharyngeal squamous carcinoma who received concomitant CRT as primary therapy and PPS chemotherapy as secondary therapy when the metabolism recurrence was identified on follow-up PET/CT. It is encouraging that he has survived for more than 5 years with a good quality of life. We report this case to discuss the role



**Figure 1.** Pathology image (A) and P16 immunohistochemistry staining (B). The pathology of this malignant lesion was confirmed as a low-differentiated squamous carcinoma. The P16 positivity rate was about 40%.

of triplet chemotherapy and PET/CT in long-term stable cancer survival.

### Case report

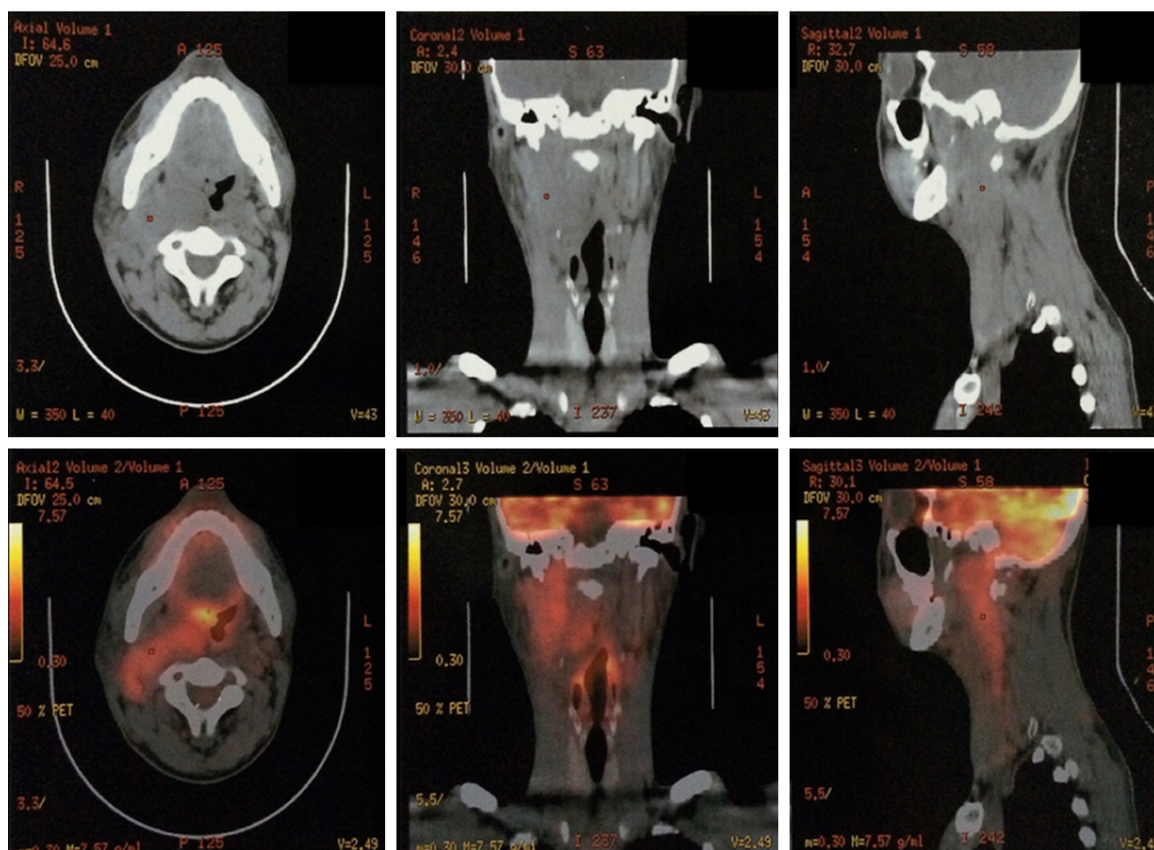
The institutional review board approved this study for human investigation. In May 2011, a 31-year-old Chinese man presented with a 5-cm mass under the right mastoid. On CT, the lesion located in the oral pharyngeal displayed inhomogeneous low intensity and could not be separated from the soft tissues, which suggested a malignant tumor. An open biopsy was performed for pathological tissue collection, which showed that the internal carotid arteries, sublingual nerve, vagus nerve, and accessory nerve was wrapped. The tumor was diagnosed as a poorly differentiated squamous carcinoma and immunohistochemical (IHC) staining was positive for P16. According to previous studies, P16+ meant this patient likely had HPV-positive OPC. The pathological, IHC, and PET/CT imaging results of the newly diagnosis are shown in **Figures 1** and **2**.

PET/CT showed high aberrant accumulation in the oropharyngeal area measuring  $4.8 \times 3.3 \times 6.6$  cm ( $SUV_{max} = 3.2$ ) with no sign of distant metastasis and no evidence of lymph node metastasis (**Figure 2**). In conclusion, the tumor was diagnosed as OPC and classified T4a N0 M0 stage IVA according to the American Joint Committee on Cancer Staging Manual (7<sup>th</sup> Edition).

