patients experienced photosensitization through glass, which is highly suggestive of a UV-A–induced mechanism.\(^6\) Photosensitization is an adverse effect of many kinase inhibitors such as imatinib, sorafenib, and vemurafenib. Imatinib inhibits the adenosine triphosphate–dependent transporter ABCG2 resulting in intracellular porphyrin accumulation and phototoxic effects in vitro.\(^7\) Since vandetanib also inhibits the transporter activity of ABCG2, a similar porphyrin-induced mechanism might explain the similar effect.\(^8\)

In a report of 2 cases, vandetanib-associated cutaneous pigmentation was preceded by photosensitization.\(^9\) In our more extensive experience, only half of the patients with cutaneous pigmentation had prior or concomitant skin photosensitization, making the hypothesis of post-photosensitization pigmentation less likely. In 3 patients, a multinucleated giant-cell granuloma was found in the dermis, which could result from a direct deposit of the drug in the skin.

Vandetanib is being tested in the treatment of several types of cancers. In patients with medullary thyroid cancer, it has already demonstrated a significant efficacy,\(^3\) which led the US Food and Drug Administration and European Medicines Agency to label the drug for patients with advanced disease in 2011. Dermatologists should be aware of the spectrum of vandetanib toxic effects, and careful photoprotection should be used to facilitate compliance with treatment.

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Accepted for Publication: July 31, 2012.

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Conflict of Interest Disclosures: Drs Schlumberger and Robert serve as consultants to AstraZeneca, a manufacturer of vandetanib, and Dr Schlumberger has received research funds from AstraZeneca. Dr Schlumberger also serves as a consultant to Amgen Eisai and Exelixis and has received research funds from Amgen and Exelixis. Dr Robert is consultant for Bristol-Myers Squibb, Roche, GlaxoSmithKline, and Novartis.

Additional Contributions: We are indebted to Lorna Saint Ange for editing.


Integrated Positron-Emission Tomography and Computed Tomography Manifestations of Cutaneous T-Cell Lymphoma

Mycosis fungoides (MF) and Sézary syndrome (SS) represent the most common types of primary cutaneous T-cell lymphomas (CTCLs).\(^1\) Current guidelines recommend [18F]-fluorodeoxyglucose positron-emission tomography (FDG-PET) plus computed tomography (CT) scan for staging purposes in all patients except in cases of early-stage disease (IA-IB).\(^3\) However, the application of FDG-PET in CTCL has not been widely documented.\(^2\) In this study, we retrospectively evaluated the findings of FDG-PET/CT scans in 41 patients with CTCL.

Methods. Patients with MF and SS who underwent FDG-PET/CT scans (Gemini TOF 64 slice PET/CT scanner; Philips Healthcare Inc) either at the time of diagnosis or at the time of suspected relapse or progression over a 4-year period at our cutaneous lymphoma clinic were retrospectively enrolled in this study. Twenty patients (stage IA-IB) did not undergo PET/CT scans because patients...
with limited disease were not scanned systematically. The clinical follow-up period was a minimum of 6 months. Disease was staged according to a well-recognized staging system.¹

An experienced nuclear medicine physician reviewed all scans, and FDG avidity was assigned to lymphomatous involvement if it was in agreement with histologic, clinical, and/or radiographic data. Results were graded visually as equivocal and positive when FDG avidity above background level was slightly and markedly enhanced, respectively. Relative uptake value was defined as the ratio of the mean FDG signal from the metabolically active lesion with the highest FDG uptake to the mean background activity in the liver (tumor to liver ratio [T:L]). Lymphadenopathy was diagnosed when the longest transverse diameter of the lymph node was 1.5 cm or longer. Data are presented as median values with respective ranges. The Danish Bioethics Committee for the Capital Region waived the need for ethical approval.

