

RESEARCH ARTICLE

Imaging Anatomy of Waldeyer's Ring and PET/CT and MRI Findings of Oropharyngeal Non-Hodgkin's Lymphoma

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Abstract

Background: This study was conducted to analyze positron emission tomography (PET) / computed tomography (CT) and magnetic resonance imaging (MRI) performance with oropharyngeal non-Hodgkin's lymphoma (ONHL). **Materials and Methods:** The complete image data of 30 ONHL cases were analyzed, all patients were performed PET / CT and MRI examination before the treatment, with the time interval of these two inspections not exceeding 14 days. The distribution, morphology, MRI signal characteristics, enhancement feature, standardized uptake value (SUV) max value and lymph node metastasis way of the lesions were analyzed. **Results:** Among the 30 cases, 23 cases were derived from the B-cell (76.7%), 5 cases were derived from the peripheral T cells (16.7%) and 2 cases were derived from the NK/T cells (6.7%). 19 cases exhibited the palatine tonsil involvement (63.3%). As for the lesion appearance, 10 cases appeared as mass, 8 cases were the diffused type and 12 cases were the mixed type. 25 cases exhibited the SUVmax value of PET / CT primary lesions as 11 or more (83.3%). MRI showed that all patients exhibited various degrees of parapharyngeal side-compressed narrowing, but MRI still exhibited the high-signal fat, and the oropharyngeal mucosa was intact. 25 cases were associated with the neck lymph node metastasis, among who 22 cases had no necrosis in the metastatic lymph nodes, while the rest 3 cases exhibited the central necrosis in the metastatic lymph nodes. **Conclusions:** PET / CT and MRI have important value in diagnosing and determining the lesion extent of ONHL.

Keywords: Oropharynx - lymphoma - anatomy - PET / CT - magnetic resonance imaging

Asian Pac J Cancer Prev, 16 (8), 3333-3338

Introduction

The oropharynx includes the palatine tonsil, tongue, soft palate and corresponding lateral and rear pharyngeal wall. The oropharynx was rich in the lymphoid tissues, thus it is also the common site of extranodal non-Hodgkin's lymphoma (NHL). And in recent years, the incidence was significantly increased (Etemad-Moghadam et al., 2010; Salplahtha et al., 2012). Because these parts were relatively deep, it would be difficult for the conventional clinical examination to determine the scope and depth of tumor violations, which was especially difficult towards the examination of submucosal lesions. Furthermore, the clinical manifestations of oropharyngeal NHL (ONHL) were complex, lack of characteristic, which often brought certain difficulties towards the accurate clinical diagnosis (Kato et al., 2013). Thus, the accurate diagnosis of NHL had important significance towards the selection of appropriate clinical treatment, as well as to the relative prognosis (Illidge et al., 2014; Yahalom, 2014).

The imaging diagnosis had important clinical values

towards the NHL diagnosis, but the NHL's imaging findings lacked the specificity (Ito et al., 2012; Loggers et al., 2014). The conventional computed tomography (CT) had certain advantages in displaying the tumor location, size and calcification situation of ONHL, but when used to determine whether the local lesion mucosa was destructed, as well as the violation degrees of surrounding tissues, its limitations were significant (Wolach et al., 2014). Magnetic resonance imaging (MRI) could perform the multi-dimensional imaging, which was conducive to display the location, scope and size of the lesion, and because of its high resolution towards the soft tissues, it could clearly exhibit whether the local lesion mucosa was destructed, as well as the signal characteristics of soft tissue mass. Meanwhile, it could easily exhibit the relationship between the lesion and the surrounding tissues, thus, currently, its application in the lymphoma diagnosis had drawn wide attention (De Paepe et al., 2013; Kato et al., 2013; Matsuzaki et al., 2012). Positron emission tomography (PET)/CT combined the dual advantages of PET functional imaging and CT

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anatomical imaging, improved the accuracy of disease detection, thus exhibiting the important clinical values towards the clinical diagnosis of lymphoma, staging accuracy, malignancy and treatment efficacy evaluation, tumor recurrence identification and prognosis evaluation (Chiewvit *et al.*, 2014; Kostakoglu and Cheson, 2014). Currently, the joint application of PET/CT and MRI into the diagnosis of ONHL was rarely reported, 30 ONHL cases, confirmed by the pathological and immunohistochemical evidences, were collected, and their PET/CT and MRI performance were retrospectively analyzed, aiming to improve the diagnosis and identification levels towards the oropharyngeal lymphomas.

