

# Detection of Richter's Transformation of Chronic Lymphocytic Leukemia by PET/CT

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Our objective was to evaluate the accuracy of PET/CT for the diagnosis of Richter's transformation of chronic lymphocytic leukemia (CLL) to diffuse large cell lymphoma. **Methods:** A retrospective study was performed of 37 patients with CLL who underwent <sup>18</sup>F-FDG PET/CT at our institution between March 2003 and July 2005. All PET/CT scans were reviewed in consensus by 2 diagnostic radiologists. Sites of abnormal <sup>18</sup>F-FDG uptake with a maximum standardized uptake value (SUVmax) of greater than 5 were considered highly suggestive of Richter's transformation. The PET/CT findings were correlated with histologic findings from bone marrow or lymph node biopsy performed within 6 wk of PET/CT and with clinical follow-up. **Results:** The 37 patients (26 men and 11 women; mean age, 61 y, range, 40–82 y) underwent 57 PET/CT scans. In 10 (91%) of 11 patients with Richter's transformation, PET/CT detected sites of abnormal <sup>18</sup>F-FDG uptake having an SUVmax of greater than 5. Richter's transformation was missed in 1 patient who had only low-grade <sup>18</sup>F-FDG uptake (SUVmax < 5). Nine patients had false-positive PET/CT findings; in 3 of these patients, alternative malignancies were diagnosed (Hodgkin's disease; metastatic neuroendocrine carcinoma; non-small cell lung cancer). In all remaining patients, PET/CT correctly excluded Richter's transformation. For the specific diagnosis of Richter's transformation of CLL to diffuse large B-cell lymphoma, PET/CT had overall sensitivity, specificity, and positive and negative predictive values of 91%, 80%, and 53% and 97%, respectively. **Conclusion:** PET/CT can detect Richter's transformation of CLL to diffuse large B-cell lymphoma with a high sensitivity and a high negative predictive value.

**Key Words:** chronic lymphocytic leukemia; Richter's transformation; lymphoma; PET; PET/CT

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Chronic lymphocytic leukemia (CLL) is the most frequent type of leukemia in the Western world. It predominantly affects adults in the 6th and 7th decades of life, although a third of patients are less than 60 y old at the time of diagnosis (1). CLL follows a protracted clinical course,

often remaining asymptomatic for years, and is characterized by a lack of apoptosis of monoclonal small B-cell lymphocytes and progressive infiltration of the lymph nodes, bone marrow, liver, and spleen. In 4% of patients, the disease may undergo Richter's transformation, most commonly to diffuse large B-cell lymphoma (2,3), which is much more aggressive than the underlying CLL (2,4,5). The risk of Richter's transformation is independent of disease stage, duration, or response to prior treatment, and it has a poor prognosis, with a median survival of less than 6 mo (6–9). The most effective therapies include a combination of rituximab and chemotherapy, and patients who achieve remission appear to benefit from myeloablative stem cell transplantation if a donor is available (5). Prompt diagnosis is necessary for optimal management (10).

Unfortunately, the clinical features of Richter's transformation are nonspecific, and suggestive laboratory findings such as raised levels of lactate dehydrogenase (LDH) and  $\beta$ -2 microglobulin can also frequently be seen in patients without Richter's transformation. There have been reports of the successful detection of Richter's transformation with high-dose <sup>67</sup>Ga scintigraphy (11) stemming from its role in the staging and monitoring of Hodgkin's lymphoma and non-Hodgkin's lymphoma (12). However, the limited availability of this isotope, the requirement for delayed scanning beyond 24 h, and suboptimal sensitivity for the detection of lymphoma in certain anatomic regions (such as the liver, spleen, abdomen, and inguinal regions) (13) have restricted the use of <sup>67</sup>Ga scintigraphy as a routine imaging test for lymphoma.

