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The Role of ^{18}F-FDG PET/CT for Initial Staging of Nasal Type Natural Killer/T-Cell Lymphoma: A Comparison with Conventional Staging Methods

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The utility of ^{18}F-FDG PET/CT in patients with nasal-type natural killer (NK)/T-cell lymphoma has not been established. Therefore, we evaluated the role of ^{18}F-FDG PET/CT for determining cancer staging by comparing its results to those of conventional staging methods (CSMs) (physical examination, CT with intravenous contrast, biopsies from primary sites, and bone marrow examinations) in patients with nasal-type NK/T-cell lymphoma. **Methods:** In this study, 52 consecutive patients (34 men, 18 women; mean age, 49.4 y) with newly diagnosed nasal-type NK/T-cell lymphoma were studied. Anatomic regions (n = 1,300; 16 nodal and 9 extranodal regions per patient) were assessed with an ^{18}F-FDG PET/CT scan and with CSMs, and each anatomic region was classified as positive or negative for malignancy. Biopsy and clinical follow-up, including additional imaging studies, were used as the gold standard for diagnosis. **Results:** Of the 59 nodal and 71 extranodal anatomic regions that were truly positive for malignancy, ^{18}F-FDG PET/CT detected 58 nodal and 69 extranodal. CSMs, however, detected only 44 of the nodal and 61 of the extranodal anatomic regions that were positive for malignancy (nodal comparison of PET/CT vs. CSMs, $P < 0.001$; extranodal comparison of PET/CT vs. CSMs, $P = 0.008$). PET/CT scans exhibited a significantly better sensitivity (97.7% vs. 80.7%, $P < 0.001$) than CSMs for the detection of malignant lesions. PET/CT findings altered the original staging category for 12 patients (21.2%) and affected treatment planning in 23 cases (44.2%). **Conclusion:** Our study demonstrated that ^{18}F-FDG PET/CT scanning is a valuable modality for staging and treatment planning in patients with nasal-type NK/T-cell lymphoma.

Key Words: ^{18}F-FDG; PET/CT; staging; nasal-type NK/T-cell lymphoma

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Extranodal natural killer (NK)/T-cell lymphoma, nasal-type, is a rare and aggressive form of lymphoma with a marked geographic preference for Asia, Mexico, and South America (*1–3*). Although it constitutes less than 1% of all lymphomas in Western countries, it accounts for 3%–9% of all malignant lymphomas in Asia (*3–5*). In western countries, most sinonasal lymphomas are diffuse large B-cell lymphomas, whereas in Asia, 40%–74% of sinonasal lymphomas are NK/T-cell lymphomas (*1,3*). Nasal-type NK/T-cell lymphoma frequently involves extranodal sites, including skin, the gastrointestinal tract, testis, kidneys, and the respiratory tract (*6*). However, unlike other lymphomas, nasal-type NK/T-cell lymphoma less frequently involves the bone marrow and lymph nodes (*3,6*). Another significant difference between nasal-type NK/T-cell lymphoma and other types of lymphoma is that, although NK/T-cell lymphoma has a good response to radiation therapy, it usually has a poor response to conventional chemotherapy (*7,8*). Radiation therapy with or without chemotherapy is now considered the optimal treatment for stage I or II nasal-type NK/T-cell lymphoma; thus, knowing the exact stage of this cancer is critical in determining the appropriate treatment (*9–11*).

^{18}F-FDG PET/CT is part of clinical practice for evaluating aggressive B-cell and Hodgkin lymphomas (*12–15*). Research indicates that ^{18}F-FDG PET/CT scans are useful for staging, evaluating treatment response, predicting prognosis, and looking for recurrence during follow-up in patients with various lymphomas. However, using ^{18}F-FDG PET/CT scans for staging patients with nasal-type NK/T-cell lymphoma is not well established. Until now, conventional staging methods (CSMs), including physical examination, CT with intravenous contrast, biopsies from primary sites, and bone marrow examinations, have been used to stage the disease as a standard method (*6*). There are few studies that have investigated the utility of ^{18}F-FDG PET/CT scans for staging purposes in this disease, and those that have been conducted were limited by their sample size (*16–19*). Therefore, the purpose of this study was to investigate the effectiveness of ^{18}F-FDG PET/CT scans, as compared with CSMs, for staging patients with nasal-type NK/T-cell lymphoma.

