Evaluation by ^{18}F-FDG-PET of patients with anal squamous cell carcinoma

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Abstract

Anal squamous cell carcinoma (ASCC) is a rare cancer of the gastrointestinal tract, representing less than 5% of the digestive malignancies. The cytological and/or histological confirmation of a suspected lesion should be followed by a complete imaging evaluation to determine the extent of disease. We are presenting our experience with ^{18}F-FDG PET in ASCC. *This is a retrospective case series of patients* diagnosed and treated for ASCC at our institution(s). A total of 14 ^{18}F-FDG PET scans (8 for initial staging, 6 for evaluation of response to chemotherapy and radiation therapy) were performed in 8 patients (6 men, 2 women). The patients were 33 - 60 years old (average: 44 ± 9). *Our results* showed that PET demonstrated the primary lesion at initial evaluation in 7 of 8 anal cancers and showed FDG-avid lymph nodes in 4 patients. Metastatic nodal involvement was confirmed by pathology in 2 patients; in the other 2 patients pathology showed reactive follicular hyperplasia. In another patient, follow-up PET demonstrated progression of disease despite treatment, prompting a change in disease management. In the remaining 5 patients with follow-up PET, the scans confirmed interval resolution of the ^{18}F-FDG uptake in the primary lesion, suggesting good treatment response. *In conclusion,* PET provides valuable diagnostic information in initial staging and evaluation of treatment response in ASCC that may significantly alter the clinical management. The emergence of the combined PET/CT scanner enhanced the accuracy of the imaging procedure in view of the precise anatomic localization of metabolic abnormalities.

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Introduction

Anal squamous cell carcinoma (ASCC) is a rare cancer of the gastrointestinal tract, representing less than 5% of the digestive malignancies. According to American Cancer Society estimates, a total of 5.070 (2.020 males, 3.050 females) newly diagnosed anal cancers were expected in 2008, with 680 expected deaths (250 males, 430 females) [1]. Although ASCC is relatively rare, it is the fourth most common reported malignancy among men with human immunodeficiency virus (HIV) infection [2]. Over the past decade, ASCC diagnosis and treatment have been revisited and new approaches have emerged. The cytological and/or histological confirmation of a suspected lesion should be followed by a complete imaging evaluation to determine the extent of disease.

Molecular imaging with positron emission tomography (PET) has an important role in the imaging evaluation of patients with various malignancies [3]. Fluorine-18-fluorodesoxyglycose (^{18}F-FDG PET) facilitates detection of local recurrence and metastatic disease, guidance at biopsy sites, prediction and monitoring response to treatment and assessment of prognosis. The information available about the diagnostic utility of ^{18}F-FDG PET in ASCC is limited [4-7]. However, recent data suggests that PET can aid in anal cancer staging and identification of residual, recurrent and metastatic disease [8]. We were therefore prompted to review our experience with ^{18}F-FDG PET in ASCC.

Materials and methods

This study is a retrospective case series (2000-2003) of patients diagnosed and treated for ASCC at our institution. Records from our hospital's cancer registry were obtained and reviewed after Institutional Review Board approval was obtained. A total of 32 patients with ASCC were identified. They were managed according to the algorithm described in Table 1. For 8 of the patients ^{18}F-FDG PET scans were performed and these are the cases included in this report.

Study entry criteria included a pathologically proven diagnosis of anal cancer and the ^{18}F-FDG PET imaging done as part of the patients' management. The PET scanner used was a dedicated ECAT EXACT camera (Siemens CTI, Knoxville, TN) on a mobile PET platform. The images were processed on computer stations from Sun Microsystems (version 7.2.2). Glucose levels were measured prior to the injection of radiotracer and only those patients with a blood glucose level less than 200mg/dl underwent PET scanning. PET images were acquired approximately 1h after intravenous injection of ^{18}F-FDG. Data were acquired in 2D mode, with attenuation correction calculated from a 3min transmission scan. Each data set consisted of 31 contiguous, 3.375mm thick, tomographic sections, for a total field of view of 10cm.

Semi-quantitative analysis of the ^{18}F-FDG uptake in the suspected lesions was based on calculation of standard uptake value (SUV), defined as the ratio of activity per milliliter of tissue to the activity in the injected dose corrected by decay and per patient's body weight or body surface. Accuracy is greater than 3 significant digits for maximum SUV (SUVmax) value [9]. Regions of interest were placed around the regions of increased ^{18}F-FDG uptake for SUVmax determination.

Computed tomography (CT) images of the chest, abdomen and pelvis were acquired on a GE HiSpeed single-slice spiral scanner and were used for assistance in the anatomic localization of the lesions noted on the ^{18}F-FDG PET scans. The thickness of the CT sections ranged from 3 to 9mm.