Whole-body PET scanning with <sup>18</sup>F-FDG is approved for the initial staging and restaging of Hodgkin's disease and non-Hodgkin's lymphoma and may therefore be used for this purpose in patients with CLL; however, as far as we are aware, no studies have been published on the diagnostic performance of PET or PET/CT for the detection of Richter's transformation in patients with CLL. The objective of our study was to evaluate the accuracy of PET/CT for the diagnosis of Richter's transformation of CLL to diffuse large cell lymphoma.

## MATERIALS AND METHODS

A retrospective analysis of consecutive patients with CLL who underwent PET/CT at our institution between March 2003 and

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July 2005 was performed. The indication for PET/CT was initial staging or monitoring of treatment outcomes. Patients were excluded from the study if they had not undergone bone marrow or lymph node biopsy within 6 wk of PET/CT, if they had insufficient clinical follow-up information for at least the 3 mo after PET/CT, or if they had a previous history of Richter's transformation. The study was approved by the Institutional Review Board, with a waiver of consent.

All PET/CT examinations were performed on an integrated PET/CT scanner (Discovery ST-8; GE Healthcare). The patients fasted for at least 6 h before undergoing scanning. Blood glucose was checked approximately 4 h before scanning; no patients in our study had hyperglycemia requiring deferment of scanning. Approximately 1 h before being scanned, the patients received an injection of  $^{18}\text{F}$ -FDG (mean, 555 MBq; range, 444–740 MBq). PET studies were acquired from the skull base to the upper thighs in the 2-dimensional mode for 3 min per bed position. PET images were reconstructed using standard vendor-provided reconstruction algorithms, which incorporated ordered-subset expectation maximization. PET images were corrected for attenuation using data from the CT component of the examination; emission data were corrected for scatter, random events, and dead-time losses using the manufacturer's software.

The CT component of the study comprised an unenhanced multidetector CT examination from the base of the skull to the upper thighs (120 mA; 140 kVp; table speed, 13.5 mm/rotation). Axial CT images were reconstructed with a slice thickness of 3.75 mm.

All PET/CT studies were retrospectively reviewed in consensus by 2 diagnostic radiologists, each of whom had previously interpreted more than 500 PET/CT scans. Both radiologists examined the PET images, the CT images, and the fused PET/CT images at a combined reading session. Images were reviewed at a dedicated PACS workstation (Advantage Workstation; GE Healthcare). Both axial and multiplanar images were examined; the CT images were examined first, followed by analysis of the PET images. The fused PET/CT images were used primarily for localizing lesions and for differentiating abnormal metabolic activity from physiologic  $^{18}\text{F}$ -FDG uptake within adjacent organs (such as the kidneys, ureters, and gastrointestinal tract). Metabolic activity within sites of abnormal  $^{18}\text{F}$ -FDG uptake was analyzed qualitatively and semiquantitatively on the PET images; a semiautomated tool was used to calculate the maximum standardized uptake value (SUVmax) within the volume of interest according to the following formula:  $\text{SUVmax} = \text{mean measured activity within the volume of interest (MBq/mL)} / \text{injected dose of } ^{18}\text{F}\text{-FDG (MBq)} / \text{body weight (g)}$ . The volume of interest was determined using a vendor-specific software tool that allowed automatic calculation of the SUVmax within a user-specified cubic volume drawn in 3 planes (axial, coronal, and sagittal) to include the site of abnormal  $^{18}\text{F}$ -FDG accumulation.

On the PET/CT images, sites of abnormal  $^{18}\text{F}$ -FDG uptake were documented with respect to the intensity of the uptake and its anatomic location. For the purposes of our study, a SUVmax of at least 5 within a lymph node or extranodal site was considered strongly suggestive of Richter's transformation, whereas values of less than 5 indicated a more indolent phase of CLL. A cutoff SUVmax of 5 was chosen empirically on the basis of our institutional practice, in which our experience has been that values of less than 5 tend to be less specific indicators of malignancy. When abnormal  $^{18}\text{F}$ -FDG uptake was observed within enlarged lymph nodes, the pattern of uptake was classified as diffuse if it involved

all sites of lymphadenopathy, suggesting diffuse transformation of CLL, or patchy if it involved some sites of lymphadenopathy but not others, suggesting more localized transformation. Extranodal disease was suspected if abnormal  $^{18}\text{F}$ -FDG uptake was observed within an extranodal soft-tissue mass or in the liver, spleen, bone marrow, or another organ.

