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Case report

Early prediction of response to cetuximab and radiotherapy by FDG-PET/CT for the treatment of a locoregionally advanced squamous cell carcinoma of the hypopharynx

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ARTICLE INFO

Article history:
Received 16 May 2014
Accepted 15 September 2014
Available online 29 September 2014

Keywords:
Cetuximab
Head and neck cancer
Predictive marker
FDG-PET/CT
Radiotherapy

ABSTRACT

Cetuximab (CTX) is used for the concurrent treatment with radiotherapy (RT) in squamous cell carcinoma of head and neck (HNSCC). There are no reliable clinical predictive markers of effectiveness of CTX at yet. We describe the clinical case of patient who received a CTX/RT to cure locoregionally advanced hypopharyngeal SCC. 2-Deoxy-2-[^{18}F]fluoro-D-glucose positron emission tomography and computed tomography (^{18}FDG-PET/CT) was performed before the treatment and repeated 10 days after CTX induction dose. A repeated ^{18}FDG-PET/CT scan showed dramatic decrease of metabolic parameters. Patient had a complete response after treatment and is still alive and cured after 5 years.

1. Introduction

Head-and-neck cancer refers to a group of the malignant tumors arising at a variety of sites in the upper aerodigestive tract, the most commonly in the oral cavity, the oropharynx, the hypopharynx and the larynx. The squamous cell carcinoma (SCC) is the predominant histological type (about 90%) and the sixth leading neoplasm by incidence worldwide with more than 650,000 new cases diagnosed per year [1]. At the time of diagnosis most patients have the locally advanced disease and lymph node metastases [2]. Despite advances in therapy during past decade,

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Peer review under the responsibility of the Lithuanian University of Health Sciences.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.medici.2014.09.003

prognosis and long-term survival of patients with locoregionally advanced head and neck squamous cell carcinoma (LAHNSCC) are poor.

Combined chemoradiotherapy, including monoclonal antibodies, represents state-of-the art treatment for LAHNSCC. Cetuximab (CTX) is a monoclonal antibody targeted to epidermal growth factor receptor (EGFR). It has been approved for use in combination with radiation during treatment of primary locoregionally advanced (stage III to IVB) HNSCC or as monotherapy for the treatment of recurrent or metastatic HNSCC after the failure of platinum-based chemotherapy, and also in combination with platinum/5-fluorouracil for the treatment of the recurrent or metastatic disease. Treatment with this anti-EGFR antibody is expensive and absolute difference in median overall survival at 3 years in LAHNSCC patients is 19.7 months (29.3 months in RT only group vs. 49 months in RT/CTX group). This corresponds to 10% absolute benefit in median overall survival in the RT/CTX group [3]. The majority of patients with LAHNSCC do not take advantage either because they have been cured by RT alone or are unresponsive on the long term. Hence, it is desirable to early predict the efficacy of the treatment with CTX/RT to better select good responders.

2. Case report

A 66-year-old man with dysphagia, pain in the left jaw and ear, and hoarseness lasting since January 2009 was admitted to the out-patient clinic in March 2009. Ulcero-proliferative lesion in the left pyriform sinus, aryepiglottic folds, left arytenoid and cricoid region with immobility of the left vocal cord was diagnosed by fiberoptic endoscopic examination. Histological examination of the lesion biopsy showed the poorly differentiated SCC. One enlarged lymph node was detected in the level II on the left side of the neck during clinical examination. No distant metastasis was detected.

A hypopharyngeal SCC of the left side was diagnosed, clinically cT3N1M0, stage IVa according to the Union for International Cancer Control (UICC) 6th edition. Concomitant chemoradiotherapy was foreseen for the treatment, but hepatitis C with the advanced cirrhosis was diagnosed before the commencement of RT. Therefore, treatment with CTX was proposed instead of platinum-based chemotherapy.

The first ^{18}FDG-PET/CT was carried out on April 23, 2009. Standard induction dose of CTX (400 mg/m^2) was administered on April 27, 2009, and was followed by radiosensitizing doses on a weekly basis.