MATERIALS AND METHODS

Patients

From May 2003 to December 2009, 52 patients with recently diagnosed nasal-type NK/T-cell lymphoma, who underwent an ^{18}F-FDG PET/CT scan for initial staging at Samsung Medical Center, were enrolled in this retrospective study. The pathologic diagnosis was determined on the basis of the World Health Organization lymphoma classification criteria (*20*). Immunohistochemistry, flow cytometry, and Epstein–Barr virus in situ hybridization analysis were performed for pathologic confirmation.

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Follow-up evaluations included clinical examinations, CT scanning with intravenous contrast, or PET/CT scanning. These were performed every 1–3 mo for the first 2 y after diagnosis, every 5–6 mo for the next 3 y, and annually thereafter. Further diagnostic work-up was performed if clinically indicated. Recurrence was diagnosed either by a positive biopsy result or by clinical or radiographic evidence of disease progression. Because diagnosis was established on the basis of clinical follow-up, which included additional imaging studies for all patients and an additional biopsy for 8 patients, we excluded patients who did not undergo follow-up imaging studies due to cancer-related death or who were lost to follow-up within 3 mo of the initial ^{18}F-FDG PET/CT scan and CSMs. The ethics committee of our institution reviewed and approved the protocol of this retrospective study.

PET/CT Imaging

Patients were instructed to fast for at least 6 h before the ^{18}F-FDG PET/CT scan. Blood glucose levels before the injection of ^{18}F-FDG were lower than 200 mg/dL in all patients. PET/CT imaging was performed using 1 of 2 dedicated PET/CT scanners (Discovery LS for 37 patients or Discovery STe for 17 patients; GE Healthcare), without intravenous or oral contrast material.

With the Discovery LS device (8-slice helical CT scanner), a whole-body CT scan was obtained, using a continuous spiral technique (140 keV, 40–120 mA adjusted on the basis of the patient's weight, and a section width of 5 mm), at 60 min after the injection of ^{18}F-FDG (5.5 MBq/kg). After the CT scan, an emission scan from the thigh to the head was obtained for 4 min per frame in 2-dimensional mode. Attenuation-corrected PET images (voxel size, 4.3 × 4.3 × 3.9 mm) were reconstructed from the CT data, using an ordered-subset expectation maximization algorithm (28 subsets, 2 iterations). With the Discovery STe device (16-slice helical CT scanner), a whole-body CT scan was obtained, using a continuous spiral technique (140 keV, 30–170 mA in AutomA mode, and a section width of 3.75 mm), at 60 min after the injection of ^{18}F-FDG (5.5 MBq/kg). After the CT scan, an emission scan was obtained from the thigh to the head for 2.5 min per frame in 3-dimensional mode. Attenuation-corrected PET images (voxel size, 3.9 × 3.9 × 3.3 mm) were reconstructed from the CT data using a 3-dimensional ordered-subset expectation maximization algorithm (20 subsets, 2 iterations). When follow-up PET/CT was performed, we used the same scanner with the same reconstruction algorithm as in the initial scan.

CSMs

All patients underwent initial CSMs, including physical examinations, CT scans (neck, chest, and abdomen) with intravenous contrast, biopsies of primary sites, and bone marrow examinations. Contrast-enhanced CT scans were acquired with a HighSpeed Advantage or Lightspeed scanner (GE Healthcare). Chest CT scans were obtained throughout the thorax with a collimation of 2.5 mm, pitch of 1.35, and reconstruction intervals of 2.5 mm. Neck CT scans were obtained with a collimation of 3 mm and reconstruction intervals of 2.5–3.0 mm. Abdominal CT scans, including whole abdomen and pelvis views, were obtained with 2.5- to 5.0-mm collimation and 2.5–5.0 reconstruction intervals. Both CSMs and ^{18}F-FDG PET/CT scans were acquired within a 3-wk interval for all patients.