The PET/CT findings were then correlated with histologic findings from bone marrow or lymph node biopsy performed within 6 wk of PET/CT. In addition, all patients had clinical follow-up information for at least the 3 mo after PET/CT, and this information was recorded. Histologic confirmation was regarded as the gold standard for the diagnosis of Richter's transformation. Richter's transformation was considered unlikely if no large cells were detected at biopsy or fine-needle aspiration of the suspected site of disease involvement and if the clinical course over the subsequent 3 mo was inconsistent with Richter's transformation.

Descriptive analyses were performed of patient age, sex, clinical characteristics, and laboratory and imaging findings. Sensitivity, specificity, and positive and negative predictive values for the PET/CT diagnosis of Richter's transformation of CLL were calculated. The Fisher exact test was used to calculate the statistical significance of a difference in LDH levels between patients with and patients without Richter's transformation.

## RESULTS

Thirty-seven patients with biopsy-proven CLL were analyzed. Their mean age at the time of their first PET/CT scan was 61 y (range, 40–82 y). There was a male predominance (26 men [70%] vs. 11 women [30%]). Fifty-seven PET/CT scans were performed during the study period; 26 patients underwent PET/CT once, and 11 patients more than once (mean, 2.5; range, 2–4). PET/CT was indicated in 18 patients for staging of CLL before initial or salvage therapy, in 22 patients for restaging after treatment, and in 17 patients for exclusion of Richter's transformation when disease was progressive or refractory to treatment.

The mean interval between the initial diagnosis of CLL and the first PET/CT scan was 8 y (median, 7 y; range, 1–19 y). Patients had received chemotherapy for their CLL before 56 of the 57 PET/CT scans; the mean interval between the end of treatment and PET/CT was 34 wk (median, 14 wk; range, 3 d to 4 y). Of 11 patients with histologically proven Richter's transformation, 10 had positive PET/CT findings.

The PET/CT results are detailed in Table 1. Of the 57 PET/CT scans, 19 demonstrated foci of abnormally increased  $^{18}\text{F}$ -FDG uptake ( $\text{SUVmax} > 5$ ), whereas 38 demonstrated no or only low-grade  $^{18}\text{F}$ -FDG uptake ( $\text{SUVmax} < 5$ ). The 19 PET/CT scans with abnormal findings were in 18 patients. In 10 of these 18 patients, Richter's transformation was diagnosed; this diagnosis was confirmed within 6 wk of PET/CT by lymph node biopsy ( $n = 6$ ), by biopsy of an extranodal soft-tissue mass ( $n = 3$ ), or by bone marrow biopsy and aspiration ( $n = 1$ ). Clinical details concerning these patients are summarized in Table 2. On PET/CT, all 10 patients (91%) had foci of abnormal

**TABLE 1**  
PET/CT Findings in Study Population

Diagnosis	Sites of increased uptake (SUVmax > 5)			Distribution of nodal uptake*	Sites of extranodal uptake	Intensity of uptake
	Nodal	Nodal and extranodal	Extranodal			
Richter's transformation ( <i>n</i> = 10) <sup>†</sup>	5	3	2	Diffuse (7); patchy (1)	Extranodal mass (3); liver (1); spleen (1)	Mean, 17.6; range, 7.4–39.4
Accelerated phase CLL ( <i>n</i> = 2)	1		1	Patchy	Bone marrow	Mean, 8.4; range, 7.4–9.3
Hodgkin's lymphoma ( <i>n</i> = 1) <sup>‡</sup>		1		Diffuse	Liver, spleen, and bone marrow	22.4
Non-small cell lung cancer ( <i>n</i> = 1)			1		Lung mass	8.8
Neuroendocrine carcinoma ( <i>n</i> = 1)	1			Diffuse		10.2
CLL without transformation or other malignancy ( <i>n</i> = 42)	4			Diffuse (2); patchy (2)		Mean, 4.5; range, 2–7.9