RT treatment planning was performed using standard contrast-enhanced CT and ^{18}FDG-PET/CT data. Then RT was administered between May 4, 2009, and June 15, 2009, inclusive. Accelerated fractionation (2 Gy/fx, 6 fx/week) was used. A therapeutic dose of 70 Gy was prescribed to the hypopharyngeal tumor and the lymph node in the level II on the left side of the neck. A prophylactic dose of 50 Gy was prescribed to the lymph nodes in the level III and IV on the left side of the neck and the level II to IV on the right side of the neck.

The second infusion of CTX was administered on May 4, 2009, and intensity modulated radiotherapy (IMRT) was used for delivery of highly conformal RT. ^{18}FDG-PET/CT was repeated on May 7, 2009, following RT of a cumulative dose of 6 Gy.

The first ^{18}FDG-PET/CT revealed pathological ^{18}FDG uptake in the left side of hypopharynx and in one lymph node in level II on the left side of the neck. The second ^{18}FDG-PET/CT on May 7, 2009, showed significant decrease in ^{18}FDG uptake in the tumor and the metastatic lymph node (Fig. 1). The main parameters of both ^{18}FDG-PET/CT scans are summarized in Table 1.

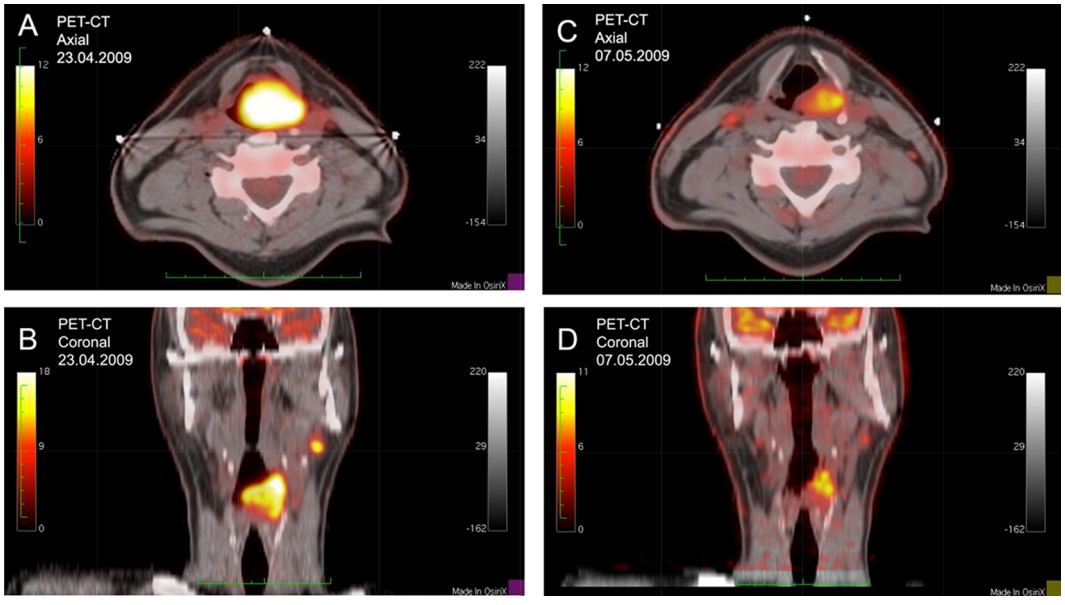

Fig. 1 – ^{18}FDG uptake before (A and B) and after (C and D) administration of 2 doses of CTX. The first ^{18}FDG-PET/CT (axial (A) and coronal (B)) revealed pathological ^{18}FDG uptake in the left side of hypopharynx and one lymph node in level II on the left side of the neck. The second ^{18}FDG-PET/CT (axial (C) and coronal (D)) on 07.05.2009 showed significant decrease in ^{18}FDG uptake in the tumor and the metastatic lymph node. SUV threshold value of 2.5 was used for image acquisition.