Image Interpretation

An experienced nuclear medicine physician interpreted the ^{18}F-FDG PET/CT scans. Lymph nodes were classified as positive if there was focally increased ^{18}F-FDG uptake, compared with the uptake in surrounding normal soft tissue (Fig. 1). In cases of lymphoid tissue, such as tonsils, the lymphoid tissue was classified as positive if there was asymmetric uptake or morphologic changes. Splenic tissue was classified as positive if there was abnormal focal ^{18}F-FDG uptake, compared with normal splenic uptake in surrounding tissue, or diffusely increased uptake, compared with the liver. Other organs were classified as positive if there was focal ^{18}F-FDG uptake, compared with the surrounding normal organ, or ^{18}F-FDG uptake that was not explained by physiologic activity (Fig. 2). [Fig. 1]

An experienced radiologist interpreted the contrast-enhanced CT scans according to the general criteria of lymph node size and extranodal structural abnormalities.

Stage and Region-Based Analysis

Disease stage was determined by the Ann Arbor classification system (*21*). The determination of the final stages was based on CSM-positive-lesion findings and on ^{18}F-PET/CT scans. Staging was confirmed by clinical follow-up or biopsy. The body was divided into 16 nodal regions and 9 extranodal anatomic regions for analysis (Table 1). Eight hundred thirty-two lymph node regions and 468 extranodal anatomic regions were analyzed.

Standard of Reference

Biopsy and clinical follow-up, including additional imaging studies, were used to establish the gold standard for diagnosis. Other than the primary site, only a small number of positive lesions that were identified by ^{18}F-FDG PET/CT scan or CSMs were biopsied, because of ethical and practical reasons. Biopsies of

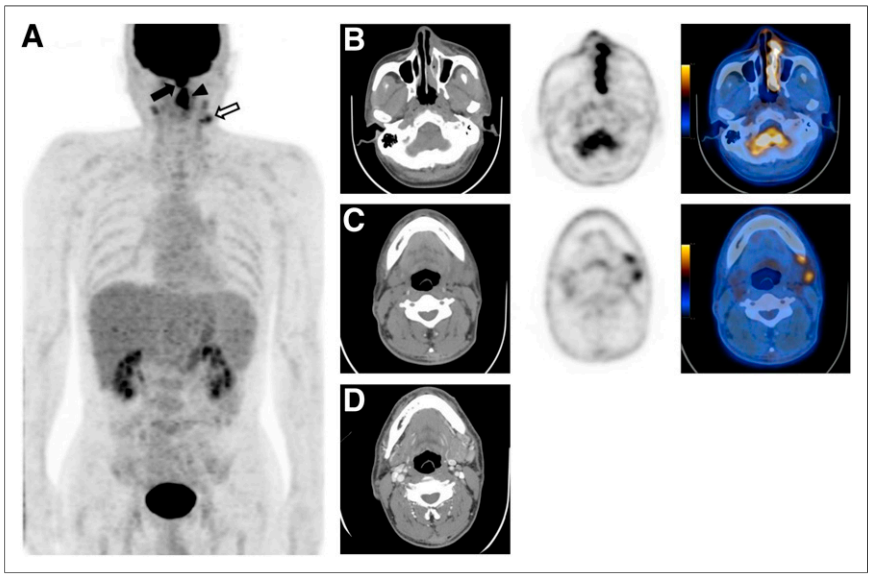

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FIGURE 1. A 46-y-old man with recently diagnosed nasal-type NK/T-cell lymphoma underwent ^{18}F-FDG PET/CT scan (A–C) and enhanced CT scan (D). Maximum-intensity-projection image (A) shows hypermetabolic lesions in nasal cavity (arrow), left tonsil (arrowhead), and left side of neck (empty arrow). Transaxial images of ^{18}F-FDG PET/CT scan shows ^{18}F-FDG–avid mass in left nasal cavity that was pathologically proven NK/T-cell lymphoma (B). ^{18}F-FDG PET/CT scan shows lymph nodes with increased ^{18}F-FDG uptake in left submandibular area, suggesting malignancy (C). However, contrast-enhanced CT shows lymph nodes, with less than 1 cm of short-axis diameter, which is not consistent with malignancy (D). Results of fine-needle aspiration cytology were positive for lymphoma involvement. Therefore, stage was changed from I to II.