\*Diffuse uptake = <sup>18</sup>F-FDG uptake within all sites of lymphadenopathy; patchy uptake = <sup>18</sup>F-FDG uptake within some sites of lymphadenopathy but not others.

<sup>†</sup>One patient had Richter's transformation and false-negative PET/CT findings and was not included in table.

<sup>‡</sup>Richter's transformation developed 6 mo later in patient with Hodgkin's lymphoma.

Numbers indicate numbers of scans.

<sup>18</sup>F-FDG uptake with an SUVmax of greater than 5 (mean, 16.5; range, 6–39.4). Sites of abnormal <sup>18</sup>F-FDG uptake were observed within lymph nodes only in 5 patients, within lymph nodes and extranodal sites in 3 patients (Fig. 1), and within extranodal sites only in 2 patients (Fig. 2). In 8 of these patients, the diagnosis of Richter's transformation had already been strongly suspected clinically (*n* = 7) or had been known from prior biopsy (*n* = 1), and the PET/CT scan had been requested to obtain additional objective evidence of transformation as well as provide information required for staging of the B-cell lymphoma. Richter's transformation was clinically unsuspected before PET/CT in 2 patients (Fig. 2).

Nine patients had PET/CT scans showing foci of abnormally increased <sup>18</sup>F-FDG uptake (SUVmax > 5) that were due to disease other than Richter's transformation. In 3 of these, a malignancy other than diffuse large B-cell lymphoma was diagnosed (1 case of Hodgkin's lymphoma, 1 case of non-small cell lung cancer, and 1 case of metastatic neuroendocrine carcinoma). In the other 6 patients, the false-positive PET/CT findings were due to an accelerated phase of CLL (*n* = 2) (Fig. 3), refractory CLL with extensive bone marrow involvement (*n* = 3), or atypical pneumonia (*n* = 1).

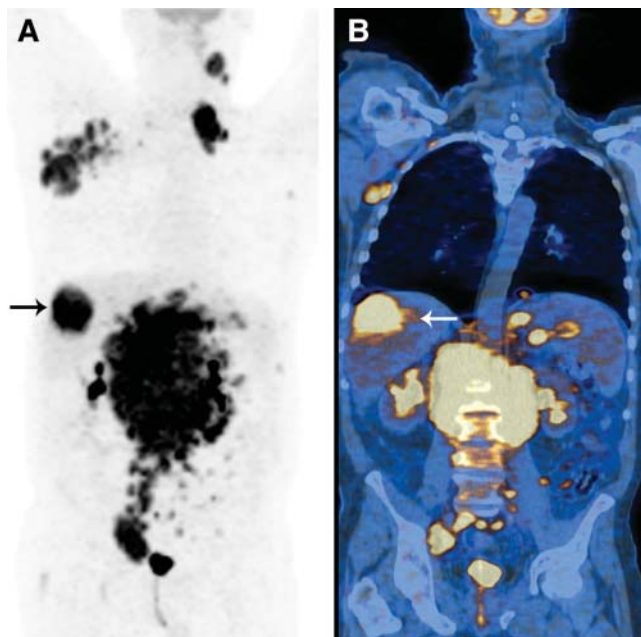
Thirty-seven PET/CT examination in 19 patients showed true-negative findings: no sites of abnormal <sup>18</sup>F-FDG

