Differential Diagnosis of Sinonasal Lymphoma and Squamous Cell Carcinoma on CT, MRI, and PET/CT

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Abstract

Objective. The purpose of this study was to analyze computed tomography (CT) and magnetic resonance (MR) images and to evaluate the maximum standardized uptake value (SUV max) of positron emission tomography (PET)/CT parameters between sinonasal non-Hodgkin’s lymphoma (NHL) and squamous cell carcinoma (SCC), knowing the imaging features that distinguish sinonasal NHL from SCC.

Study Design. Case series with chart review.

Setting. University tertiary care facility.

Subjects and Methods. We analyzed the features on CT, MR imaging, and PET/CT of 78 patients diagnosed with sinonasal NHL or SCC histopathologically. The CT (n = 34), MRI (n = 25), and PET/CT (n = 33) images of 39 patients with sinonasal NHL and the CT (n = 38), MR (n = 28), and PET/CT (n = 31) images of 39 patients with SCC were evaluated. The sinonasal NHL was diagnosed as natural killer/T-cell lymphoma (n = 28) and diffuse large B-cell lymphoma (n = 11).

Results. Patients with sinonasal NHL had a larger tumor volume and higher tumor homogeneity than patients with SCC on T2-weighted and postcontrast MR images. Most of the sinonasal NHL and SCC showed a high degree of enhancement. The apparent diffusion coefficient (ADC) values and adjacent bone destruction were significantly lower in sinonasal NHL than in SCC. However, cervical lymphadenopathy, Waldeyer’s ring involvement, and PET/CT SUV max showed no significant differences between sinonasal NHL and SCC.

Conclusion. CT and MR images of sinonasal masses showing a bulky lesion, marked homogeneity, and low ADC values without adjacent bone destruction are more suggestive of sinonasal NHL than SCC.

Keywords

lymphoma, non-Hodgkin, carcinoma, squamous cell, paranasal sinus neoplasms, tomography, spiral computed, magnetic resonance imaging, positron emission tomography

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Primary malignant tumors of the sinonasal cavity are rare, accounting for less than 5% of all head and neck cancers and 1% of all malignancies.1 Despite its relatively small anatomic size, the sinonasal cavity can give rise to a tremendously diverse group of neoplasms ranging from carcinomas to lymphomas and sarcomas of various types.2 Sinonasal malignancies may be classified into epithelial and nonepithelial categories. The most commonly encountered epithelial subtypes are squamous cell carcinomas (SCCs), whereas the most common nonepithelial sinonasal malignancies are malignant lymphomas.3

Non-Hodgkin’s lymphoma (NHL) is a cancer that arises in the nodal and extranodal lymphoid tissue. Although SCC constitutes 40% to 50% of all sinonasal malignancies, primary sinonasal NHL is less common, comprising 6% to 13% of all extranodal head and neck lymphomas.4,5 The most common presenting symptoms of sinonasal malignancies are nasal obstruction, localized pain, epistaxis, unilateral facial or nasal swelling, nasal discharge, and headache.5 However, these findings are nonspecific and make differential diagnosis between sinonasal NHL and SCC quite difficult.

Comparative image analysis of sinonasal NHL and SCC can be helpful in differential diagnosis and is important clinically because they require completely different treatment strategies. Although the patients with sinonasal NHL

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are usually treated with the combination of radiotherapy and chemotherapy, surgical resection is the mainstay of treatment for patients with sinonasal SCC. However, few studies have compared radiologic imaging findings between NHL and SCC that originated from nasal cavity and paranasal sinuses.

The purpose of this study was to analyze computed tomography (CT) and magnetic resonance (MR) images and to evaluate the maximum standardized uptake value (SUV max) of positron emission tomography (PET)/CT between sinonasal NHL and SCC.

**Subjects and Methods**

**Subjects**

We reviewed and analyzed the medical records and imaging findings of 39 patients diagnosed with sinonasal NHL and 39 patients diagnosed with SCC histopathologically between 1999 and 2016 at Pusan National University Hospital and Pusan National University Yangsan Hospital.