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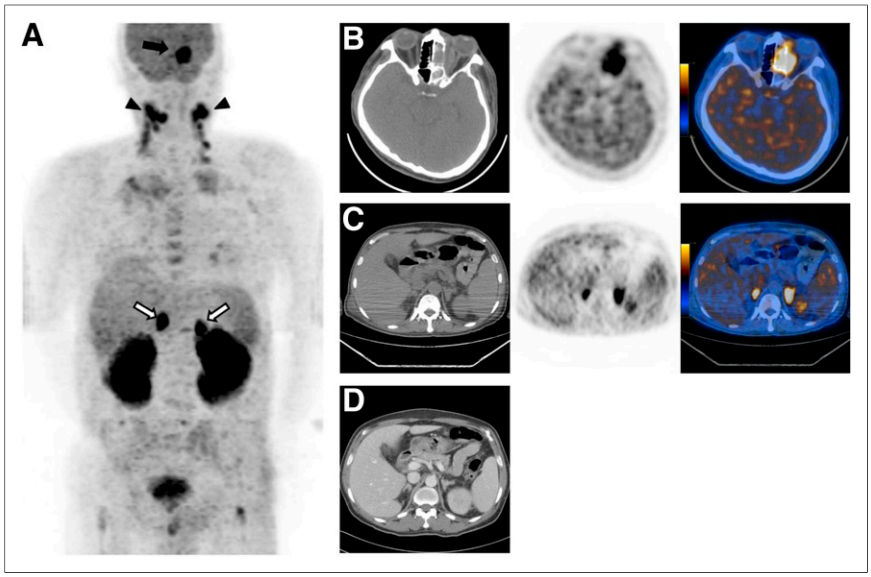

FIGURE 2. A 60-y-old man with newly diagnosed nasal-type NK/T-cell lymphoma underwent ^{18}F-FDG PET/CT scan (A–C) and enhanced CT scan (D) for initial staging. Maximum-intensity-projection image (A) shows hypermetabolic lesions in left ethmoid sinus (arrow), both cervical lymphatic chains (arrowhead), and both suprarenal areas (empty arrow). Transaxial images of ^{18}F-FDG PET/CT scan shows ^{18}F-FDG–avid mass in left ethmoid sinus (B). ^{18}F-FDG PET/CT scan showing intense ^{18}F-FDG uptake in both adrenal glands, suggesting malignancy (C). However, enhanced CT scan shows only mild nodular thickening in both adrenal glands (D). Finally, after obtaining PET/CT scan, stage was changed from II to IV. After 4 cycles of chemotherapy, follow-up ^{18}F-FDG PET/CT scan showed normalized ^{18}F-FDG uptake in both adrenal glands.

additional lesions were performed in only 9 of 52 patients (17.3%). Clinical follow-up included additional imaging, consisting of CT scanning, MR imaging, or ^{18}F-FDG PET/CT scanning, which was performed for at least 6 mo for all patients.

Methods of lesion classification were similar to those of previous studies (*22,23*). Concordant findings in both diagnostic methods (^{18}F-FDG PET/CT scans and CSMs) and clinical course were regarded as true-positives (TPs) or true-negatives (TNs) for disease. If a patient entered remission, lesions that were resolved on follow-up imaging were regarded as TPs. Conversely, lesions that had progressed were regarded as TPs if the patient's disease had developed. If a site remained disease-free during the course of follow-up, it was regarded as a TN.

Discordant findings between the predictions from diagnostic methods and the clinical course were regarded as false-positives (FPs) or false negatives (FNs) for disease. If a patient entered remission, lesions that were seen to remain stable or progress were regarded as FPs. In the case of patients who suffered disease progression, lesions that appeared to be resolved or remain stable were regarded as FNs. If a lesion met the criteria for a TP, but was not identified or was considered nonmalignant by ^{18}F-FDG PET/CT scanning or CSMs, it was regarded as FN. Anatomic regions that were disease-free by diagnostic methods were also considered FNs if disease developed at that site during the following 2 mo of follow-up.