Materials and Methods

Clinical data

A total of 30 ONHL cases, who had the complete clinical data and were confirmed by the clinical surgery and pathology, were collected in our hospital from January 2010 to December 2013, including 18 males and 12 females, aged 23 to 79 years old, with an average age as 43 years old. The main clinical manifestations were throat discomfort, obstruction feeling when swallowing, throat lumps or neck mass accidentally found, partial patients might exhibit the fever and systemic superficial lymphadenectasis. All patients were performed the PET/CT and enhanced MRI before the treatment, the time interval between the two examination methods was not more than 14 days (average 3 days). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Guangdong Academy of Medical Sciences. Written informed consent was obtained from all participants.

PET/CT examination

Siemens Sensation Biograph Somatom 16 PET/CT instrument was used. The positron drug, 18F-deoxy-2-fluoro-d-glucose (18F-FDG) was produced by the RDS111 cyclotron (Crystal Technology and Industries, Inc., USA) in the PET center of our hospital, and qualified by the rigorous tests of radiochemical purity, sterilization, non-pyrogen, non-endotoxin. The patient was placed in the supine position, and performed torso image scanning from the thigh to the upper nasopharynx, the CT scanning was performed firstly, followed by the PET scanning towards

the same range. The patient was generally scanned seven bed positions, with 2 min collection in each bed position. The patient was asked to empty the bladder before the scanning, and kept calm breathing during the scanning.

Based on the lesion situations showed by PET/CT, the enhanced CT scanning was performed towards the neck, the contrast enhancer was the non-ionic contrast agent (Niopam 370 mg I/ml), with the dose as 90 ml, and injected with the flow rate as 3~5 ml/s by a high-pressure syringe through the elbow vein. 18~24 s after the injection, the scanning was started. All data were transmitted to the Wizard workstation for the image fusion, which generated the coronal, sagittal and axial PET, CT and PET/CT fusion images, respectively.

MR examination

The MR imaging used the Sigma Infinity Echospeed Plus 1.5T superconductive MR scanner (GE, USA), and the data acquisition used the head and neck phased-array coil. Scanning method: cross section (from the skull base to the thoracic inlet) and coronal FSE-T2WI, TR 3500 ms, TE 104 ms, as well as the conventional chemical shift saturation method and fat suppression (Fat Sat); cross section SE-T1WI, TR 500 ms, TE 8.6 ms, the conventional enhancement used GD-DTPA, with the dose as 0.1 mmol/kg, injected through the anterior elbow vein, after injected the contrast agent, the cross-sectional and coronal SE T1WI were performed.

Image analysis

Observation contents: *i*) MRI: the anatomical locations, scopes, numbers, shapes, sizes of soft tissue mass, conventional signals and enhancement levels, situations of lymph node metastasis of the lesions; *ii*) PET/CT: the anatomical locations, scopes, numbers, glucose metabolism and radiological uptake situations of the lesions, as well as the maximum standardized uptake value (SUVmax).

Results

Pathological typing, involvement of anatomic sites and lymph node metastasis

According to the classification scheme of lymphomas (WHO, 2001), the situations of pathological types, involvements of anatomic sites and lymph node metastasis of the 30 ONHL cases were shown in Table 1. 23 cases

Table 1. The Pathological Typing and Involved Area in Oropharyngeal NHL

Pathological type	One anatomic site involvement of the inner ring	Multiple anatomic site involvements of the inner ring	Number of metastatic lymph nodes				
			Partition I	Partition II	Partition III	Partition IV	Partition V
B cell-origin lymphoma(n=23)	10	13	8	15	5	3	2
Peripheral T cell-origin lymphoma(n=5)	1	4	2	4	1	1	0
Extranodular NK/T-origin lymphoma(n=2)	0	2	1	3	2	0	0

were derived from the B cells (76.7%), 7 cases were derived from the peripheral T cells and extranodal NK/T cells (23.3%). A total of 11 cases showed the involvement in single anatomic site of inner ring, which meant that the lesion only involved one anatomic site of the inner ring of Waldeyer's ring, while regardless of the lymph node metastasis; 19 cases exhibited the involvements in multiple anatomic sites of inner ring, which meant that the lesion involved two or more anatomic sites of the inner ring of Waldeyer's ring, while regardless of the lymph node metastasis, among which the palatine tonsil involvement had the most cases, with a total of 20 cases, accounting for 67.7% (Figure 1).

