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Response Monitoring by Positron Emission Tomography during Radiotherapy of a Squamous Cell Skin Carcinoma

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Key Words

Skin neoplasms · Squamous cell carcinoma · Radiotherapy · Positron emission tomography (PET)

Summary

Background: Radiotherapy of skin cancer in a previously irradiated area is a challenging task with regard to cumulative total dose and consecutive normal tissue toxicity. Methods of biological response monitoring might be helpful in achieving a favorable therapeutic ratio. **Patient and Methods:** We report the case of a 77-year-old patient with squamous cell skin carcinoma originating within a previous radiotherapy field. Initially, the patient refused surgical resection. 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography (FDG-PET) was performed before reirradiation and after 44 Gy. **Results:** FDG-PET showed no change in the standardized uptake value, i.e. no metabolic response. Clinically, the tumor failed to shrink after radiotherapy with a total dose of 64 Gy and progressed rapidly within the first 8 weeks of follow-up. Confirmatory biopsies were obtained and salvage surgery attempted. **Conclusion:** In this case, FDG-PET after 44 Gy correctly identified a non-responding patient with squamous cell skin cancer. Thus, further assessment of this method for response evaluation and treatment optimization appears warranted.

Schlüsselwörter

Hautkrebs · Plattenepithelkarzinom · Strahlentherapie · Positronenemissionstomographie (PET)

Zusammenfassung

Hintergrund: Die Strahlentherapie von Hauttumoren in einem vorbestrahlten Areal ist bezüglich der kumulativen Gesamtdosis und der resultierenden Normalgewebetoxizität eine große Herausforderung. Methoden zur biologischen Verlaufsbeobachtung könnten hilfreich sein, um ein günstiges therapeutisches Verhältnis zu erzielen. **Patientin und Methoden:** Wir beschreiben den Fall einer 77-jährigen Patientin mit Plattenepithelkarzinom der Haut in einem vorbestrahlten Areal. Die Patientin lehnte ein operatives Vorgehen initial ab. Wir führten vor der Zweitbestrahlung und nach 44 Gy eine 2-Deoxy-2-[18F]fluoro-D-glucose Positronenemissionstomographie (FDG-PET) durch. **Ergebnisse:** Es ergab sich keine Veränderung des «Standardized-uptake-Wertes», d.h. kein metabolisches Ansprechen. Klinisch sprach der Tumor ebenfalls nicht auf die Bestrahlung mit insgesamt 64 Gy an und war in den ersten 8 Wochen der Nachbeobachtungszeit rasch progredient. Es wurden konfirmatorische Biopsien veranlasst und eine Salvage-Operation angestrebt. **Schlussfolgerung:** In diesem Fall identifizierte die FDG-PET nach 44 Gy korrekt eine nicht ansprechende Patientin mit Plattenepithelkarzinom der Haut. Daher erscheint die weitere Untersuchung dieser Methode zur Verlaufsbeobachtung und Behandlungsoptimierung gerechtfertigt.

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Introduction

Besides different other risk factors, skin cancer might be induced by ionizing radiation [1]. Curative treatment options include surgical excision and primary radiotherapy [2, 3]. However, the latter might be difficult to administer in previously irradiated areas due to the compromised normal tissue tolerance. Thus, adjustment of the total dose to the lowest possible level by means of response monitoring methods would be prudent. Most of these skin lesions will be amenable to simple clinical inspection. However, if tumor shrinkage does not occur early during retreatment, definitive judgement might require alternative methods. 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography (FDG-PET) has been studied in both malignant melanoma and basal cell carcinoma of the skin [4]. Besides staging purposes, FDG-PET can also be used to monitor response to treatment, for example in neoadjuvant radiochemotherapy of non-small cell lung cancer (NSCLC) and esophageal cancer [5–8]. Based on this experience, we used FDG-PET to monitor the response of skin cancer to reirradiation.

Case Report

In May 2004, a 77-year-old female patient presented with a slightly ulcerating tumor of the right cheek which was histologically diagnosed as well differentiated (G1, focal G2) squamous cell carcinoma. Magnetic resonance imaging (MRI) demonstrated a lesion of 2.5 cm maximum diameter infiltrating deep into the buccal mucosa of the oral cavity without any bone involvement or lymph node metastasis. The patient had severe trismus and xerostomia resulting from a previous radiochemotherapy series. In 1996, this treatment had been administered sequentially (chemotherapy followed by radiotherapy) for a squamous cell carcinoma of the right maxilla, stage T4 N2b M0 G2. Total dose of radiotherapy was 66 Gy in 33 fractions (lateral opposed beam technique with inclusion of both neck sides for the first 50 Gy, i.e. shrinking field; combination of 6-MV photons and dorsal electron fields for spinal cord sparing). The patient had been in complete remission for almost 8 years. The new lesion clearly developed within the pretreated area, which showed moderate skin atrophy and subcutaneous fibrosis. Because of the significant late sequelae resulting from the previous treatment, we recommended surgical excision rather than additional radiotherapy. However, the patient refused surgery and presented again in September, asking for definitive radiotherapy. Corresponding to the clinical examination at that time, an FDG-PET scan showed a region of enhanced uptake (now 3 cm in maximum diameter, fig. 1A, B) without any lymph node or organ metastases.