Results

Fourteen scans were performed in 8 patients. The clinical indication was staging (8 scans) and follow-up after combined radiation and chemotherapy (6 scans). Data about the 8 patients included in this case series is summarized in Table 2. Six patients were males and 2 females. The age of the patients ranged from 33 - 60 year(s) old (average: 44 ± 9). Four patients were HIV positive. The interval between the initial scan and the follow-up imaging ranged from 4 to 10 months. All patients received a combination of neo-adjuvant chemotherapy (mitoxantrone and 5-fluorouracil) and local radiation therapy prior to the follow-up PET scan.

In this case series, ^{18}F-FDG PET at initial disease evaluation demonstrated the primary cancer in 7 of the 8 biopsy proven anal cancers. In addition, ^{18}F-FDG PET identified hypermetabolic lymph nodes in 4 of the 8 patients. Metastatic involvement was confirmed by pathology examination in 2 cases, thus changing the stage of disease. The other 2 cases were reactive follicular hyperplasia, in patients with HIV. The management was changed in a patient with equivocal pelvic lymph nodes on CT: no uptake on the PET scan in this area prompted cancellation of a lymph node biopsy.

Follow-up studies were done in 6 of the 8 patients. In one of these patients, more intense ^{18}F-FDG uptake in the primary lesion suggested absence of response to treatment or disease recurrence, prompting a change in the chemotherapy regimen and cancellation of surgery. For the remaining patients, ^{18}F-FDG PET demonstrated decrease in the metabolic activity of the tumor, suggesting good response to treatment.

Figure 1 presents the initial PET scan of a patient with symmetric axillary ^{18}F-FDG uptake (arrowheads; SUVmax 1.9 on the left and 2.7 on the right), corresponding to lymph nodes increased in size on CT. Biopsy of the right axillary lymph nodes demonstrated reactive changes. The primary rectal lesion showed ^{18}F-FDG uptake as well (arrows).

The initial evaluation of another patient by PET imaging confirmed the primary cancer of the anus (SUVmax 7.4) with

Table 1. *Algorithm for diagnostic and therapeutic approach in anal SCC*

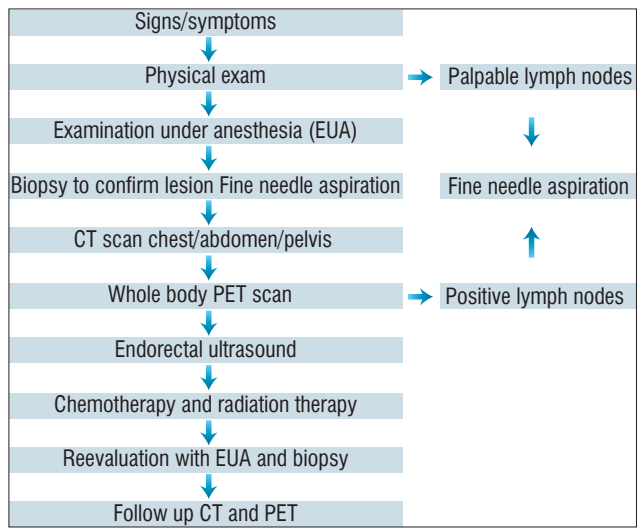

Table 2. *Data about the patient population included in this case series*

Case	Age	Sex	Signs and symptoms at presentation	Histology	Stage
1	33	M	Anorectal pain, bright red blood per rectum, weight loss	Well to moderately differentiated ASCC	T2N0M0
2	40	M	Perianal abscess	Moderately differentiated ASCC	T1N0M0
3	46	M	Constipation	Well to moderately differentiated ASCC	T3N0M0
4	44	M	Bright red blood per rectum	Poorly differentiated ASCC	T3N3M0
5	35	M	Anal lump	Moderately differentiated ASCC	T2N0M0
6	44	F	Anorectal pain	Moderately to poorly differentiated ASCC	T2N1M0
7	54	M	Anal lump	Moderately differentiated ASCC	T2N0M0
8	60	F	Rectal discharge, inguinal lump	Moderately differentiated ASCC	T2N2M0

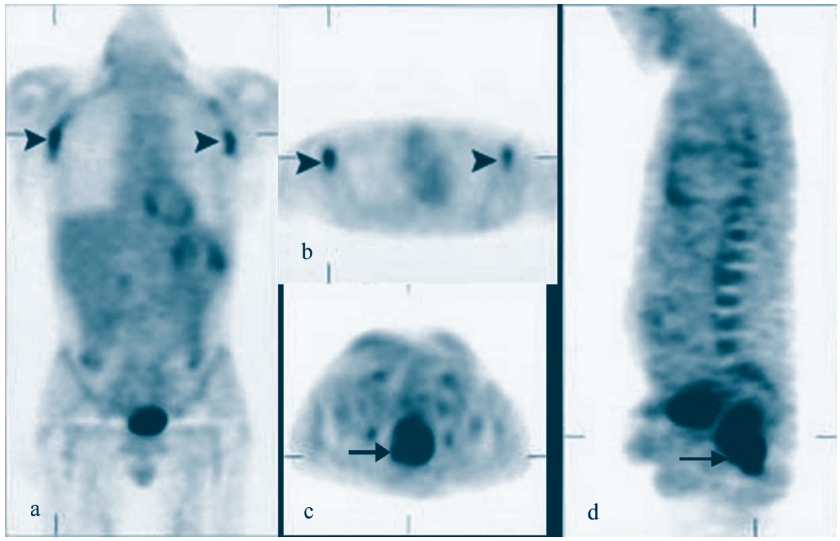

Figure 1. A 40 years old man with moderately differentiated ASCC. a) and b) Initial PET scan showed mild ^{18}F-FDG uptake in the axillae (arrowheads), proved to be reactive lymph nodes on biopsy; c) and d) the primary tumor is also metabolically active (arrows).