Patients diagnosed with NHL were aged 28 to 86 years, with a mean age of 57.9 years (26 males, 13 females). Patients diagnosed with SCC were aged 40 to 88 years, with a mean age of 66.4 years (23 males, 16 females). The CT (n = 34), MR (n = 25), and PET/CT (n = 33) images of 39 patients with NHL and the CT (n = 38), MR (n = 28), and PET/CT (n = 31) images of 39 patients with SCC were available for evaluation. Seventeen patients with NHL and 27 patients with SCC underwent both enhanced CT and MR examination.

Clinical stages were stage I in 17 NHLs and 18 SCCs, stage II in 16 NHLs and 17 SCCs, stage III in 3 NHLs and 2 SCCs, and stage IV in 3 NHLs and 2 SCCs. The immunophenotypes of NHL included natural killer (NK) T cell (28 cases) and diffuse large B cell (11 cases). SCCs were well, moderately, and poorly differentiated in 17, 13, and 9 patients, respectively. The nasal cavity was the most common site of NHL and SCC, followed by the maxillary sinus and ethmoid sinus. The patients' characteristics are summarized in Table 1. This study was approved by the Institutional Review Board of Pusan National University School of Medicine.

**CT Imaging**

CT examinations were performed on either of the 2 scanners after injection of contrast material (iopromide, Ultravist 300; Bayer Schering Pharma, Berlin, Germany): SOMATOM Definition Dual Source 64 (Siemens, Forchheim, Germany) or SOMATOM Definition AS+128 (Siemens). Their parameters were as follows: field of view (FOV) = 200 × 200, KVp = 120, mAs = 120, and slice thickness = 2 mm.

**MR Imaging**

MR imaging was performed using the 3T MR scanner (Magnetom Tim Trio; Siemens). MR imaging parameters were as follows: for T2 coronal and axial images, repetition time (TR) = 5462 to 5500 ms, echo time (TE) = 92 ms, field-of-view (FOV) = 190 × 210 for the coronal image and 199 × 220 for the axial image, slice thickness = 4 mm, number of excitations (NEX) = 3 for the coronal image and 2 for the axial image, and phase/frequency encoding steps = 384 × 244. For T1 axial images, TR = 591 to 600 ms, TE = 9.4 ms, FOV = 199 × 220, slice thickness = 4 mm, NEX = 1, and phase/frequency encoding steps = 384 × 244. Diffusion-weighted imaging was performed using an echoplanar sequence. The imaging parameters were as follows: an FOV of 230 × 230 mm, 128 phase-encoding steps, a section thickness of 5 mm, a gap of 0.1 mm, and an acquisition matrix of 192 × 192. The diffusion sensitizing gradient was oriented at the 3 axes with b values of 1, 500, and 1000 s/mm². The apparent diffusion coefficient (ADC) map was obtained simultaneously with custom software. Contrast-enhanced axial and coronal images were obtained with 2 mmol/kg gadolinium (Magrevist; Bayer Schering Pharma). Postcontrast axial images were obtained with the same parameters as the precontrast T1-weighted image (T1WI) plus fat suppression. Postcontrast coronal images were obtained with the following parameters: TR = 600 ms, TE = 10 ms, FOV = 190 × 210 mm, slice thickness = 4 mm, phase/frequency encoding steps = 320 × 203, NEX = 2, and fat suppression.

