Malignant Lymphomas

## Positron emission tomography with [18F] 2-fluoro-D-2-deoxyglucose in primary cutaneous T-cell lymphomas

**Whole body positron emission tomography using 18-2-fluoro-2-deoxy-glucose (18F-FDG-PET) was performed in 13 consecutive patients with histologically verified cutaneous T-cell lymphomas (CTCL). None of the patients in stage Ia had a positive scan, whereas all patients with stage IV disease did so; 18F-FDG-PET might add valuable clinical information in this latter context.**

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Mycosis fungoides (MF) is the most common form of cutaneous T-cell lymphomas (CTCL).[1] The disease is characterized by indolent patches and plaques in early stages, and extracutaneous involvement occurs in advanced stages.[2] Patients with generalized patch/plaque disease have a relatively high likelihood of disease progression (24%),[3] highlighting the importance of monitoring and staging. In addition to a correct classification,[1,4] determination of the extent of disease in patients with CTCL is of critical importance for planning treatment. Whole body positron emission tomography (PET) using 18-2-fluoro-2-deoxy-glucose (18F-FDG) has been shown to be highly sensitive and specific for imaging lesions in patients with lymphomas.[5] Following preliminary data from two patients with cutaneous lymphoma,[6] we evaluated the clinical usefulness of 18F-FDG-PET for staging and follow-up of patients with CTCL. Thirteen consecutive patients (9 females, 4 males) with histologically verified CTCL were included in our series. Their characteristics are described in Table 1. The stage of disease was established by physical examination, chest radiography, sonography and computed tomography (CT) in patients with internal organ involvement. The staging system used was that proposed by the Mycosis Fungoides Cooperative Group.[7] All patients underwent scanning with 18F-FDG-PET before initiation of treatment. Results were compared to those of conventional staging and examination of cutaneous lesions. Whole body 18F-FDG-PET scans were performed on a GE Advance PET scanner (GE Medical Systems, Waukesha, WI, USA) and

**Table 1. Characteristics of patients with primary CTCL at the time of 18F-FDG-PET scan.**

| *Patient No.* | *Sex/ Age (yr)* | *Histology* | *Clinical signs/ Location* | *Stage*[2] | *PET result* | *Status* |
|---|---|---|---|---|---|---|
| 1 | M/44 | MF[1] | Patch-plaque/ groin, lower back | Ia | negative | alive |
| 2 | F/80 | Sézary syndrome - *large cell peripheral T-cell lymphoma | Erythroderma; axillary lymph node/ generalized | IVa | positive | dead |
| 3 | F/85 | CD30+ T-cell lymphoma | Central necrotic papules/ generalized | Ia | negative | alive |
| 4 | F/68 | MF[1] | Patch-plaque/ lower back | Ia | negative | alive |
| 5 | M/63 | MF[1] | Plaques, tumors; axillary, inguinal lymph nodes; bone marrow;peripheral blood /groins, axilla, lower back | IVb | positive | alive |
| 6 | F/87 | MF[1] – *large cell peripheral T-cell lymphoma | Plaques, tumors; axillary, inguinal lymph nodes/ generalized | IVa | positive | dead |
| 7 | F/44 | MF[1] | Patch-plaque trunk | Ia | negative | alive |
| 8 | F/77 | MF[1] | Patch-plaque back | Ia | negative | alive |
| 9 | F/63 | MF[1] - *large cell peripheral T-cell lymphoma | Plaques, tumors; muscle involvement left thigh/generalized | IVb | positive | dead |
| 10 | F/46 | MF[1] | Patch-plaque back | Ia | negative | alive |
| 11 | M/55 | MF[1] | Patch-plaque generalized | Ia | positive (HD) | alive |
| 12 | M/61 | MF[1] generalized | Patch-plaque | Ia | positive (lung cancer) | alive |
| 13 | F/38 | CD30+ T-cell lymphoma | Patch-plaque lower back, lower extremity | Ia | negative | alive |

*[1]Mycosis fungoides; *transformation in the course of the disease, [2]at the time of imaging. The patients had a performance status < 2 according to WHO criteria. HD: Hodgkin's disease.*

**Figure 1. Coronal F18-FDG-PET image in a 62-year old female with MF which transformed into large cell peripheral T-cell lymphoma. The significant FDG-uptake in the left thigh is indicative of muscle involvement.**

images were reconstructed using previously published standard methods.[8] Of the 13 patients, 9 patients had stage Ia (7 MF patients, 2 with CD30$^+$ T-cell lymphoma) and 4 patients had stage IV (2 patients IVa and 2 IVb) (Table 1).

None of the 9 patients in stage Ia had a positive $^{18}$F-FDG-PET scan at the sites of CTCL, irrespective of CD30 expression on tumor cells. In 2 of these patients, positive $^{18}$F-FDG-PET scan led to the detection of a squamous cell carcinoma of the lung in one and mediastinal Hodgkin's lymphoma in the other patient.

The $^{18}$F-FDG-PET scan was positive in all 4 patients with stage IV disease. In 1 patient uptake correlated well with two cutaneous localizations and axillary lymph nodes (Table 1, patient #5), but no tracer accumulation was seen in the bone marrow despite lymphomatous involvement. In 3 patients, subsequent transformation to a large cell peripheral T-cell lymphoma at the sites $^{18}$F-FDG accumulation had occurred. One female patient had a positive $^{18}$F-FDG-PET scan in axillary lymph nodes (Table 1, patient #2), another female patient, in the left thigh, corresponding to muscle involvement (Table 1, patient #9) (Figure 1). Skin lesions, however, were not visualized in either case. The last patient, showed focal accumulation both in involved lymph nodes and in skin lesions (Table 1, patient #6). The clinical course of MF is usually indolent, but is characterized by a high rate of recurrences following treatment.[3] Transformation to an aggressive T-cell lymphoma may also occur during the course of disease and is associated with a poor outcome.[9,10] As the prognosis of MF is also based on the extent of disease at presentation,[3,4] staging is as important as consequent follow-up.

Seventy percent of our 13 patients were classified as having stage Ia disease and, according to our results, $^{18}$F-FDG-PET does not appear to be useful for staging in such patients. By contrast, $^{18}$F-FDG uptake, in histologically verified sites of disease was seen in all patients with stage IV disease. Nevertheless, $^{18}$F-FDG-PET did not provide identify all sites involved. Three patients had transformation to a large cell peripheral T-cell lymphoma in the foci of $^{18}$F-FDG uptake. These findings suggest that a positive $^{18}$F-FDG-PET scan heralds transformation to a more aggressive type of lymphoma and might thus provide clinically relevant information for the management of patients with CTCL.

The negative results in all 9 cases with stage Ia disease are not readily explainable by recent concepts. One might speculate that the biology of MF stage Ia would *per se* implicate a low glucose metabolism in the skin lesions, resulting in negative scan results. Recent data in other indolent lymphomas of B-cell lineage, however, show positive $^{18}$F-FDG uptake in spite of low proliferation of tumor cells.[8]

Based on our results, we do not recommend the use of $^{18}$F-FDG-PET for routine staging of patients with CTCL. In patients with advanced disease, $^{18}$F-FDG-PET might add valuable clinical information and assist in locating sites for potential biopsy, to facilitate planning of therapy and follow-up.

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