The partition of cervical lymph node referred to the partition scheme proposed by Som, which was revised in 1999 and combined the clinical applications. The partition I had the lymph node maximum diameter ≥ 10 mm, while the rest partitions set the lymph node maximum diameter ≥ 8 mm as the diagnostic criteria of cervical lymph node metastasis. Among the 30 NHL cases, 25 cases had the cervical lymph node metastasis (83.3%),

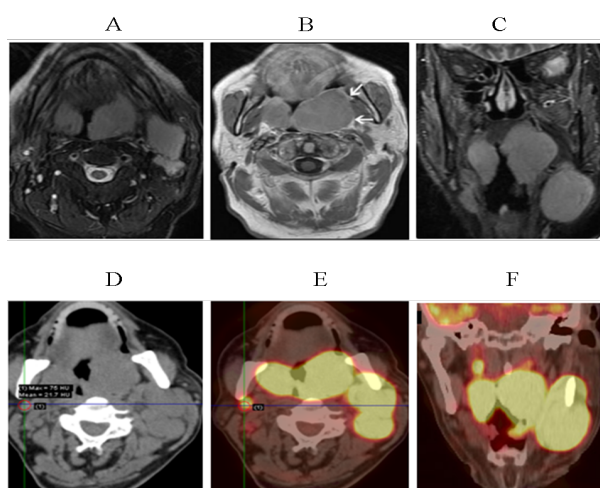


Figure 1. The NHL of tonsil: A. Axial T2WI; B. Axial T1WI; C. Coronal T2WI; D. CT imaging; E. Axial PET/CT; F. Coronal PET/CT. The homogeneous soft mass were showed in bilateral enlarged tonsils in MRI and PET/CT, the cases show the parapharyngeal space were narrowed, but the high signal of the fat was showed on MRI, coincidentally, mucosae of pharynx oralis was continuous. SUVmax of primary tumor was increased significantly in PET/CT

8 cases were of the unilateral involvement, and 17 cases were of the bilateral involvement, the specific metastasis partitions were shown in Table 1. Most enlarged lymph nodes showed the uniform densities and clear boundaries, after the enhancement, they exhibited the moderate enhancement (Figure 2). 3 cases showed the uneven densities, the enhanced images showed the low central density, while the edge was ring-shape enhanced.

MRI and PET/CT signs

In this study, 10 mass-type cases showed that the shadow of soft tissue mass exhibited the clear boundary and broke into the oropharyngeal cavity (Figure 1). The maximal mass was 43 mm $\times$ 36 mm, while the minimal one was about 11 mm $\times$ 10 mm. 8 diffuse-type cases showed that the irregular soft tissues were thickened, and the boundaries were poorly defined (Figure 2). The 12 mixed-type cases showed that the soft tissues were irregularly diffused on the pharyngeal wall, thickened, and concomitant with the shadows of palatine tonsil or tongue mass.

In the MRI examination, T1WI all showed the equal or slightly lower signal, while T2WI showed the equal or slightly higher signal (Figure 2), after the enhancement,

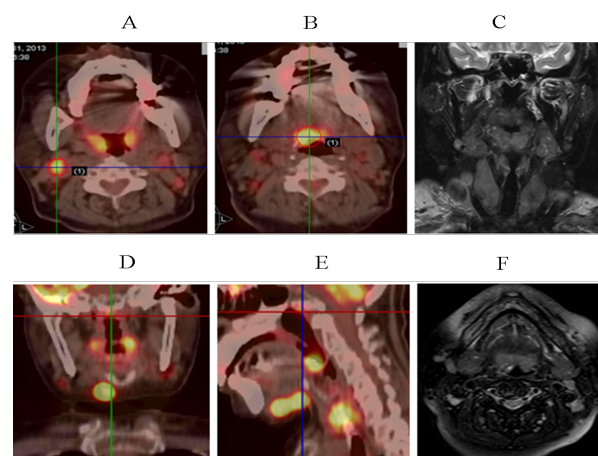


Figure 2. A, B. Axial PET/CT; C. Coronal T2WI; D. Coronal PET/CT; E. Sagittal PET/CT; F. Axial T2WI. The case of NHL with simultaneous invasion of the lingual root and bilateral tonsils which lymph nodes showed homogeneous density and SUVmax=16 in PET/CT.