Statistical Analysis

Statistical analyses were performed using PASW Statistics (version 18; IBM Inc.). The specificity, sensitivity, and accuracy of ^{18}F-FDG PET/CT scanning and CSMs were calculated on the basis of the standard of reference. A McNemar test was used to compare the accuracy of ^{18}F-FDG PET/CT scans and CSMs in detecting malignant lesions and initial staging. A P value of less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

The patient characteristics are summarized in Table 2. Fifty-two patients (34 men, 18 women), with a mean age of 49.4 ± 11.3 y (age range, 24.4–74.1 y), were included in the study. Mean follow-up duration was 34.4 ± 22.8 mo (range, 6.8–93.1 mo). In 44 of the 52 patients (84.6%), the primary tumor site was the nasal cavity. In the remaining 8 patients (15.4%), the primary tumor site was the skin (n = 2), duodenum (n = 1), pharynx (n = 4), and larynx (n = 1). All patients underwent a biopsy of the primary tumor site and bone marrow. Of the 17 patients (32.7%), for whom there was a discrepancy between the findings of their ^{18}F-FDG PET/CT scan and CSMs, 8 underwent an additional biopsy to confirm the lesion. Additional biopsy sites included the neck (n = 2), tonsil (n = 1), stomach (n = 2), duodenum (n = 2), and lung (n = 1). The maximum standard uptake value of primary lesions was 12.4 ± 5.8 and ranged from 3.1 to 35.2. [**Table 2**]

^{18}F-FDG PE/CT Scanning Versus CSMs: Anatomic Region–Based Analyses

^{18}F-FDG PET/CT scans detected more anatomic regions with malignant tumors than did the CSMs. Among the 832 nodal regions and 468 extranodal anatomic regions analyzed, 59 nodal and 71 extranodal anatomic regions were TPs. The scans detected

TABLE 1
Nodal and Extranodal Regions for Lesion-Based Analysis

Nodal regions (n = 16)	Extranodal regions (n = 9)
Waldeyer ring	Upper aerodigestive tract
Right neck*	Skin/subcutaneous
Left neck*	Central nervous system and spinal canal
Right infraclavicular	Lung
Left infraclavicular	Myocardium
Right axillary and pectoral	Bone and bone marrow
Left axillary and pectoral	Liver
Mediastinal	Bowel
Hilar	Renal and adrenal
Spleen	
Paraaortic	
Mesenteric	
Right iliac	
Left iliac	
Right inguinal and femoral	
Left inguinal and femoral	

*Included cervical, supraclavicular, occipital, and preauricular regions.

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TABLE 2
Patient Characteristics

Characteristic	Patients	
	n	%
Age (y)		
≤60	43	82.7
>60	9	17.3
Sex		
Male	34	65.4
Female	18	34.6
Stage		
I	22	42.3
II	19	36.5
III	0	0.0
IV	11	21.2
Eastern Cooperative Oncology Group performance status		
0–1	43	82.7
2–4	9	17.3
Bone marrow involvement		
Positive	3	5.8
Negative	49	94.2
Lactate dehydrogenase elevation*		
Positive	18	34.6
Negative	34	65.4
B symptom		
Positive	21	40.4
Negative	31	59.6

*Upper limit of normal, 480 IU/L.

58 nodal and 69 extranodal anatomic regions that were TPs, whereas CSMs detected only 44 nodal and 61 extranodal anatomic regions that were TPs (nodal comparison ^{18}F-FDG PET/CT vs. CSMs, $P < 0.001$; extranodal comparison ^{18}F-FDG PET/CT vs. CSMs, $P = 0.008$). Consequently, the sensitivity, specificity, and accuracy of ^{18}F-FDG PET/CT scans and CSMs for the detection of malignant lesions were 97.7%, 99.7%, and 99.5%, respectively, and 80.7%, 99.8%, and 97.9%, respectively (Table 3). [Table 3]