**TABLE 2**  
Clinical Characteristics of 11 Patients with Richter's Transformation

Characteristic	No. of patients	%
Male-to-female ratio	5:6	45:50
Age at diagnosis of CLL (y)	Mean, 58 (range, 37–70)	
Time to diagnosis of Richter's transformation (y)	Mean, 8 (range, 1–15)	
Patients older than 60 y at diagnosis of Richter's transformation	9	82
Symptoms and signs		
Rapidly enlarging lymph nodes	5	45
Painful lymphadenopathy	4	36
Night sweats	4	36
Weight loss	2	18
None	3	27
White cell count < 4,000/ $\mu$ L	4	36
Platelet count < 100 $\times$ 10 <sup>9</sup> /L	1	9
Lactate dehydrogenase > 1.5 times normal level (1.5 $\times$ 618 IU/mL)	2	18
Raised $\beta$ -2 microglobulin level ( $\geq$ 1.9 mg/L)	9* (mean $\beta$ -2 microglobulin level, 6.4; range, 2–10.2)	100*

\* $\beta$ -2 microglobulin levels were not obtained at time of diagnosis in 2 patients.





**FIGURE 1.** 70-y-old man with 1-y history of CLL, who had completed chemotherapy. PET/CT was requested because of increasing abdominal pain and constitutional symptoms of B-cell lymphoma. Maximum-intensity-projection PET (A) and coronal fused PET/CT (B) images demonstrate diffusely increased  $^{18}\text{F}$ -FDG uptake within bulky multicompartmental lymphadenopathy and within right lobe of liver (arrow). Fine-needle aspiration of a neck lymph node confirmed diagnosis of Richter's transformation to diffuse large B-cell lymphoma. PET/CT allowed concurrent staging of lymphoma.

uptake ( $n = 31$ ) or diffuse low-grade metabolic activity ( $\text{SUV}_{\text{max}} < 5$ ) in chronically enlarged lymph nodes ( $n = 6$ ) (mean  $\text{SUV}_{\text{max}}$ , 3.2; range, 2–4.7). None of these patients had evidence of Richter's transformation on anal-

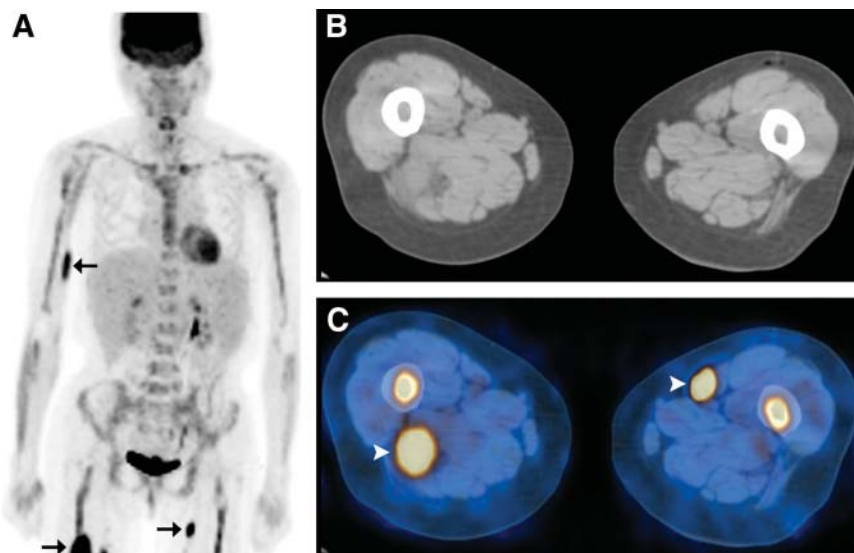
ysis of bone marrow or lymph node specimens or on clinical follow-up.

One PET/CT examination had false-negative findings in a patient who subsequently died and in whom Richter's transformation was diagnosed only at postmortem examination.