Table 2. The Imaging Features of Oropharyngeal NHL

Examination method	n	Imaging features
MR	30	T2WI: equal or slightly higher signal, without necrotic cystic lesion
	27	The parapharyngeal space was compressed and narrowed, while the high signal of fat gap existed
	30	The oropharyngeal mucosa was intact, with no interruption
	44	Numbers of metastatic lymph nodes detected
PET/CT	26	The density was even in the conventional CT scanning, and homogeneously mildly enhanced after the enhancement
	25	SUVmax value ≥ 11
	5	Combined with extra- cervical organ involvement
	47	Numbers of metastatic lymph nodes detected

the images were homogeneously enhanced, none of the primary foci exhibited the necrotic cystic lesion (Figure 2); all the cases all exhibited the intact oropharyngeal mucosa, with no interruption (Figure 1); except that three cases exhibited the unclear observation towards the local fat gap because of the huge mass, MRI of the rest 27 cases could exhibit the pressure-caused narrowed fat gaps (Figure 1); in addition, MRI showed a total of 44 cervical lymph nodes (Table 2).

PET/CT examination exhibited that most cases showed the uniform while slightly lower density in the conventional CT scanning, with the CT values as 38~47HU, while homogeneously mildly enhanced after the enhancement, with the CT values as 57~63HU, the conventional CT scanning of other 4 cases showed that the densities were less uniform; the SUVmax values of 25 primary tumors were over 11, and those of cervical metastatic lymph nodes basically matched the primary foci; PET/CT also found two cases of peripheral T-cell lymphoma combined with the systemic lymphadenectasis and hepatosplenomegaly, three cases of diffused large B-cell NHL combined with jejunoileal or colonic lesions; PET/CT found 47 intumescent cervical lymph nodes, slightly higher than the number detected by MRI (Table 2).

Discussion

Imaging anatomy of Waldeyer's ring: The oropharyngeal lymphoid tissues were rich, besides the scattered lymph nodes, the intensive lymphoid tissues aggregated and formed the tonsil-like tissues, and formed the Waldeyer's ring. The Waldeyer's ring was also divided into the inner ring and the outer ring; the inner included the pharyngeal tonsil (adenoid) of nasopharynx, palatine tonsils on both sides of the oropharynx, tongue tonsil and lateral pharyngeal bands on both sides of the tongue root, lymphoid follicles on the posterior pharyngeal wall; the lymph of inner ring flew towards the neck lymph nodes, while the latter bonded with each other and self-formed a ring, namely the outer ring, mainly composed by the retropharyngeal lymph nodes, submandibular lymph nodes and submental lymph nodes. In the normal conditions, CT and MRI could exhibit several major lymphoid organs of the inner ring, such as the pharyngeal tonsil, palatine tonsil and tongue tonsil, especially MRI, because of its good soft tissue differentiation ability, it could clearly outline the contours of several important lymphoid organs. The oropharyngeal Waldeyer's ring had rich in lymphoid tissues, and was the most common incidence site of head and neck extranodal NHL, and NHL occurred in the palatine tonsil accounted for about half in the head and neck extranodal NHL, and most of them were B-cell origin (Carlos Bregni *et al.*, 2012). In this study, 21 cases were of the palatine tonsil involvement (67.7%), and among the 30 cases, 23 cases were of the B-cell origin (76.7%), consistent with the literature.

Scope and lymph node metastasis of pharyngeal lymphoma involvement: The ranges of oropharyngeal lymphomas were wide, which often involved two or more anatomical sites of the inner ring. In this study, 11 cases exhibited the involvement of single anatomical site of the

inner ring, while 19 cases exhibited the involvements of multiple anatomical sites of the inner ring (63.3%), which showed multiple centers changed in CT and MRI. It might be related to that the Waldeyer's ring had many lymphatic tubes, so it would be easy for the tumor to spread to the surroundings along the connected lymphatic tubes, thus the lesion involvements were wide. This differed from the oropharyngeal epithelial cell-derived squamous cell carcinoma, the malignant tumors of epithelial cells often originated in the focal center and invaded the surrounding tissues, but the maximum diameter of tumor would still be in the primary site. The anatomical site involvements of Waldeyer's inner ring of the patients in this study mostly lied in the palatine tonsil, with a total of 20 cases, and accounting for 67.7%, which might be associated with that the palatine tonsil was the largest lymphoid organ inside the Waldeyer's ring.