In June 2011, a course of chemotherapy consisting of PPS (paclitaxel 135 mg/m<sup>2</sup> d1, cisplatin 25 mg/m<sup>2</sup> on days 1-3, and S-1 orally 40 mg/m<sup>2</sup> on days 1-14, 21 days each course) with

concurrent intensity-modulated radiation therapy (radiotherapy started with the begin of the first course of chemotherapy; simultaneously integrated boosted technology, planning therapy volume covers the primary gross tumor on the contrasted CT, and the high- and low-risk regions are 70 Gy, 66 Gy, and 60 Gy) were administered. During the hospitalization, the adverse reactions included grade 2 gastrointestinal tract reaction, grade 2-3 leucopenia, and grade 2-3 mucosal reaction, which could be controlled with symptomatic relief and supportive treatment. Three and 12 months after the primary therapy, the PET/CT series showed that both the size and the  $SUV_{max}$  of the tumor decreased, which reflected the therapeutic efficacy.

However, 22 months after the primary therapy, the PET/CT imaging showed that the  $SUV_{max}$  was significantly increased ( $SUV_{max} = 6.5$ ). We considered this metabolic recurrence. However, physical examination, nasopharyngoscope, CT, and MRI revealed no obvious changes. Since the patient refused to undergo salvage surgery, six courses of chemotherapy with PPS (the same regime as before) were performed from December 2013 to June 2014. Due to the lack of radiotherapy, only grade 2-3 leucopenia was found in each course that could be controlled with support therapy. Three months later, PET/CT showed that the  $SUV_{max}$  decreased significantly. After the therapy for the metabolic recurrence, the follow-up PET/CT found no evidence of recurrence until now. The patient has survived for more than 5 years with good quality of life after the first recurrence (2012-02-09). A review of the imaging series is shown in **Figure 3**.



**Figure 2.** Positron emission tomography/computed tomography imaging before any therapy. The highly aberrant accumulation after paclitaxel, platinum, and S-1 treatment measured  $4.8 \times 3.3 \times 6.6$  cm (maximum standardized uptake value = 3.2) with no evidence of distant or lymph node metastasis.

## Discussion

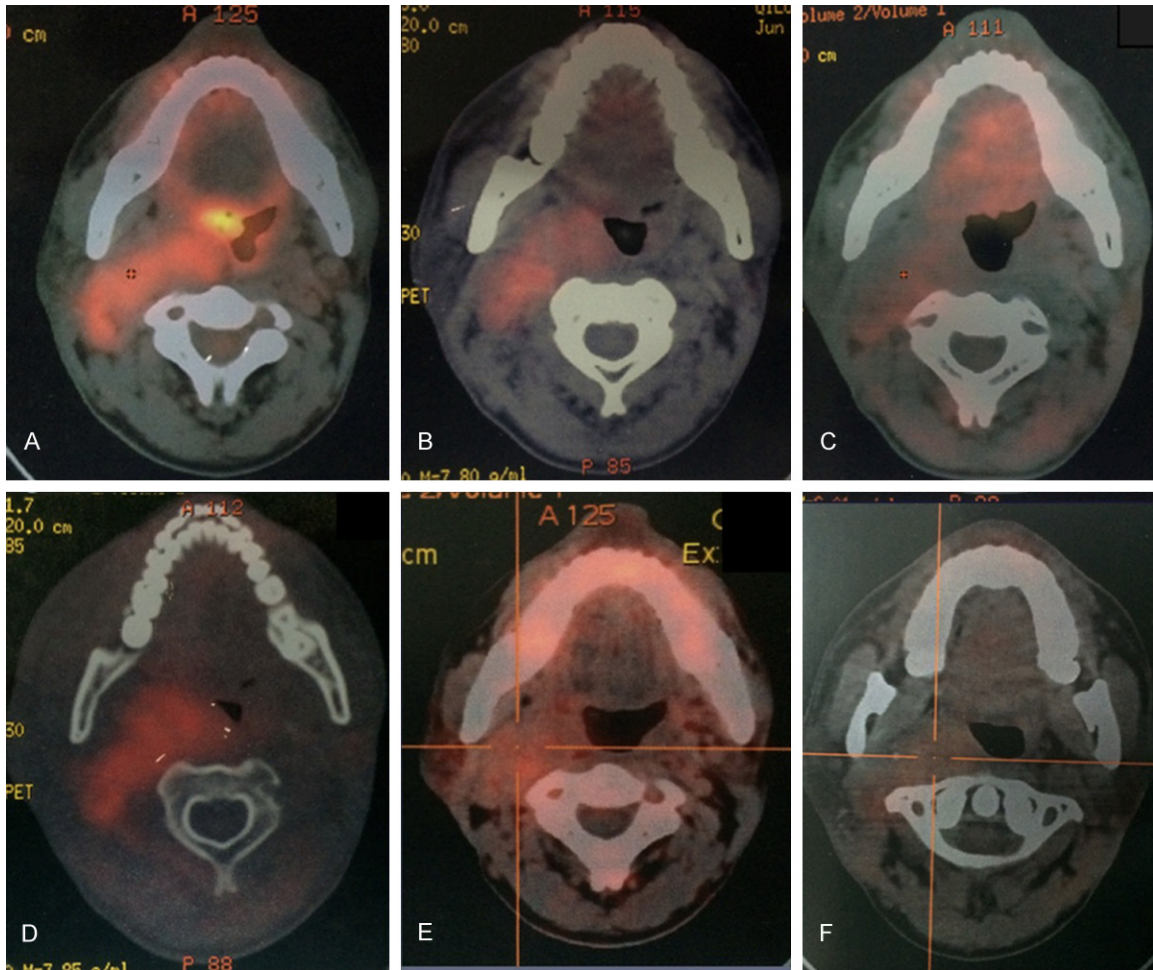
Since 2000, concomitant CRT has been considered the standard treatment for unresectable HNSCC since it can achieve high rates of locoregional control, survival, and preserved organ function. Nevertheless, the recurrence at the primary site or in the neck was approximately 20-30% and 10-15% of patients, respectively [3]. The median overall survival after treatment failure is poor at <1 year [2]. The next problem is that many patients are medically unfit or unwilling to undergo surgery, and reirradiation is less effective with a high incidence of complications [5]. Although systemic therapy was once considered less effective than reirradiation or salvage surgery, oncologists frequently struggled about whether chemotherapy could be used as an alternative treatment for patients with unresectable locoregional recurrent HNSCC. Response rates of chemotherapy are approximately 30% and response duration does not exceed 6-8 months with a median overall survival of 6-9 months [6]. The triplet regimen of PPS had comprehensive effects,