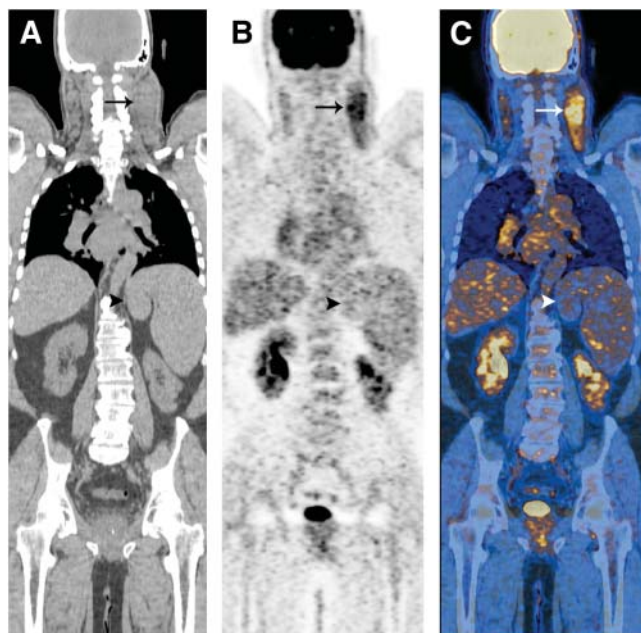
At the time of PET/CT, data on LDH levels were available for all patients; the levels were raised in 2 patients (18%) with Richter's transformation and in 8 patients (17%) without Richter's transformation ( $P = 0.69$ , Fisher exact test). Serum  $\beta$ -2 microglobulin levels were available at the time of PET/CT in 29 patients; the levels were raised in all (9 patients with Richter's transformation and 20 patients without Richter's transformation).

Of the 17 patients in whom Richter's transformation was suspected clinically before scanning, PET/CT confirmed the diagnosis in 8 patients and detected accelerated-phase CLL or an alternative malignancy in 5 patients (accelerated-phase CLL in 2, metastatic neuroendocrine carcinoma in 1, non-small cell lung cancer in 1, and Hodgkin's lymphoma in 1). PET/CT correctly excluded Richter's transformation in 2 of these patients. In the remaining 2 patients, PET/CT findings were falsely negative in 1 patient (who was found to have Richter's transformation on postmortem examination 6 wk later) and falsely positive in 1 patient (who had pneumonia causing fever and night sweats and  $^{18}\text{F}$ -FDG-avid hilar lymphadenopathy). Finally, in 2 other patients, PET/CT detected a case of Richter's transformation that had not been clinically suspected before scanning.

A cutoff  $\text{SUV}_{\text{max}}$  of 5 provided the greatest discriminatory information between patients with and patients without Richter's transformation. Values lower than 5 were less specific, whereas values higher than 5 were less sensitive.



**FIGURE 2.** 66-y-old woman with 8-y history of CLL, which had been clinically responsive to chemotherapy. In posterior right thigh and right forearm, patient had nontender masses thought to represent spontaneous hematomas secondary to low platelet count, but she was otherwise asymptomatic. On restaging PET/CT, coronal maximum-intensity-projection PET image (A) demonstrated focal areas of increased  $^{18}\text{F}$ -FDG uptake within right forearm and both upper thighs (arrows). Diffusely increased  $^{18}\text{F}$ -FDG uptake within bone marrow represented physiologic marrow stimulation secondary to therapy. Thighs showed no obvious corresponding abnormality on axial CT images (B), but hypermetabolic intramuscular masses (arrowheads) were evident on axial fused PET/CT images (C). Fine-needle aspiration of a right forearm nodule revealed diffuse large cell lymphoma.



**FIGURE 3.** 60-y-old man with 3-y history of CLL with bulky multicompartmental lymphadenopathy. Coronal CT (A), PET (B), and fused PET/CT (C) images from restaging PET/CT after chemotherapy demonstrate patchy increased  $^{18}\text{F}$ -FDG uptake within lymphadenopathy on left side of neck (arrows). Enlarged lymph nodes at other sites (right side of neck, mediastinum), as well as prominent splenomegaly (arrowhead), demonstrate only mild  $^{18}\text{F}$ -FDG accumulation. PET/CT findings helped guide fine-needle aspiration of  $^{18}\text{F}$ -FDG-avid lymph nodes on left side of neck. Increased numbers of large B cells, consistent with CLL in accelerated phase, were detected.