Because there were many lymphatic tubes connecting the inner and outer rings, and connected with 5 large cervical lymph nodes (submental, submandibular, anterior cervical, cervical superficial and cervical deep lymph node groups) through the lymphatic tubes (de Leval *et al.*, 2012). Therefore, it would be easy for the oropharyngeal lymphoma to metastasize towards each lymph node group through the lymphatic tubes, thus this metastasis mode might be the sequential metastasis way which was from the inner ring to the outer ring, then towards the cervical lymph node groups or the saltatory metastasis might occur. In this group, 25 cases exhibited the cervical lymph node metastasis (83.3%), among who 8 cases were of the unilateral involvement, and 17 cases were of the bilateral involvements, with most cases in the partition I, II and III, and it was considered to be related with that the anatomical location was close to the Waldeyer's ring. The densities of cervical lymph node metastatic lesions were relatively uniform, equal to or slightly higher than the muscle density, and the boundaries were regular. There were three cases in this study that showed the ring-shape enhancement, but the ring wall was relatively smooth, without wall nodules, the inner structures were uniform and low-density necrotic, the cervical lymph node biopsy showed the infiltration and necrosis of tumors.

MRI and PET/CT signs: The MRI signals of ONHL primary lesions of the patients in this study were uniform, with clear boundaries, and homogeneously enhanced after the enhancement. The conventional CT scanning showed that most cases exhibited the uniform densities, normally without the cystic degeneration, necrosis or calcification. Only four cases in this study showed that the palatine tonsil lesions exhibited less uniform densities in the conventional CT scanning, and non-homogeneously enhanced after the enhancement, the pathology confirmed that the partial cells were arranged unevenly and appeared the small focal necrosis and focal inflammatory cell infiltration.

The lymphoma would rarely have the deep violation, when the mass was big, the parapharyngeal space would be compressed and became narrower. Because the density of tonsil was equal to those of the surrounding muscles, thus it would sometimes be difficult to identify whether the mass invaded the peripheral soft tissues by CT. MRI had the soft tissue identification ability than CT, T2WI could

clearly show the existence of high signal fat that were shifted because of the parapharyngeal space compression. NHL on the palatine tonsil and tongue root had certain characteristic in the morphological appearance, which were all manifested as the para-round soft tissue mass shadow breaking into the oropharyngeal cavity, and the oropharynx mucosal was intact, the enhanced CT scan and MRI T2WI could display the intact mucosa, without damage and interruption. While the oropharyngeal epithelial cell-derived SqCa would easily involve into the parapharyngeal space and peripheral soft tissue structures, the edges would normally unclear, and the local oropharyngeal mucosal line would be interrupted, these could be used as the important identification signs towards these two types of diseases.

18F-FDG PET/CT was an imaging technology that combined the radionuclide scanning and CT scanning, and had been widely used in the diagnosis, staging and therapeutic evaluation of lymphomas currently (Hosokai et al., 2011; Zanoni et al., 2011; Qiu et al., 2013). Clinically, SUVmax >2.5 was often set as the criteria of malignant lesions. Certain studies had shown that (Juweid and Cheson, 2005) the higher the SUVmax value, the higher the degree of malignancy. Another study pointed out (Schöder et al., 2005), that the SUVmax value of aggressive lymphoma was higher than that of the indolent lymphoma, and it was found that when SUVmax >11, the likelihood of aggressive lymphoma was greater. In this study, the SUVmax values of 25 primary tumors were higher than 11, and the SUVmax value of cervical metastatic lymph node basically matched that of the primary tumor. Because the sample size in this group was less, no further analysis was performed towards the SUVmax value of lymphoma and its aggressiveness. In this study, PET/CT detected 47 cases of cervical lymph node metastasis, slightly higher than MR (n=44). The author thought that, 18F-FDG PET/CT reflected the molecular metabolism of tumor cells to some extent, and the detection rate towards the small lymph node was slightly better than MRI. NHL had the trend of multi-center origin or distant spread, and the most commonly involved organs were the abdominal organs (Saito et al., 2001). Therefore, the other obvious advantage of PET/CT towards the diagnosis and staging of ONHL was that it could perform the whole body imaging, so that it could make clear whether the distant organs were involved. In this study, PET/CT also found two cases of hepatosplenomegaly, and three cases were combined with the involvements of jejunum, ileum and colon. Therefore, towards the diagnosed ONHL patients, the gastrointestinal symptoms should be paid the particular attention to during the follow-up, and performed the PET/CT examination if necessary in order not to miss the lesions.

In short, a thorough understanding of imaging anatomy of Waldeyer's ring could help to understand the mechanism and peripheral violation method of ONHL, thus deepen the understanding towards their MRI and PET/CT signs. The pathogenetic location, shape, and peripheral tissue invasion of ONHL had certain anatomical and imaging features, the complementation of MRI and PET/CT had important values towards the diagnosis and lesion range identification of NHL.

Acknowledgements

This study was supported by grants from National Scientific Foundation of China (Grant 81171329) and Guangdong Science Foundation (Grant S2011010000790).

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