Impact of PET/CT on initial staging, restaging and treatment management of anal cancer: A clinical case with literature review

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Summary

Distant extrapelvic metastases appear in approximately 10% of the patients with squamous cell anal cancer (SCAC) and survival depends on the treatment strategy. Exact staging leads to optimal planning of multimodality therapy and the adequate evaluation of treatment response can improve the prognosis of the disease. Diagnosis and staging of SCAC are commonly performed using contrast-enhanced computerized tomography (CT) and interpretation of the findings are based on anatomical size criteria with limitations for tumor biological behavior. F18-fluoro-2-deoxy-D glucose positron emission tomography (¹⁸F-FDG PET) reveals aspects of tumor function and allows metabolic measurements. Combined PET/CT scans permit exact localization with anatomical criteria of the hypermetabolic ¹⁸F-FDG avid malignant lesions. We present a patient with SCAC in whom, according to PET/CT findings, the initial stage was changed from II (T2N0M0) to III A (T2N2M0). Radiation therapy (RT) and chemotherapy achieved a good therapeutic response but early follow up revealed new para-aortic lymph node (LN) metastases, as well as an uncommon left supraclavicular LN metastasis from the same primary carcinoma. The disease was restaged as stage IV (T2N2M1) and radiation therapy was substituted by chemotherapy.

Key words: computerized tomography, positron emission tomography, squamous cell anal cancer, staging, supraclavicular nodal metastasis

Introduction

Despite that malignancies of the anal canal are relatively rare, accounting for 4% of the lower gastrointestinal (GI) carcinomas [1-3], SCAC most commonly occurs in 47-60% of these cases [4]. The risk of invasive SCAC associated with poor prognosis increases 2-6 times in HIV-positive patients [5]. The probability of nodal involvement is directly related to the main risk factors such as the tumor size, site and cell differentiation. Above the dentate line, tumor drainage flows to perirectal and paravertebral nodes and below this line drainage is through the inguinal and femoral nodes [6]. Distant extrapelvic metastases occur approximately in 10% of the patients, predominantly to the lung and liver, most commonly following the dual lymphatic drainage to the portal and systemic nodal basins [7]. Accurate staging followed with an optimal planning of radiation therapy and chemotherapy can extend the survival of the patients. The anatomical imaging techniques [CT, ultrasound (US) and/or magnetic resonance imaging (MRI)] cannot evaluate tumor biology and behavior [8]. Functional PET imaging can have a role in assessing hypermetabolic ¹⁸F-FDG avid lesions inconclusive by the other imaging modalities [9]. In combined PET/CT, PET with ¹⁸F-FDG is known to be sensitive enough for detecting viable tumor tissue, whereas CT permits vi-
sualization of anatomic changes and exact localization of the metabolic proliferative changes [10]. Meta et al. in their retrospective review of the impact of PET on the treatment of rectal cancer reported that it changed both the staging in 42% of the patients and treatment in more than 60% [11]. We did not find PET/CT data on SCAC staging in the accessible clinical reports and any clinical reports with supraclavicular LN metastasis from SCAC.

The interest of this case lies in the PET/CT impact on the exact primary staging and restaging with metastatic extension including unexpected SCAC supraclavicular LN metastasis, as well as on the assessment of multimodality radiochemotherapy efficacy or further treatment planning.

Case presentation

A 45-year-old HIV-positive white male with stage II (T2N0M0) poorly differentiated SCAC was diagnosed in January 2005 following diagnostic work-up of anal condylomata acuminata.

The surgical specimen pathology reported invasive poorly differentiated squamous cell carcinoma. Past history was significant for HIV for 12 years with several episodes of pneumonia and encephalitis. PET/CT was requested for initial staging and restaging and was performed 80 min post-injection of the $^{18}$F-FDG, using a PET/CT Discovery ST-General Electric Medical System. A low dose x-ray CT was used for attenuation, correction and anatomical localization of the $^{18}$F-FDG emission PET scan. The scan was performed from the mid thigh to the base of the skull. Oral contrast was given. Intravenous contrast was not used.

The results of PET/CT were evaluated for primary staging, chemotherapy and RT response, restaging and planning further therapy.

The primary staging PET/CT study suggested a hypermetabolic ano-rectal tumor with increased uptake of $^{18}$F-FDG with maximum standardized uptake value (SUV max) 5.1 and regional metastasis to the left side of the pelvis, as well as to iliac LNs at the level of L4-5 with SUV max 5.3 (Figure 1a,b). The prompt pretreatment PET/CT findings led to upstaging from T2N0M0 (stage II) to T2N2M0 (stage III A).

Five months later after completion of combination chemotherapy with 5-fluorouracil (5-FU), mitomycin C, and cisplatin and RT to the groin/anal region, a whole body PET/CT scan was carried out to evaluate treatment response. The study demonstrated marked improvement of the hypermetabolic lesions in the ano-rectal region and pelvic LNs compared with the previous scan, suggesting good response to chemoradiotherapy (Figure 2a). Biopsies taken from the site of the primary lesion and treated regions showed squamous mucosa with hyperplastic changes and moderate to severe epithelial dysplasia without invasive carcinoma.