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**Table 1. Patient Characteristics.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>NHL</th>
<th>SCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (95% CI), y</td>
<td>57.9 (53.4-62.8)</td>
<td>66.4 (62.1-70.7)</td>
</tr>
<tr>
<td>Sex, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (66.7)</td>
<td>23 (59.0)</td>
</tr>
<tr>
<td>Female</td>
<td>13 (33.3)</td>
<td>16 (41.0)</td>
</tr>
<tr>
<td>Modality, No.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>34</td>
<td>38</td>
</tr>
<tr>
<td>MRI</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>PET/CT</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>Clinical stage, No.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>II</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Histological subtypes, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>11 (28.2)</td>
<td></td>
</tr>
<tr>
<td>NK T-cell lymphoma</td>
<td>28 (71.8)</td>
<td>39 (100)</td>
</tr>
<tr>
<td>SCC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well differentiated</td>
<td></td>
<td>17 (43.6)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>13 (33.3)</td>
<td>3</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>9 (23.1)</td>
<td>2</td>
</tr>
<tr>
<td>Tumor origin site, No. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal cavity</td>
<td>30 (76.9)</td>
<td>28 (71.8)</td>
</tr>
<tr>
<td>Maxillary sinus</td>
<td>6 (15.4)</td>
<td>7 (17.9)</td>
</tr>
<tr>
<td>Ethmoid sinus</td>
<td>3 (7.7)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>Sphenoid sinus</td>
<td></td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Frontal sinus</td>
<td></td>
<td>1 (2.6)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CT, computed tomography; MRI, magnetic resonance imaging; NHL, non-Hodgkin's lymphoma; NK, natural killer; PET, positron emission tomography; SCC, squamous cell carcinoma.
PET/CT imaging was performed using a Gemini PET/CT scanner (Philips, Milpitas, California). Patients were instructed to fast for 6 hours, and blood glucose was measured to ensure a level lower than 11 mmol/L prior to injection of 370 to 444 MBq fluorine-18 fluoro-2-deoxyglucose (18F-FDG). FDG-PET/CT acquisition protocol included an initial CT (140 Kv, 80 mA, 2 slices helical, 0.5 seconds per rotation, pitch 6:1, slice thickness 5 mm), followed by FDG-PET acquisition in 2-dimensional mode for 4 minutes per field of view.

Image Analysis

An experienced head and neck radiologist with 27 years’ experience in imaging the head and neck and 2 otolaryngologists with 5 and 15 years’ experience in the field of rhinology reviewed all images retrospectively by consensus. Interrater reliability was determined using $\kappa$ statistics. Weighted $\kappa$ values were used to assess interrater agreement. The results of the weighted $\kappa$ values were interpreted as follows: 0.00 to 0.20, slight; 0.21 to 0.40, fair; 0.41 to 0.60, moderate; 0.61 to 0.80, good; and 0.81 to 1.00, excellent agreement.

Images were assessed for tumor volume, homogeneity, ADC value, degree of enhancement, adjacent bone destruction, Waldeyer’s ring involvement, retropharyngeal and cervical lymph node (LN) metastasis, and PET/CT SUV max. Tumor volume was measured by region-of-interest (ROI) measurement in the PACS (picture archiving communications system) program. It was calculated by multiplying the axial cross-sectional area by the interval of the slice (mm) and the number of every slice showing mass (Figure 1). Tumor homogeneity was classified as homogeneous or heterogeneous on CT and MR images, respectively. If tumor density or signal density was within 10% median values on 90% of voxels within the tumor, the lesion was considered homogeneous (Figure 2). The ADC values were measured in the ADC map images by placing ROIs over the tumors and mean ADC values were tabulated (Figure 3).

Statistical Analysis

Before starting our study, we performed power analysis using G*Power software (Franz Faul, Universitat Kiel, Germany) and calculated that we would need a total sample size of 26 to achieve 80% confidence and $\alpha = .05$. Tumor volume and PET/CT SUV max were analyzed by independent $t$ test (SPSS version 18.0; SPSS, Inc, an IBM Company, Chicago, Illinois). Tumor homogeneity, degree of enhancement, adjacent bone destruction, Waldeyer’s ring involvement, and retropharyngeal and cervical LN metastasis were analyzed by $\chi^2$ test (SPSS version 18.0). ADC value was analyzed by the Mann-Whitney $U$ test (SPSS version 18.0). Data are presented as mean and 95% confidence interval (CI). A value of $P < .05$ was considered to be significant.

Results

The weighted $\kappa$ values were more than 0.90 at all parameters. Therefore, the interrater agreement between sinonasal NHL and SCC was excellent at all parameters irrespective of the CT, MR, and PET/CT images.