Of the 3 malignant lesions missed by ^{18}F-FDG PET/CT scanning, one was bone marrow infiltration, detected by the bone marrow biopsy, and another was leptomeningeal seeding, detected by a spinal tap. The final malignant lesion that was missed by ^{18}F-FDG PET/CT scanning was a nasopharyngeal lesion that was correctly identified as positive by CSMs. Though it was not biopsied, the patient entered remission and it was resolved on follow-up imaging. The scans also detected 3 FP lesions. One was a duodenal lesion that showed suggestive focal ^{18}F-FDG uptake; this was confirmed to be negative by esophagogastroduodenoscopy with biopsy. A second FP lesion by ^{18}F-FDG PET/CT scanning was on the thyroid that had focal ^{18}F-FDG uptake, which was shown to be negative by fine-needle aspiration cytology. The final FP identified by ^{18}F-FDG PET/CT scanning was a tonsil lesion with asymmetric ^{18}F-FDG uptake. This was not biopsied, but after clinical follow-up, including additional imaging, it was considered to be incidental tonsillitis. All of the FP lesions identified by the scans were correctly categorized as negative by CSMs.

^{18}F-FDG PET/CT Versus CSMs: Staging

PET/CT scans were more accurate in defining the clinical stage of nasal-type NK/T-cell lymphomas than CSMs in this study. PET staging was consistent with the final stage determination in 96.2% (50/52) of patients, whereas CSM staging was correct in final stage determination in 75.0% (39/52) of patients (Table 4). In 2 patients, for whom PET staging differed from the final staging determination, the PET/CT scan incorrectly downstaged patients with stage IV disease, by missing bone marrow infiltration and leptomeningeal seeding. [Table 4]

PET staging and CSM staging differed in 13 patients. Among these patients, PET staging was consistent with the final stage determination for 12. However, the CSM stage corresponded with the final stage determination for only 1 patient. In 11 of 12 patients, ^{18}F-FDG PET/CT scanning correctly showed that the stage should be increased, by detecting additional malignant lesions, including positive cervical lymph nodes ($n = 8$), a tonsillar lesion ($n = 1$), a lung lesion ($n = 1$), and an adrenal gland lesion ($n = 1$). In 1 patient, the ^{18}F-FDG PET/CT scan correctly decreased the staging, because the scans showed negative uptake in the mediastinal and hilar lymph nodes.

Clinical Impact of ^{18}F-FDG PET/CT on Patient Management

The results of the ^{18}F-FDG PET/CT scans affected treatment planning in 44.2% of patients (23/52) (Supplemental Table 1; supplemental materials are available online only at http://jnm.snmjournals.org). Treatment plans changed from chemoradiation to chemotherapy in 3.8% of patients (2/52), because of an increase in the initial stage from stage II to IV. Radiotherapy planning was modified according to ^{18}F-FDG PET/CT scan findings in 40.4% of patients (21/52). In 19 of the 21 patients, the radiotherapy field was increased to cover both cervical lymphatic chains and the primary lymphomatous site. Among them, 12 patients had the same staging for the ^{18}F-FDG PET/CT scan and CSMs overall. The reason was that indeterminate lymph nodes, which were classified as benign, were covered in radiotherapy fields, because the scans identified ^{18}F-FDG uptake. For small lymph nodes that are close to the ^{18}F-FDG–avid malignant mass, if the nodes have ^{18}F-FDG uptake, the radiotherapy field extends to cover the nodes, because they are considered as indeterminate lesions, which could not be completely ruled out for the possibility of malignancy. In many such cases, ^{18}F-FDG uptake was not significantly higher than for surrounding normal tissue or was not focally increased. Therefore, the nodes were classified as benign rather than malignant. These nodes were also classified as benign by radiologists because of their small size or benign features.

TABLE 3
Comparison Between PET/CT and CSMs for Region-Based Detection of Nodal and Extranodal Disease

Parameter	Region-based analysis					Diagnostic performance		
	TP	TN	FP	FN	Total	Sensitivity	Specificity	Accuracy
PET/CT	127	1167	3	3	1300	97.7%	99.7%	99.5%
CSMs	105	1168	2	25	1300	80.7%	99.8%	97.9%
P						<0.001	Not significant	<0.001

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TABLE 4
Comparison Between PET/CT and CSMs for Staging

	Concordant with final stage (n = 52)		Discordant with final stage (n = 52)	
Parameter	n	%	n	%
PET/CT	50	96.2	2	3.8
CSMs	39	75.0	13	25

P value = 0.003.