In this highly selective population of patients with CLL, the overall sensitivity and specificity of PET/CT for Richter's transformation were 91% and 80%, respectively, with positive and negative predictive values of 53% and 97%, respectively. For the diagnosis of Richter's transformation, an accelerated phase of CLL, or a new malignancy of any nature, PET/CT had a sensitivity, a specificity, and positive and negative predictive values of 94%, 90%, and 79% and 97%, respectively.

## DISCUSSION

Our results show that PET/CT can detect Richter's transformation of CLL to large cell lymphoma with a high sensitivity, specificity, and negative predictive value. The rationale for using PET/CT in the diagnosis of Richter's transformation is based on the high sensitivity of this test for the detection of an elevated metabolic rate in large cell lymphoma and the relatively low  $^{18}\text{F}$ -FDG accumulation in cells with a low turnover rate, such as the small lymphocytes of CLL.

We found that the main value of PET/CT in patients with CLL was its ability to exclude the diagnosis of Richter's transformation with a high degree of confidence, with a negative predictive value of 97%. In our series, PET/CT

correctly excluded the diagnosis in all but 1 of the patients who did not have Richter's transformation. In 2 of these patients with negative scan findings, there were clinical symptoms and signs to suggest possible Richter's transformation (one was a patient with a painful lymph node in the neck; the other was a patient with constitutional symptoms of B-cell lymphoma and raised levels of  $\beta$ -2 microglobulin and LDH), but the PET/CT scans showed no evidence of abnormal  $^{18}\text{F}$ -FDG uptake and the imaging findings were more consistent with indolent CLL. Histologic analysis and subsequent follow-up confirmed the absence of Richter's transformation.

In addition, in patients in whom Richter's transformation was strongly suspected, abnormal findings on PET/CT supported the clinical impression of Richter's transformation and was able to identify lymph nodes or extranodal masses amenable to biopsy to confirm the diagnosis. Richter's transformation had already been strongly suspected before PET/CT in most patients in our series (9/11 patients); however, the detection of specific sites of elevated  $^{18}\text{F}$ -FDG uptake helped guide decisions on which lymph nodes or masses should undergo biopsy. In addition, PET/CT was able to identify clinically unsuspected Richter's transformation in 2 other patients. Although PET/CT was requested as a diagnostic examination in most cases to exclude or confirm Richter's transformation, concurrent staging by PET/CT was also possible in cases in which lymphoma was confirmed.

Compared with its high sensitivity, the relatively lower specificity and positive predictive value (80% and 53%, respectively) of PET/CT for the diagnosis of Richter's transformation has several explanations. Our study had 9 PET/CT scans with false-positive findings. One source of diagnostic difficulty in patients with abnormal PET/CT findings is the inability of PET/CT to distinguish between Richter's transformation and other  $^{18}\text{F}$ -FDG-avid malignancies. CLL may undergo transformation to malignancies other than large B-cell lymphoma (so-called Richter's variants, such as Hodgkin's lymphoma (14), and other hematologic malignancies (15–19)), and patients with CLL also have a high incidence of second malignancies, such as of the skin, breast, prostate, or lung (20). In our group of patients, PET/CT detected the development of Hodgkin's lymphoma in 1 patient and of nonhematologic cancer in 2 other patients (1 patient with non-small cell lung cancer and 1 patient with metastatic neuroendocrine carcinoma), all of which cases were  $^{18}\text{F}$ -FDG-avid. Because the treatment of these second malignancies may differ markedly from the management of large cell lymphoma, it is important that abnormal PET/CT findings always be confirmed histologically before the treatment is decided.

