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PET in T-Cell Lymphoma

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Abstract Most non-Hodgkin lymphomas (NHL) are of B-cell origin; only about 10% are T-cell or NK-cell lymphomas. The clinical features of T/NK-cell lymphomas differ from those of B-cell lymphomas: advanced stage and extranodal disease are more common and the prognosis is worse. Several studies have confirmed that 2-[fluorine-18]fluoro-2-deoxy-D-glucose (18FDG) uptake varies among different subtypes of lymphoma, a disparity that can be explained by the differences in histology, proliferation of tumor cells, and the ratio of viable tumor and reactive cells in the environment. These observations are based on investigation of B-cell lymphomas. Positron emission tomography (PET)/computed tomography (CT) was found to be useful both at staging and at measuring the therapeutic outcome after two to three cycles of chemotherapy (interim PET/CT). Several meta-analyses have confirmed the role of PET in evaluating the viability of the residual tumor mass after treatment. 18FDG-PET has been proved to have an excellent negative predictive value. Conversely, only a few studies have investigated the role of FDG-PET in T/NK-cell lymphomas. This paper summarizes the current information regarding the potential use of PET/CT in patients with T-cell lymphoma.

Keywords T-cell lymphoma · Peripheral T-cell lymphoma · Cutaneous T-cell lymphoma · PET scan · CT scan · SUV · Positron emission tomography · PET/CT · Staging · Prognosis

Introduction

For decades, the Ann Arbor staging system has been used to stage the extent of B-cell non-Hodgkin lymphomas (NHL) and peripheral T-cell NHL (T-NHL) based primarily on physical examination and bone marrow evaluation; computed tomography (CT) scans subsequently were incorporated [1]. Numerous papers have shown that positron emission tomography (PET) is more sensitive and specific than CT and identifies more lesions. Nevertheless, PET is currently not part of standard lymphoma staging, primarily because of its expense and because PET generally detects additional disease sites that modify clinical stage in only a small percentage of patients (15%–20%); this modification alters management or outcome in even fewer patients (10%–15%) [2–5]. PET and CT are 80% to 90% concordant in staging of patients with diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL) [3, 6]. In those patients with discordant results, PET typically results in upstaging due to the additional presumed sites of nodal, hepatic, or splenic disease. Although PET identifies more lesions than CT, PET alone does not currently replace CT for pretreatment staging [7–10].

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FDG Avidity and Histology

The various lymphoma histologies vary in their FDG avidity. The more common subtypes in the United States and Europe (e.g., DLBCL, FL, MCL, Hodgkin's lymphoma [HL]) are routinely FDG-avid [3, 11, 12].

The data for PET in T-NHL are more limited and suggest that FDG avidity is less predictable in T-NHL than in other lymphomas. Elstrom et al. [13] reported a retrospective analysis of FDG-PET scans in 172 NHL patients with a variety of histologies. The diagnosis was histologically confirmed and the imaging studies were performed either at diagnosis or at relapse, prior to further treatment. Whereas DLBCL, FL, MCL, and HL were almost uniformly FDG-avid,

the scan was positive in only two of five patients with peripheral T-cell lymphoma (PTCL).

Tsukamoto et al. [14] staged disease in 255 patients with lymphoma. FDG-PET was 100% avid in patients with noncutaneous anaplastic large cell lymphoma (ALCL), angioimmunoblastic T-cell NHL (AITCL), and natural killer (NK)/T-cell lymphoma, and 98% in PTCL, but the likelihood was lower (71%) in subcutaneous panniculitis-like T-cell lymphoma. Khong et al. [15•] evaluated pretreatment FDG-PET in 30 patients with T-cell lymphomas or NK-cell lymphomas. In 12 NK-cell lymphomas, all nasal and extranasal lesions were positive. Nasal maxillary lesions were more localized than on CT, suggesting an effect of inflammation. PET failed to identify marrow involvement in several patients. These researchers found that AITCL, PTCL–not otherwise specified (NOS), and ALCL were concordant with CT scans, but cutaneous ALCL and mycosis fungoides (MF) had minimal FDG uptake. They were unable to identify a correlation between standard uptake value (SUV) and prognosis.

Other studies have confirmed FDG avidity in patients with NK/T-cell lymphoma [16•]. Kako et al. [17] retrospectively evaluated FDG-PET scans from 41 patients with NK/T-cell lymphoma. FDG-PET identified at least one lesion in 36 patients, but the likelihood of detecting a lesion was lower for cutaneous disease. Overall, the likelihood of FDG avidity for PTCL-NOS was 91%; extranodal NK-cell lymphoma (ENKL), 100%; ALCL, 60%; AILT, 100%; and MF/Sézary syndrome (SS), 33%. However, the results were disappointing for patients with cutaneous lesions: the overall positive rate was 50%, including 0% for MF/SS and 40% for cutaneous ALCL. This group noted discordance between cutaneous and other lesions. They also concluded that FDG-PET was poor for identifying bone marrow disease.

Suh et al. [18] included PET scans in the initial evaluation of 21 patients with previously untreated ENKTCL of the head and neck. All pretreatment lesions were considered positive by PET scan, with a median SUV of 5.3. This group identified a correlation between the intensity of the FDG uptake and tumor aggressiveness and failure to respond to therapy. Because PET scans were not performed following treatment, they were unable to predict outcome.

Horwitz et al. [19] evaluated PET scans as part of initial staging for 107 patients with T-cell lymphoma, including cutaneous T-cell lymphoma with suspected extracutaneous disease. PET was considered positive in 89%, with SUVs from 1.1 to 20.5. Of 12 patients with a negative scan, 58% had no disease on CT. PET detected additional sites in 32% of patients, including three new malignancies, but stage was altered in less than 10%. Thus, though additional sites of extranodal disease were identified, stage was not changed because patients were already known to have advanced disease.