However, evaluation of the abdomen and pelvis revealed several new foci of intense $^{18}$F-FDG uptake with max SUV 12.0 in the left paraaortic LN chain at the level of the L2-3 vertebrae (Figure 2b). There was also enhanced $^{18}$F-FDG uptake (max SUV 3.7) that fused to a normal sized aorto-caval LN and borderline right paraaortic LN (max SUV 3.7). Evaluation of the head and neck, other LN groups, lung parenchyma, mediastinum, both axillae, chest wall, liver and spleen revealed normal uptake of $^{18}$F-FDG. Biopsy showed metastatic squamous cell carcinoma in a paraaortic LN.

One month later a PET/CT study was requested for RT planning which showed persistent $^{18}$F-FDG increased uptake in multiple bulky abdominal and retroperitoneal LNs with max SUV ranging from 5.0 to 11.5, unchanged since the prior study. Evaluation of the head and neck showed a new low-grade focal $^{18}$F-FDG uptake with max SUV 2.2 in a left subcentimeter supraclavicular LN (Figure 3a). This LN was not well delineated, but was worrisome for disease involvement. Diagnostic enhanced contrast CT scan revealed no significant LN metastases in the supraclavicular region bilaterally (Figure 3b). Biopsy of the mild hypermetabolic supraclavicular LN noted by PET and localized by fusion low dose x-ray CT scan showed metastatic involvement, histologically similar to the primary tumor lesion. RT was substituted by chemotherapy.

Discussion

Two-year survival rate is about 10% in patients with extrapelvic metastases of SCAC and depends on the treatment strategy [1,12]. Daniaud-Alexandre et al. in a series of 305 SCAC patients reported that prompt treatment of recurrences with RT and concurrent chemotherapy, usually with 5-FU plus either mitomycin-C or cisplatin, can lead to remission in up to 25% of advanced anal carcinomas [13]. RT and chemotherapy promote an important prolongation of survival but they need accurate staging and an early treatment response evaluation [14,15].

PET/CT imaging with the glucose analogue $^{18}$F-FDG is increasingly used to stage different malignant diseases [10,16]. Furthermore, therapy-induced
Figure 1. A: PET evaluation of GI tract demonstrates increased uptake in the lower rectum with max SUV of 5.1 (black arrows). There is no tumor extension outside the rectum. In the pelvis there are multiple lymph nodes along the left pelvic sidewall demonstrating increased activity (black arrows). B: Two additional lymph nodes are seen along the left iliac artery with increased $^{18}$F-FDG uptake at the level of L4-5 with max SUV of 5.3 and fusion with an enlarged lymph node at the same location (black arrows). There is no evidence of liver, upper abdomen, pulmonary, osseous or rest of the body $^{18}$F-FDG hypermetabolic metastases.

changes in tumors are related to changes in $^{18}$F-FDG uptake and treatment response can be monitored using the standardized uptake value of $^{18}$F-FDG [9].

In a comparative study by Adams et al. US, CT, MRI and $^{18}$F-FDG metabolic PET image findings were evaluated in head and neck cancer [17]. Their data confirmed 90% sensitivity, 94% specificity and 93% accuracy of $^{18}$F-FDG for LN staging of squamous cell cancer of the head and neck, and respectively, 82%, 85%, 85% for CT, 80%, 79%, 79% for MRI and 72%, 70%, 70% in cases where US had been used. New developments in CT, MRI, and US have improved image quality and made possible better structural lesion detection, but they lack the critical information about metabolic activity.

Kalff et al. reported metastatic disease in 7% of the patients with colorectal cancer being negative before $^{18}$F-FDG-PET evaluation [18]. Relapse was confirmed in 98% (49/50) of PET-positive patients and the management plan for 56% was altered as a direct result of unexpected PET findings. $^{18}$F-FDG PET imaging was more accurate (92%) than CT (71%) for
extrahepatic metastases [16]. Whole body PET/CT improved the detection of lesions on both CT and $^{18}$F-FDG-PET scans.

In conclusion, in this clinical case, based on PET/CT, primary stage changed from II (T2N0M0) to III A (T2N2M0). The diffuse lymphadenopathy in this HIV-positive patient with SCAC was distinguished from metastatic LN involvement. Subsequent follow up demonstrated further progression to stage IV (T2N2M1). PET/CT accurately identified treatment response and helped choose adequate treatment strategy. The unique advantage of PET/CT fusion imaging was the ability to correlate the findings of anatomic and functional imaging modalities and played a more important role than diagnostic CT alone in choosing the proper treatment.
References


Figure 3. A: PET/CT evaluation shows new low grade focal 18F-FDG uptake with max SUV 2.2 in a left supraclavicular subcentimeter lymph node (arrow); B: CT scan of the neck soft tissues with contrast reveals no lymph node metastases in this region (arrow).