fewer adverse effects, and lower cost since it did not include cetuximab [12-15]. Considering that the standard first-line therapy for HNSCC consisting of the triplet chemotherapy regimen was effective in primary therapy, we recommend that use of the same chemotherapy regimen may show effectiveness when recurrence occurs 1 year after the primary therapy. The findings in this case supported our suggestions.

Another challenge is that when the therapy for recurrent patients cannot achieve complete remission, the patients must survive with cancer. Surviving with cancer stably is a strategy that requires patients to have good prognosis factors such as no smoking, no other diseases, good performance score, and young age. To maintain cancer stability over the long term, active follow-up and early therapy for early recurrence are necessary.

The early detection of metabolic recurrence may provide a chance for early salvage treatment and, therefore, a survival benefit [7]. However, regular standard examinations includ-





**Figure 3.** Summary of the follow-up imaging series. A: At diagnosis, the tumor measured  $4.8 \times 3.3 \times 6.6$  cm and the maximum standardized uptake value ( $SUV_{max}$ ) = 3.2. B: Three months after the primary therapy, the tumor measured  $4.0 \times 2.4 \times 4.5$  cm,  $SUV_{max}$  = 1.5. C: Twelve months after the primary therapy, the tumor measured  $3.7 \times 2.2 \times 4.4$  cm,  $SUV_{max}$  = 1.3. D: Twenty-two months after the primary therapy at the time of metabolic recurrence, the tumor measured  $4.5 \times 2.3 \times 5.6$  cm,  $SUV_{max}$  = 6.5. E: Three months after the second-line therapy, the tumor measured  $3.7 \times 2.1 \times 5.3$  cm,  $SUV_{max}$  = 2.2. F: Thirty months after the second-line therapy, the tumor measured  $3.5 \times 2.0 \times 4.5$  cm,  $SUV_{max}$  = 1.8.

ing physical examination, endoscopy, CT, and MRI have the disadvantage of interfering with postsurgical or radiation-induced changes to detect early recurrence [8]. Functional imaging techniques such as PET/CT could reflect the metabolism of malignant lesions with a sensitivity of 79.9% and specificity of 87.5% for the post-treatment assessment of recurrence [4]. It was noted that a 3-month scan following primary treatment had better accuracy for assessing effectiveness [4]. In addition, the negative of recurrence on 3-month imaging after the initial therapy is associated with favorable prognosis [9].

As discussed above, we chose to perform 3-month imaging after each therapy to assess

therapeutic efficacy. Routine post-treatment PET/CT imaging is controversial for asymptomatic patients. Considering that the patients survived with cancer, we think that performing follow-up PET/CT scans in the first 2 years will provide a survival benefit whether the patient is symptomatic or asymptomatic. Abgral R found that PET/CT scanning at 1 years had an overall accuracy of 90% for the detection of HNSCC recurrence [10]. The patients received the first scans just 3 months after the first therapy, and then the scans were performed every 6 months once the patients were surviving with cancer and needing more care. Using this strategy, we identified the metabolic recurrence in time. However, the value of follow-up PET-CT after 2 years requires investigation. Moreover, its cost-

effectiveness is a major consideration in its routine use [11]. All in all, this series of PET/CT scans leads to the early discovery of recurrence and effective therapy, which comprise the basis of long survival.

## Conclusion

PPS triplet chemotherapy is expected to improve the outcomes of patients with local advanced metabolic recurrent HNSCC. The dose and course of treatment must be identified in each individual case. Our patient has survived for a long time with a good quality of life. The follow-up PET/CT scans could provide useful information about recurrence and prognosis.

## Disclosure of conflict of interest

None.

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