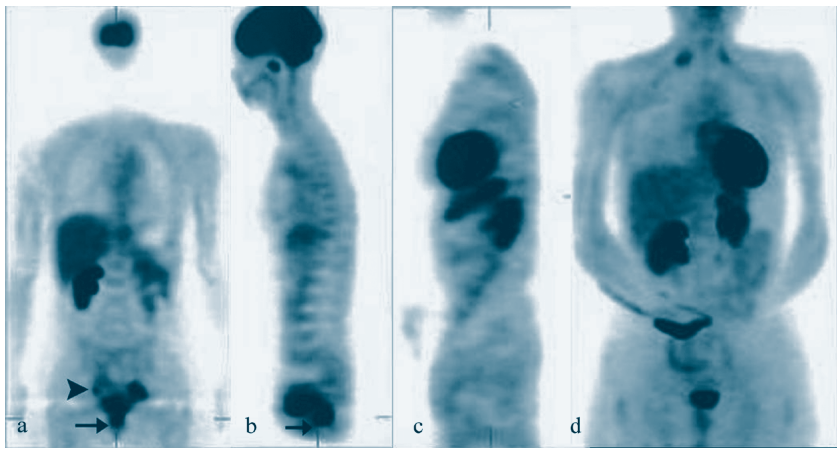

Figure 2. A 44 years old woman with moderately to poorly differentiated ASCC. a) and b) The initial PET imaging confirmed the ASCC with local extension into the pelvis (arrows) and raised the possibility of malignant involvement of a right inguinal lymph node (arrowhead), which was confirmed by the biopsy results; c) and d) Four months later, after radiation therapy and chemotherapy, the follow-up ^{18}F-FDG PET scan was negative.

local extension into the pelvis and raised the possibility of malignant involvement of a right inguinal lymph node (Fig. 2a and b). Pathologic examination of the lymph node confirmed the presence of metastatic disease. Four months later, a follow up PET scan was normal (Fig. 2c and d).

Discussion

Anal cancer can be cured by synchronous radiation and chemotherapy and patient care should be managed by a multidisciplinary team [10].

CT, MRI and endoscopic rectal ultrasonography recognize abnormalities based on changes in anatomy. ^{18}F-FDG PET imaging allows three-dimensional observation of glucose metabolism. There is evidence to suggest its role as the standard of care in initial staging, monitoring the response to treatment, and management of head and neck and esophageal squamous cell carcinomas [11]. In a case series including four patients with anal cancer, PET appeared to be useful for the diagnosis of recurrent disease [12]. ^{18}F-FDG PET, in conjunction with CT scanning, provides additional staging information in cancer of the anal canal, but post-treatment PET scans appear to be of little value in predicting durability of response [4]. PET detects the primary anal tumor more often than CT and detects substantially more abnormal inguinal lymph nodes than are identified by standard clinical staging with CT and physical examination [5].

With one exception, all the initial staging PET scans demonstrated intense ^{18}F- FDG uptake at the site of the primary tumor. From a surgical standpoint, regional lymph nodes are difficult to be accessed and providing means to assess their involvement by tumor is needed. PET scanning identified regional lymph node metastases in 2 patients, confirmed by pathologic assessment, and was negative in lymph nodes described as equivocal on CT in another patient. ^{18}F-FDG PET findings may be false positive, as demonstrated in 2 patients with hypermetabolic lymph nodes, but reactive follicular hyperplasia on biopsy. Reports in the literature suggest that a subset of patients infected with HIV demonstrates a syndrome of persistent generalized lymphadenopathy and lymph node biopsies reveal benign reactive changes with a pattern of follicular hyperplasia [13]. Incidental ^{18}F-FDG uptake is not always associated with underlying pathology [14].

Recent articles describe results of the use of combined PET/CT in anal cancer. Furthermore, there are reports on the use of ^{18}F-FDG PET/CT to predict response to therapy in anal

cancer. One study suggests that a partial metabolic response in the anal tumor as determined by post-therapy ^{18}F-FDG PET is predictive of significantly decreased progression-free and cause-specific survival after chemoradiotherapy for anal cancer [15]. *In conclusion,* ^{18}F-FDG PET and PET/CT may be an effective tool in the imaging of anal cancer by providing reliable information regarding the staging and management of this disease and the need for surgical biopsy. In addition, PET imaging might be useful in assessing the response to treatment. Combined PET/CT scanners enhance the ability to detect pathologic changes and differentiate them from variants of normal anatomy.

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