Karantanis et al. [20] evaluated 21 FDG-PET/CT scans performed on 10 patients with NK/T-cell lymphoma. Four studies were performed for initial staging, nine during therapy, and eight after completion of therapy. For those patients with nasal involvement, five scans were true positive, whereas 15 were true negative; one was considered positive but unconfirmed. For those patients with extranodal disease, the scan was true positive in 3, true negative in 16, and false negative in 2. The mean highest SUV (SUVmax) for nasal lesions was 16, versus 10.9 for extranasal lesions.

FDG-PET is more sensitive than conventional CT in enteropathy-associated T-cell lymphoma (EATL) [21]. Higher FDG uptake can be seen in inflammatory deviations/tissues (e.g., refractory celiac disease), but then the SUV value is lower than in EATL (0.0–4.6 vs 6.4–8.0) [21].

Okada et al. investigated the occurrence of relapse related to SUV value before treatment in the course of 34 previously untreated patients (3 HL, 31 NHL). During the follow-up time of 15 to 50 months, 22 patients achieved complete remission and did not relapse (SUV, 6.4±3.0). Six other patients who achieved complete remission did relapse (SUV, 10.2±2.9), and six patients did not achieve remission (SUV, 14.4±5.5) [22]. Those patients whose SUV was less than 8 had a longer survival.

Other Histologies of PTCL

Anecdotal case reports suggest FDG avidity in adult T-cell leukemia/lymphoma (ATLL) [23]. PET scans may also be positive in patients with subcutaneous panniculitis-like T-cell lymphoma [24], although the likelihood of FDG avidity may be less than with other PTCLs [14]. Hoffman et al. [25] performed staging PET/CT in four patients with enteropathy-type T-cell lymphoma; all cases were confirmed to be FDG-avid (SUVmax, 6.4–8.0). After treatment (surgery or chemotherapy), no pathologic FDG uptake was seen [22]. Of 12 celiac disease patients who also underwent PET/CT, 4 patients showed elevated FDG uptake and 5 patients showed lower-level, diffuse intestinal FDG accumulation (SUVmax, 2.2–4.6). Three patients had diffuse intestinal FDG uptake, but the SUV was not evaluated. The SUV of EATL patients was significantly higher than the value for patients with celiac disease, and the FDG uptake of patients with celiac disease did not show correspondence with the activity of their disease [25]. None of the patients with celiac disease transformed into EATL during the average duration of 22 months of follow-up (4–32 months after first PET/CT) [25].

Cutaneous T-Cell Lymphoma

The likelihood of FDG avidity in cutaneous T-cell lymphoma appears to depend on whether the tumor is cutaneous or extracutaneous. Kuo et al. [26•] reported that PET was superior to physical examination for identifying subcutaneous lesions in patients with cutaneous T-cell lymphoma. PET was useful in identifying advanced visceral disease. Of interest was the variability in FDG avidity among lymph nodes in individual patients. Tsai et al. [27] evaluated the role of FDG-PET in staging of cutaneous T-cell lymphoma in patients at risk for lymph node involvement. Whereas only 5 of 13 patients had lymphadenopathy by CT criteria, tumors from all patients were FDG avid. Those with aggressive transformation had the highest SUV values. However, the PET scan did not routinely identify cutaneous involvement. This group concluded that FDG-PET was more sensitive than CT scans for nodal disease.

Kumar et al. [28] retrospectively assessed PET in 19 patients with primary cutaneous lymphoma, including 15 with T-NHL. They found a sensitivity of 82% for local disease and 80% for distant localizations, which was superior to CT scans. Two patients with cutaneous T-cell lymphoma had no uptake at the site of disease. Kuo et al. [29] assessed the role of FDG-PET in a phase II trial of vorinostat in cutaneous T-cell lymphoma. Preliminary analysis of the data suggested that the results of the scan may correlate with lack of response. Where PET may be useful in cutaneous T-cell lymphoma is in patients for whom an aggressive transformation is suspected: a PET scan may help to identify for biopsy the lesion that is most likely to support the clinical suspicion.

Conclusions

Several studies have confirmed the utility of FDG-PET both in HL and NHL in staging, in measuring the therapeutic outcome [2–4], and as an early prognostic factor after two to three cycles of chemotherapy [30–32]. Certain lymphomas were confirmed by different FDG uptake, which can be explained by the different histology, proliferation of tumor cells, and ratio of viable tumor and reactive environmental cells [7, 8]. These observations are based on investigation of B-cell lymphomas (HL and DLBCL), whereas only a few studies with a relatively small number of patients have investigated the role of FDG-PET in T-cell and NK-cell lymphomas. Subtypes of T/NK-cell lymphomas have different pathological features, such as a prominent inflammatory background in AILT and tissue necrosis in ENKL, which can influence FDG-PET results [17].

FDG-PET has become an important component of the management of patients with B-cell NHL and HL. However, its role in T-NHL is still being defined. The limited data suggest that PET for initial assessment does not alter the clinical stage or treatment recommendations, so it cannot be recommended for routine use. Because most PTCLs are not curable, PET should be used for restaging only if complete response is a major study end point. The role of interim examinations is still challenging. Further studies based on large numbers of patients are needed to evaluate the exact role.

PET is neither sufficiently sensitive nor specific for the assessment of cutaneous T-cell lymphoma, so more traditional criteria remain standard, such as the modified Severity Weighted Assessment Tool (mSWAT) score (the percentage of affected total body surface area weighted for each lesion type [patch, plaque, or tumor]).

Thus, whereas an increasing body of data have been described for the use of PET in T-NHL, guidance as to the use of this technology is lacking. Clinical trials should provide prospective validation of PET in T-NHL before it can be considered a standard part of patient management.

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