Other causes of false-positive PET/CT findings may stem from the composition of our study population, which included patients with advanced disease who were referred to our institution for active treatment. In 2 of these patients, PET/CT demonstrated sites of increased  $^{18}\text{F}$ -FDG uptake

that corresponded to an accelerated phase of CLL rather than to frank lymphomatous transformation. Accelerated-phase CLL is characterized by increased numbers of more immature cells within the bone marrow and by lymphoid tissue with a higher rate of cell turnover. This phase can be viewed as an intermediate stage between CLL and Richter's transformation, similar to accelerated-phase chronic myeloid leukemia. Although there are insufficient histologic criteria in such patients for a firm diagnosis of Richter's transformation, we have found in our series of patients that this phase of the disease pursues an aggressive clinical course similar to that of Richter's transformation and requires treatment with rituximab and chemotherapy or stem cell transplantation (Apostolia M, Tsimberidou et al., unpublished data, 2006). PET/CT can detect this phase of acceleration by demonstrating increased  $^{18}\text{F}$ -FDG uptake within lymph nodes and in the bone marrow. With the more stringent criteria of the current study, the 2 patients in our group who were diagnosed with CLL in a phase of acceleration and who had abnormal PET/CT findings were considered to have false-positive findings; nevertheless, the PET/CT findings supported the clinical impression of rapid disease progression, and both patients were treated accordingly.

Pneumonia was a cause of false-positive PET/CT findings in 1 patient who had  $^{18}\text{F}$ -FDG-avid hilar lymphadenopathy secondary to presumed reactive lymphoid hyperplasia. Patients with CLL are particularly susceptible to recurrent infections, especially sinusitis and atypical pneumonia, because of their chronically impaired immunity, which may be related to the disease itself or to immunosuppressive treatment. Infection can therefore be the source of false-positive findings on PET/CT, and the interpreting radiologist should always take care to examine the corresponding CT images for signs suggestive of infection to avoid misinterpreting the significance of the PET abnormalities. For the clinician, even if the results of the PET/CT scan are negative for Richter's transformation, the detection of other treatable disease is important, and therefore it is valuable to interpret the results in the context of the clinical situation.

The limitations of our study stem from its retrospective nature. Our study population comprised patients with CLL at different stages of advancement. Many of these patients had received prior treatment, and all had been referred to our tertiary care cancer center for management. The diagnostic performance of PET/CT as assessed in our study therefore applies more to a high-risk group of patients than to the general population of CLL patients, who in general have a more indolent clinical course with a lower risk of malignant transformation. Furthermore, lymph node biopsy was performed almost exclusively on patients with abnormal PET/CT findings. Although most patients with normal PET/CT findings did not undergo lymph node biopsy, Richter's transformation was excluded in these patients on the basis of clinical follow-up and negative results on bone marrow biopsy and aspiration.

PET/CT should be used in patients with CLL who present with fever in the absence of infection, an elevated LDH level, and rapidly enlarging lymph nodes, all of which indicate Richter's transformation, and PET/CT should be considered if large cells are found in bone marrow biopsy samples or in the peripheral blood—a possible indication of an accelerated phase of CLL. The main purpose of PET/CT in these circumstances is for confirmation of the diagnosis and for staging of Richter's transformation to large cell lymphoma. In particular, PET/CT can identify sites of increased  $^{18}\text{F}$ -FDG uptake that are suitable for biopsy or surveillance.

## CONCLUSION

PET/CT can exclude the diagnosis of Richter's transformation with a high degree of confidence in patients with CLL. The presence of sites of abnormally increased  $^{18}\text{F}$ -FDG uptake on PET/CT of patients with CLL is predictive of Richter's transformation to large B-cell lymphoma, accelerated-phase CLL, or another malignancy. Because of this potential for detection of other malignancies, histologic confirmation of the cause of abnormal PET/CT findings is always advisable before one decides on subsequent management. The role of PET/CT for the detection and staging of Richter's transformation should be assessed in prospective trials on uniformly treated patients.

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