Results. Overall, PET findings were considered suggestive of malignancy in 14 of 44 total scans (32%): 1 of 12 in stage IA scans (8%); 1 of 12 in stage IB (8%); 5 of 7 in stage IIB (71%); 1 of 4 in stage IIIA (25%); and 6 of 9 in stage IVA (67%) (Table). While cutaneous lesions of patches, plaques, and erythroderma showed no abnormalities on PET/CT scans, tumors (T:L, 0.9 [range, 0.6-5.7]), were detected consistently. We found no evidence of differences in the T:L of tumors with different histologic subtypes.

Six patients with MF and 6 with SS (1 SS followed by transformed MF) had clinical lymphadenopathy, which in 8 patients showed FDG avidity. In patients with transformed cutaneous disease (2 stage IIB and 2 stage IVA), PET/CT scans demonstrated abnormal FDG uptake (T:L, 2.8 [range, 2.2-3.1]) and lymphadenopathy. Analysis of biopsy specimens confirmed transformed nodal histologic characteristics in 2 patients. At last follow-up, all had progressive disease or had died due to disease progression.

Seven patients with MF (1 stage IA, 3 IB, 3 IIIA), who had an FDG-positive cutaneous lesion with thickening of the skin and/or active lymph node enlargement, had FDG avidity. Three of these patients died as a result of progression of the tumors; another patient had a regressed tumor at the time of the last follow-up. One patient had negative initial scan results owing to tumors existing outside the scan view and then positive findings on a second scan owing to progression of the tumors; another patient had a regressed tumor at the time of the last follow-up.

PET scans were positive for lymphoma in 14 of 44 total scans (32%): 1 of 12 in stage IA scans (8%); 1 of 12 in stage IB (8%); 5 of 7 in stage IIB (71%); 1 of 4 in stage IIIA (25%); and 6 of 9 in stage IVA (67%) (Table). While cutaneous lesions of patches, plaques, and erythroderma showed no abnormalities on PET/CT scans, tumors (T:L, 0.9 [range, 0.6-5.7]), were detected consistently. We found no evidence of differences in the T:L of tumors with different histologic subtypes.

Tumors with stage IB, IVA, and IIB disease, respectively. Lung cancer and a tubulovillous adenoma of the colon were detected incidentally in a patient with stage IIB disease and one with stage IIIA disease, respectively. After assessment of PET scans, and guided by these results, the lesions were also visible on CT except in the case of the colon adenoma, for which the CT finding was uncertain, but colonoscopy confirmed the diagnosis.

Comment. Our results offer no evidence that PET/CT provides any information beyond that revealed by a physical examination in assessing cutaneous disease in MF and SS. In this, they concur with studies suggesting that hypermetabolic activity is rarely seen except in tumors.²,³

Assessment of nodal involvement in CTCL is difficult because many patients have dermatopathic lymphadenopathy, and lymphomatous involvement can occur in normal-sized lymph nodes.¹ The present study is limited by lack of nodal biopsy specimens, but a recent prospective study of 13 MF and SS cases demonstrated a correlation between high FDG accumulation and histologic grade of nodal involvement or large-cell transformation.²

We did not find evidence of visceral spread in our patient population but found a high rate of concomitant malignant neoplasms, which is not unusual in CTCL.¹ Though the CT component also provided information, it suggests a role for imaging techniques in disclosing concurrent neoplasia, at least in advanced CTCL phases.

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>PET Scans, No.</th>
<th>Negative</th>
<th>Mild Avidity</th>
<th>Positive</th>
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<tr>
<td>IA</td>
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<td>10</td>
<td>1</td>
<td>1³</td>
</tr>
<tr>
<td>IB</td>
<td>12</td>
<td>8</td>
<td>3</td>
<td>1²</td>
</tr>
<tr>
<td>IIA</td>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>IIB</td>
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<td>2³</td>
<td>0</td>
<td>5⁴</td>
</tr>
<tr>
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<td>4</td>
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<td>1³</td>
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<tr>
<td>IIIIB</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>IVA</td>
<td>9</td>
<td>2²</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>IVB</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CTCL, cutaneous T-cell lymphoma; FDG, fluoro-2-deoxyglucose; MF, mycosis fungoides; NA, not applicable; PET, positron-emission tomography; SS, Sézary syndrome.