Tumor Volume

NHL ranged in volume from 0.45 to 11.54 $\times 10^4$ mm$^3$ (mean, 2.45; 95% CI, 1.338-3.878) and SCC ranged from

\[ \text{Figure 1. Measurement of tumor volume. Tumor volume is measured by region-of-interest measurement (A) and calculated by multiplying the axial cross-sectional area by the interval of the slice (mm) and the number of slices showing mass (B).} \]
Figure 2. Evaluation of tumor homogeneity. The non-Hodgkin’s lymphoma is considered homogeneous (A, C) and the squamous cell carcinoma is considered heterogeneous (B, D). (A, B) Axial T2-weighted magnetic resonance (MR) images. (C, D) Axial gadolinium-enhanced T1-weighted MR images.

Figure 3. Measurement of apparent diffusion coefficient (ADC) values. The mass reveals hyperintense signal intensity on the diffusion-weighted image (A) and hypointense signal intensity on the ADC map image (B). The ADC value is $0.640 \times 10^{-3}$ mm$^2$/s.

Figure 4. Evaluation of degree of enhancement. Axial gadolinium-enhanced T1-weighted magnetic resonance images of primary sinonasal lymphoma show high (A), intermediate (B), and low degree of enhancement.
There was a significant difference in tumor volume between NHL and SCC ($P < .001$) (Table 2).

### Tumor Homogeneity

On CT images, 24 of 34 (70.5%) NHLs showed homogeneity and 18 of 38 (47.4%) SCCs showed homogeneity. Tumor homogeneity was shown in 21 of 25 (84.0%), 17 of 25 (68.0%), and 17 of 25 (68.0%) NHLs and 21 of 28 (75.0%), 7 of 28 (25.0%), and 8 of 28 (28.6%) SCCs on T1WI, T2WI, and postcontrast MR images, respectively. NHL had a higher tumor homogeneity than SCC on T2WI and postcontrast MR images ($P = .005$ and $P = .012$, respectively) (Table 2).

### ADC Values

The ADC values ranged from 0.09 to $1.69 \times 10^{-3}$ mm$^2$/s (mean, 0.59; 95% CI, 0.460-0.783) in NHL and from 0.62 to $1.77 \times 10^{-3}$ mm$^2$/s (mean, 0.97; 95% CI, 0.887-1.066) in SCC. The ADC values were significantly lower in NHL than in SCC ($P < .001$) (Table 2).

### Degree of Enhancement

Most NHLs and SCCs showed a high degree of enhancement. Both NHL and SCC had the smallest number of low degree of enhancement. There was no significant difference in the degree of enhancement between NHL and SCC ($P = .991$) (Table 2).
Adjacent Bone Destruction

The destruction of the sinus wall or bony structure adjacent to the tumor was shown in 13 of 34 (38.2%) NHLs and 32 of 39 (84.2%) SCCs. Destructive growth pattern was significantly more frequent among SCCs than among NHLs (P < .001) (Table 2).

Waldeyer’s Ring Involvement and Retropharyngeal and Cervical LN Metastasis

Waldeyer’s ring involvement was seen in 5 of 39 (12.8%) NHLs and 1 of 39 (2.6%) SCCs. However, Waldeyer’s ring involvement did not reach statistical significance between NHL and SCC (P = .206). Although NHL showed high retropharyngeal and cervical LN metastasis, there was no significant difference (P = .438 and P = .454, respectively) (Table 2).

PET/CT SUV Max

The PET/CT SUV max ranged from 2.0 to 36.4 (mean, 13.40; 95% CI, 10.578-16.396) in NHL and from 3.9 to 41.5 (mean, 15.05; 95% CI, 11.582-18.749) in SCC. There was no significant difference in PET/CT SUV max between NHL and SCC (P = .478) (Table 2).

Discussion

The diagnosis of primary sinonasal malignancies is difficult because these lesions develop in a confined anatomical space and grow silently. Initially, they may present nonspecific symptoms such as chronic rhinorrhea and nasal obstruction that are more common in chronic rhinosinusitis. SCC is the most frequent malignant tumor in the sinonasal cavity, whereas NHL is the second most frequent. Nevertheless, NHL of this region is not easily distinguished from SCC, especially because NHL often appears in extranodal localizations. Primary sinonasal NHL has been more common in Asia than in the Western populations. B-cell lymphoma tends to involve the paranasal sinuses and predominates in the Western populations, but NK T-cell lymphoma is the most common to involve the nasal cavity, with a predilection for Asian and South American populations. In this study, NK T-cell lymphoma was more common than diffuse large B-cell lymphoma.