Treatment was administered to the primary tumor plus 2 cm safety margin by use of a single 12-MeV electron field with bolus material. We used conventional fractionation, i.e. a dose of 2 Gy per fraction, 5 fractions per week. Clinically no tumor shrinkage was seen. Therefore, we performed an additional FDG-PET scan after application of 44 Gy. Our intention was to limit the total dose to this heavily pretreated area in case of a metabolic response. However, the standardized uptake value (SUV) in the region of interest remained unchanged (maximum 6.4 in September and 6.3 in November, fig. 1C). Thus, we decided to administer a total dose of 64 Gy. Treatment was finished without interruption and without severe acute toxicity. The patient was re-evaluated 8 weeks after completion of radiotherapy. Both clinical examination and MRI showed enlargement of the tumor by approximately 1 cm. No locoregional metastases were detected. 2 weeks later, 6 biopsies were taken from the periphery of the external tumor and the buccal infiltration, all of which contained viable squamous cell carcinoma. The patient was scheduled to undergo salvage surgery.

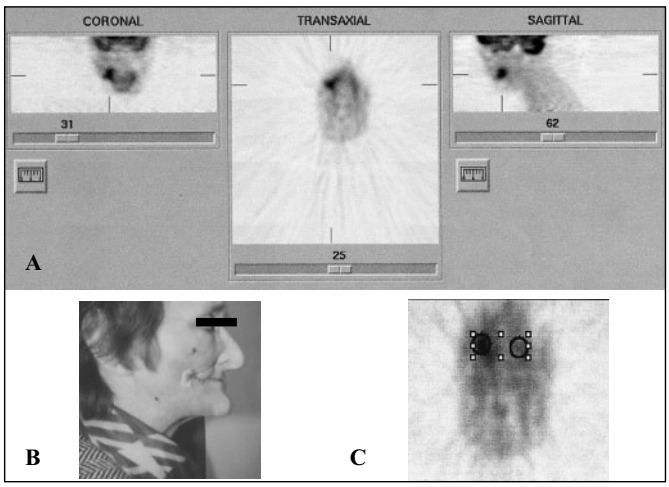

Figure 1. **A.** FDG PET scan of the spinocellular carcinoma obtained before definitive radiotherapy. **B.** Photograph of the tumor before definitive radiotherapy. **C.** Evaluation of the standardized uptake value in the region of interest compared to the contralateral cheek after 44 Gy

Discussion

The occurrence of skin cancer within an area previously exposed to therapeutic radiation doses is uncommon when compared to the total number of skin cancers [2]. However, this situation is particularly challenging if the treatment of choice is reirradiation. In the light of the long time interval of 8 years between the maxilla tumor and the skin tumor of our patient, we think that a second primary tumor is more likely than a recurrence. In the absence of a clinical response after 40 Gy, we attempted to adjust the dose of reirradiation to the metabolic response of the tumor by comparing the SUV of FDG-PET scans, based on studies in squamous cell carcinomas of other organs [5–7]. The unchanged SUV turned out to correspond well with the ultimate outcome. Despite administration of 64 Gy to the lesion, no regression was seen. It appears unlikely that this could be attributable to technical reasons. Compared to the moderate growth before reirradiation, the tumor even appeared to accelerate its growth during the first 8 weeks thereafter. Thus, salvage surgery became necessary. According to Lovett et al., newly diagnosed squamous cell skin cancer was locally controlled in 87% of cases (recurrent tumors in 65%) [9]. Comparable results were reported by other groups [10, 11].

FDG-PET has been used for response monitoring in both lung and esophageal cancer. The study by Ryu et al. included 26 patients with NSCLC treated with neoadjuvant radiochemotherapy [5]. Of these 6 had squamous cell carcinoma. Mean SUV of all 26 patients was 14.9 at baseline and 5.7 after

neoadjuvant treatment. SUV-based analysis (cut-off 3.0) had a high sensitivity (88%) but limited specificity (67%) for detecting residual tumor. The study by Swisher et al. included a majority of patients with adenocarcinoma of the esophagus [6]. The accuracy of PET SUV after preoperative radiochemotherapy was 76%. PET was more accurate than computed tomography and endoscopic ultrasonography. Wieder et al. evaluated 38 patients with esophageal squamous cell cancer [7]. Their patients were evaluated after 2 weeks of neoadjuvant radiochemotherapy and preoperatively. Mean SUV before treatment was 9.3 and decreased to 5.7 after 2 weeks and to 3.3 before surgery. In histopathologic responders, the SUV decrease after 2 weeks was significantly higher than in non-responders, suggesting that FDG-PET during treatment might predict the effectiveness of radiochemotherapy. Of course, the accuracy of FDG-PET during radiotherapy of skin cancer needs confirmation in a larger series of patients which are not suitable for clinical monitoring alone. However, this method might be helpful in predicting tumor response and in improving the therapeutic ratio in pretreated patients. Limitation of its use to a highly selected group of patients is certainly warranted from the point of cost-effectiveness. If extended experience with PET scanning should suggest that this method is suitable to guide the choice of further treatment (radiotherapy completion vs. salvage surgery), the cost-effectiveness might depend on the type of surgery, for example extensive resection with plastic reconstruction as opposed to limited local excision.

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