Table. PET Results in Patients With CTCL

Our results offer no evidence that PET/CT provides any information beyond that revealed by a physical examination in assessing cutaneous disease in MF and SS. In this, they concur with studies suggesting that hypermetabolic activity is rarely seen except in tumors.²,³

Assessment of nodal involvement in CTCL is difficult because many patients have dermatopathic lymphadenopathy, and lymphomatous involvement can occur in normal-sized lymph nodes.¹ The present study is limited by lack of nodal biopsy specimens, but a recent prospective study of 13 MF and SS cases demonstrated a correlation between high FDG accumulation and histologic grade of nodal involvement or large-cell transformation.²

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Itch and Pain in Nonmelanoma Skin Cancer: Pain as an Important Feature of Cutaneous Squamous Cell Carcinoma

Pain is a common feature of cancer with an estimated prevalence rate between 52% and 77%.1 Itch is the most common dermatologic symptom and is also a common feature of lymphoma.2 However, no studies have been performed examining the prevalence rates of pain and itch in common skin cancers. Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are the 2 most common types of nonmelanoma skin cancer (NMSC). They have a rapidly increasing incidence in the United States, with nearly 4 million new cases of NMSC diagnosed each year.3 The purpose of the present study was to assess the prevalence and intensity of pain and itch among the 2 most common skin cancers.

Methods. Data for this institutional review board–approved study were prospectively collected on a total of 576 biopsy-proven NMSCs from 478 patients with either BCC or SCC seen in the dermatologic surgery department at Wake Forest University Baptist Medical Center from July 2010 to March 2011. Patients rated their pain and itch intensity on a visual analog scale from 0 (least intense) to 10 (most intense). A multiple logistic regression model was fit to examine the relationship of pain and itch with BCC and SCC using age, sex, chronic pain- or itch-related conditions, tumor size, and depth of invasion as covariates. A subanalysis was also performed to compare SCC in situ vs invasive SCC.

Results. Of the 505 patients approached, 478 completed the study. The mean (SD) age was 68.8 (12.7) years (age range, 27-94 years), and most patients were male (304 men, 174 women). There were 353 biopsy-proven SCCs and 223 BCCs.

Itch was the most common symptom reported in both skin cancers (43.5% of SCCs and 33.4% of BCCs). This difference was not statistically significant. The prevalence of pain was 39.8% (95% CI, 35.4%-44.2%) in SCC and 17.7% (95% CI, 13.4%-21.9%) in BCC. A patient’s pain score was a highly significant predictor of having an SCC as opposed to a BCC (P < .001). For each point increase on the VAS in pain, there was a 30% increase in the odds of having an SCC compared with having a BCC (Figure, A). Further analysis revealed that patients presenting with a pain score higher than 2 had a nearly 4-fold increase in the likelihood of having an SCC compared with a BCC (odds ratio [OR], 3.94 [95% CI, 2.49-6.23]) (P < .001).

To account for potential intra-individual differences in patients with multiple skin cancers, data were stratified into 2 groups, patients with 1 skin cancer vs those with 2 or more skin cancers. Analyses were repeated in each group, and comparable results were obtained, suggesting no difference between these groups. Interestingly, pain did not significantly differ in patients with SCC in situ compared with invasive types of SCC (P = .47).

Comment. Our findings reveal that pain and itch are common symptoms of NMSC. A previous study reported tenderness in SCC,4 but to our knowledge, ours is the first study to assess the prevalence of pain and itch and their intensities in NMSC. Specifically, we have shown the intensity of pain to be a unique factor to help in differentiating SCC from BCC. This finding is of significant clinical utility in the diagnosis and treatment of NMSC. With an increasingly aging population, patients often present with numerous BCCs and SCCs, and it is often difficult for the clinician to prioritize lesion biopsy and removal. Thus, there is a need for better clinical tools to aid the physician in selecting lesions most likely to be SCCs,