In general, NHL of the sinonasal cavity has been reported as large bulky masses with remodeling or erosion of the adjacent bone, although lytic destruction can be seen, especially with the nasal NK T-cell type. In contrast, SCC shows prominent bone destruction in the adjacent sinus wall. Previous studies reported that intratumoral necrosis is more frequently observed with SCC than NHL of the sinonasal cavity. Although the definite distinction between NHL and SCC is very difficult without histopathologic examination, the tumors in the paranasal sinuses may not be easily accessible to a biopsy, and it is possible that the biopsy results may still not provide definite information to the clinician. In such cases, characteristic imaging features can be helpful in the differential diagnosis of sinonasal tumors. To our knowledge, this is the first study to identify the imaging features of CT, MR, and PET/CT that differentiate NHL from SCC that originates from nasal cavity and paranasal sinuses.

In this study, NHL had a larger tumor volume than SCC, and NHL showed higher tumor homogeneity than SCC on both CT and MR images, especially T2WI and postcontrast MR images. NHL showed homogenous tumors with moderate signal intensity on both T1WI and T2WI, but SCC was more heterogeneous due to intratumoral necrosis and hemorrhage with the same signal intensity as NHL on both T1WI and T2WI. Furthermore, the ADC values of NHLs were significantly lower than those of SCCs. Because ADC values on diffusion-weighted imaging have been reported to correlate strongly with tumor cellularity, these findings suggest that tumor cellularity was significantly greater in NHL than in SCC. However, destructive tumor growth to the adjacent sinus wall was more frequently observed with SCC than with NHL. Therefore, a large bulky tumor with marked homogeneity, low ADC values, and remodeling or erosion of the adjacent bone may suggest NHL rather than SCC.

This study showed that all MR images in both NHL and SCC revealed intermediate hypointense signal intensity on T1WI and intermediate hyperintense signal intensity on T2WI with at least moderate enhancement on postcontrast T1WI. There was no significant difference in the signal intensity and degree of enhancement on T1WI, T2WI, and contrast-enhanced CT or MR images. Although Waldeyer’s ring and nodal involvement has been found at presentation or during the course of disease in half of all patients with extranodal NHL of the head and neck, the involvement of Waldeyer’s ring and LN metastasis were not common in patients with NHL and SCC in this study. The PET/CT SUV max showed no significant difference between NHL and SCC. Therefore, LN metastasis and PET/CT SUV max were of no significant value in differentiating NHL from SCC in the nasal cavity and paranasal sinuses.

Although we analyzed the image according to the clinical stage and histological subtypes, there was no significant difference in the imaging features. Additional prospective studies with a larger sample size would be helpful to determine their contribution to the change in CT, MR, and PET/CT imaging features.

Conclusion

Although it is difficult to distinguish sinonasal NHL from SCC solely based on clinical features, CT and MR imaging can assist with the differentiation between these 2 entities. CT and MR images of sinonasal masses showing a bulky lesion, marked homogeneity, and low ADC values without adjacent bone destruction are more suggestive of sinonasal NHL than SCC.

Author Contributions
Seek-Hyun Kim, drafting the work and revising it, analysis and interpretation of data, final approval of the version to be published, agreement to be accountable for all aspects of the work;
Sue-Jean Mun, drafting the work and revising it, analysis and interpretation of data, final approval of the version to be published, agreement to be accountable for all aspects of the work; Hak-Jin Kim, conception and design, analysis and interpretation of data, drafting the work and revising it, final approval of the version to be published, agreement to be accountable for all aspects of the work; Seon Lin Kim, acquisition of data, analysis and interpretation of data, drafting the work and revising it, final approval of the version to be published, agreement to be accountable for all aspects of the work; Sung-Dong Kim, acquisition of data, analysis and interpretation of data, drafting the work and revising it, final approval of the version to be published, agreement to be accountable for all aspects of the work; Kyu-Sup Cho, conception and design, analysis and interpretation of data, revising the article, final approval, accountability for the work.

Disclosures
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