

•Original Article•

Computed tomography features of enlarged tonsils as a first symptom of non-Hodgkin's lymphoma

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[Abstract] Background and Objective: The tonsils are the most commonly involved primary part of non-Hodgkin's lymphoma (NHL) of the head and neck, which usually happens in the Waldeyer's ring. Our study describes the features of computed tomography on enlarged tonsils as a first symptom of NHL and the characteristics of the involved cervical lymph nodes. **Methods:** A retrospective review was performed on 130 patients with primary extranodal lymphomas of the head and neck over 16 years. Of them 22 untreated patients showed tonsil lesions as a first symptom. **Results:** Bilateral enlarged tonsils were involved in 13 patients, and unilateral lesions were in 9 patients. The lesions in 20 patients appeared mass-like, while 2 patients had diffuse thickening. There were 8 patients with simultaneous invasion of the nasopharynx, soft palate, and epiglottis. Of the 19 patients that underwent enhanced CT scans, 15 patients demonstrated slight homogeneous enhancement, 4 with crannied or a patch of low density, and 1 with ring-like enhancement. All 22 patients appeared to have cervical lymph nodes involvement. The upper groups of cervical lymph nodes were involved bilaterally in 13 patients, unilaterally in 9 patients. The middle groups were involved bilaterally in 7 patients, unilaterally in 10 patients. The lower groups were involved bilaterally in 2 patients, and unilaterally in 5 patients. After contrast administration, lymph nodes showed homogeneous density and slight enhancement in 11 patients, heterogeneous enhancement with necrosis and cystic changes in 6 patients, and ring-like enhancement in 2 patients. **Conclusions:** Bilateral involvement, homogeneous density, and slight enhancement are characteristics of tonsil involvement of non-Hodgkin's lymphoma. Bilateral upper groups of cervical lymph nodes are the most frequently involved lymph nodes, which are often shown with homogeneous density and slight enhancement.

Key words: Non-Hodgkin's lymphoma, tonsils, cervical lymph nodes, computed tomography

Lymphoma is a kind of systemic disease. Once pathologically diagnosed, patients should get a general physical check-up to provide a reference for clinical staging. After gastrointestinal lymphoma, lymphoma of the head and neck is the second most common site of extranodal lymphomas. About one-half of the lymphomas of the head and neck happen in the Waldeyer's ring, and almost all are non-Hodgkin's lymphoma^[1]. Approximately 40%–79% of primary non-Hodgkin's lymphomas that happen in the Waldeyer's ring invade the tonsils^[2]. Therefore, tonsils are the most common primary site, the nasopharynx is second, while the root of the tongue and the soft palate are less involved^[3]. Investigating the distribution and computed tomography (CT) features of the cervical lymph node involved tonsil has great significance in the diagnosis and the differential diagnosis.

Imaging studies of lymphomas involving tonsils have been less reported. Our study reviewed patients with lymphoma that involved the tonsils and analyzed the CT features of non-Hodgkin's lymphoma involving tonsils and the CT features of the involved cervical lymph nodes.

Materials and methods

Clinical features

A total of 130 patients with lymphoma involving the head and neck and initially diagnosed with CT imaging data, medical records, pathologic results, and follow-up records at the Cancer Hospital of Chinese Academy of Medical Sciences from January 1991 to December 2006 were reviewed. A total of 22 patients were initially diagnosed with primary lesions in the tonsils.

A total of 13 were men, 9 women, and their ages ranged from 15 to 70 years, with a median age of 50 years. Regarding pathologic classification, 14 patients had diffuse large B-cell type, 1 had diffuse B-cell type with small cleaved cell, 1 had diffuse B-cell of mixed small and large cell type, 1 had a

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mucosa-associated type, 1 had follicle center cell-derived (follicular II) type, 1 had NK/T-cell type, 1 had peripheral T-cell type, 1 had precursor T lymphoblastic lymphoma, and 1 was unclassified.

According to the 2002 American Joint Committee on Cancer (AJCC) staging system^[4], 3 patients had stage-IEA disease, 16 had stage-IIEA disease, 1 had stage-IIIEA disease, 1 had stage-IVA disease, and 1 had stage-IVBS disease. The primarily involved extra-nodal organ of stage I-II was the tonsils, and there were 6 patients with simultaneous invasion of the nasopharynx (including 2 patients with diffuse large B-cell lymphoma, 1 with T precursor T lymphoblastic lymphoma, 1 with NK/T-cell lymphoma, 1 with peripheral T-cell lymphoma, and 1 with follicle center cell-derived lymphoma), 2 with invasion in the soft palate, 1 with invasion in the epiglottis (all of three are diffuse large B-cell lymphoma). A total of 9 patients had simultaneously involved unilateral or bilateral cervical lymph nodes. One patient had stage-III simultaneous invasion of the mediastinal lymph nodes; two had stage-IV bone marrow invasion, and 1 had invasion in the spleen, bilateral kidney, mediastinal septum, and the unilateral hilar lymph nodes, and another had invasion in the bilateral axillary lymph nodes.