In 1 of the remaining 2 patients, the radiotherapy field was extended to both sides of the retropharyngeal space, from only the primary site, based on the ^{18}F-FDG PET/CT scan. In the other patient, the results of the scan prompted the radiotherapy field to be extended to cover more anatomic regions in a unilateral cervical lymphatic chain.

DISCUSSION

^{18}F-FDG PET/CT scanning is widely accepted as the most sensitive imaging modality for staging, monitoring response, and predicting prognosis for various lymphomas (*24–29*). However, given that ^{18}F-FDG uptake is often less avid, and varies by lymphoma histology, PET/CT scans are not recommended for evaluating low-grade and T-cell non-Hodgkin lymphoma. In patients with these lymphomas, enhanced CT scans remain the standard (*24*). In patients with nasal-type NK/T-cell lymphoma, the use of an ^{18}F-FDG PET/CT scan is not established, and there are limited data, probably due to the lower incidence of this disease. Our study demonstrated that ^{18}F-FDG PET/CT scans are more successful in detecting nodal and extranodal malignant lesions than CSMs. The scans correctly altered the initial disease stage for some patients, thus altering treatment planning. These data support the importance of using ^{18}F-FDG PET/CT scans for initial staging of the disease.

The value of ^{18}F-FDG PET/CT scans for this disease has been investigated in previous studies (*17–19,30–32*). However, the data from these studies were insufficient to establish the role of ^{18}F-FDG PET/CT scans. The small numbers of patients and the retrospective designs of previous studies were serious obstacles for generalizing this modality as a standard staging method. In addition, many of the studies were performed with histologically heterogeneous groups of patients, and the data were further diluted because of the more frequent histology of lymphomas (*30–32*).

There are a few studies of only nasal-type NK/T-cell lymphoma that evaluated the usefulness of the scan for staging (*17–19*). Wu et al. reported that the scan seemed to be useful for staging purposes (*18*). In this study with 15 patients (13 newly diagnosed, 2 recurrent), PET/CT scans were shown to be useful in patients with NK/T cell lymphomas, because the scans correctly localized primary lesions that had not been detected by CSMs, and PET/CT scans correctly changed the CSM-determined stage. Similarly, Karantanis et al. reported that in 10 patients with NK/T-cell lymphoma, viable tumors were ^{18}F-FDG–avid and PET/CT scanning appeared to be sensitive enough for disease detection (*19*). More recently, Fujiwara et al. reported that PET/CT scans showed a high positive rate for extranodal lesions and a low positive rate for bone marrow involvement in their study of 19 patients with extranodal NK/T-cell lymphoma (*17*). Although our study was also limited because of its retrospective design, it is the largest single study, involving 52 patients with newly diagnosed nasal-type NK/T-cell lymphoma, and shows the usefulness and influence of ^{18}F-FDG PET/CT scans in initial staging and treatment planning.

This study revealed that nasal-type NK/T-cell lymphoma is ^{18}F-FDG–avid (maximum standard uptake value, 12.4 ± 5.8). This finding is consistent with the results of previous studies, which reported that extranodal NK/T cell lymphoma is ^{18}F-FDG–avid (*16–19,30*). In some types of lymphoma with poor ^{18}F-FDG uptake, malignant lesions are often missed (*23*). However, due to the ^{18}F-FDG avidity of nasal-type NK/T cell lymphoma, the scans were able to detect more malignant lesions and add clinically important information that was not provided by CSMs. This study showed that ^{18}F-FDG PET/CT scans can detect lymphoma, even in the case of normal-appearing extranodal sites, or lymph nodes with a normal size.

In detecting extranodal lesions, our results are in accordance with those of previously published studies. ^{18}F-FDG PET/CT scans showed better performance in detecting extranodal lesions than CSMs (*17–19*). ^{18}F-FDG PET/CT scans detected more extranodal lymphomatous involvement of the skin, adrenal gland, stomach, duodenum, and lung that was falsely classified as negative by CSMs. However, it is unclear whether ^{18}F-FDG PET/CT scans are significantly better than CSMs in correctly classifying nodal lesions as positive or negative for lymphomatous involvement. Although Fujiwara et al. did not find a significant difference in the detection of nodal lesions between ^{18}F-FDG PET/CT scans and CSMs (*17*), our results indicated that the scans were better than CSMs in detecting nodal lesions.

In the present study, ^{18}F-FDG PET/CT scans staged more patients correctly than did CSMs. There were significant differences in overall staging between ^{18}F-FDG PET/CT scans and CSMs. The correction of a misclassified stage by ^{18}F-FDG PET/CT scanning has important clinical implications, because the appropriate treatment of NK/T-cell lymphomas depends on accurate staging. Although NK/T-cell lymphomas are sensitive to radiotherapy, they are refractory to conventional chemotherapy (*33,34*). Thus, before initiating treatment, it is essential to detect and find the exact localization of tumors. One of the most important findings in this study is that ^{18}F-FDG PET/CT scans altered treatment planning in a considerable portion of patients (44.2%).

Six lesions were misclassified by ^{18}F-FDG PET/CT scanning in the present study. Three lesions (including focal hypermetabolic lesions in the duodenum, thyroid, and tonsils) were falsely classified as malignant, and 3 lesions (including bone marrow involvement, leptomeningeal seeding, and nasopharyngeal involvement) were missed. CT detected the nasopharyngeal involvement correctly through image enhancement. This case reminds us of the advantage in performing the attenuation-correction CT of the ^{18}F-FDG PET/CT scan with contrast. It would improve the diagnostic quality of the scan and also reduce the number of procedures a patient has to experience.

Previous studies have reported that approximately half of the lesions that involved bone marrow, as confirmed by biopsy, were also identified to have spread to marrow by ^{18}F-FDG PET/CT scans (*17,35*). Although it is hard to mention statistical significance because of a low incidence of marrow involvement in our patients, we observed a similar result in this study. Among the 3 patients with pathologically confirmed bone marrow involvement, 2 were found to be positive for bone marrow involvement by the scan.

The present study has some limitations. The retrospective nature of this study is a critical limitation in its generalization. Another limitation is that only a small portion of the lesions (14.1%, except at the primary site and bone marrow) that were classified as positive for

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malignancy underwent biopsy and pathologic confirmation. Using clinical follow-up with additional imaging studies as the standard of reference may lead to false classification of the lesions. Nonmalignant lesions, such as focal inflammation, that were resolved on follow-up imaging studies, regardless of lymphoma treatment, may have been falsely regarded as TPs. Conversely, malignant lesions with lower ^{18}F-FDG avidity may have been falsely regarded as negative. Therefore, the sensitivity of ^{18}F-FDG PET/CT scanning may not have been correctly evaluated. However, existing published studies share the same limitations (*16–19*). Biopsies of every suggestive lesion are neither ethical nor recommended in routine clinical practice. The other limitation is that analyses of ^{18}F-FDG PET/CT scans and CT scan images were based on the initial formal reports. Therefore, the readers who interpreted the images might not be masked. Last, 2 kinds of PET/CT scanners with different protocols were used, possibly affecting the measurement of standardized uptake values. However, such a circumstance would have little impact on the results of this study, because we used visual analysis for diagnosis and used the same scanner with the same reconstruction algorithm for follow-up to the initial scan.

CONCLUSION

Our study demonstrated that ^{18}F-FDG PET/CT scans are able to detect more nodal and extranodal lesions than CSMs in patients with nasal-type NK/T-cell lymphoma. In addition, ^{18}F-FDG PET/CT scans were more accurate at staging patients than CSMs. Results of this study suggest that ^{18}F-FDG PET/CT scanning deserves to be included as a routine staging modality in addition to CSMs in nasal-type NK/T-cell lymphoma.

DISCLOSURE

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