Regarding treatment, for patients with stage-I disease, 1 underwent radiotherapy alone, 2 underwent chemoradiotherapy. For patients with stage-II disease, 3 underwent radiotherapy alone, 10 underwent chemoradiotherapy, 3 underwent chemotherapy alone. One patients with stage-III disease underwent chemoradiotherapy. Two patients with stage-IV disease underwent chemotherapy alone.

Imaging methods

Our research applied spiral CT (PQ6000, GE Lightspeed ultra and GE Lightspeed pro) to perform the imaging, with slice thickness at 5 mm, slice interval at 5 mm, 120 kV, 240 mA, and all patients had axial scans of the head and neck and direct coronal scans, or coronal and sagittal reconstructions. For the 19 patients without iodine contraindications, 95 mL nonionic iodinated contrast medium (300 mgI/mL) was applied to perform the enhanced scans, and the intravenous injection was performed by a power injector with the flow rate of 3.0 mL/s, then delayed 45s to start the scan. Three patients underwent non-contrast scans. The scanning range of the head and neck was from the base of the skull to the supraclavicular area. Six patients simultaneously underwent chest CT scans; 9 underwent abdominal and pelvic CT scans for staging.

As for the sites of lymph node invasion, imaging-based nodal classification system was used to classify cervical lymph nodes^[5]. Additionally, supraclavicular, retropharyngeal, parotid, and other superficial cervical lymph nodes were analyzed.

The diagnostic criteria of the involved lymph nodes included the measurement of the shorter diameter of the lymph node. The diagnostic threshold was 1.0 cm, and lymph nodes greater than 1.0 cm were considered abnormal. Those smaller than 1.0 cm, if they happened in a cluster, or enlarged lymph nodes were observed in adjacent sites of lymph nodes, those lymph nodes were enlarged at the follow-up CT, or shrink or disappeared after chemotherapy, were also defined as involved lymph nodes.

Follow-up diagnosis

A total of 18 patients were followed for 2–31 months, with a mean of 12 months, receiving 33 head and neck CT scans, 19 neck and chest CT scans, 13 abdominal and pelvic CT scans, 5 chest and abdominal scans, and 1 chest, abdominal, and pelvic CT scan. Four patients were not followed at our hospital.

Results

Pathologic features of tonsils

Bilateral tonsils were involved in 13 patients, of whom 3 showed symmetric tonsillar enlargement (Figure 1), 10 showed asymmetric tonsillar enlargement, and 9 had unilateral lesions (Figure 2). The lesions appeared mass-like in 20 patients, of whom 17 were well-defined, and 3 were poorly defined. For these patients, the long diameter of the lesion was 1.3–4.8 cm, with a mean of 2.7 cm. Two patients showed diffuse thickening, and the thicknesses were 1.2 cm and 2.2 cm, respectively. There were 6 patients with simultaneous invasion in the nasopharynx (Figure 3), 2 with invasion in the soft palate (Figure 1), and 1 with invasion in the epiglottis. Of the 3 patients that underwent non-contrast scans, they showed homogeneous density similar to muscle (Figure 4). Of the 19 patients that underwent enhanced CT scan, 15 had homogeneously enhancement, with a density slightly higher than muscle (Figure 2); 4 had crannied or a patch of low density (Figure 5), and 1 had ring-like enhancement.

Characteristics of the involved cervical lymph nodes

Bilateral cervical lymph nodes were invaded in 13 patients, and unilateral cervical lymph nodes were invaded in 9 patients. Among them, the upper groups of the cervical lymph nodes were involved bilaterally in 13 patients, with a mean of 1.5 cm (range 0.7–3.4 cm); unilaterally in 9 patients, with a mean of 1.5 cm (range 1.0–4.2 cm). The middle groups were involved bilaterally in 7 patients, unilaterally in 10 patients, with a mean of 1.3 cm (range 0.6–4.8 cm). The lower groups were involved bilaterally in 2 patients, unilaterally in 5 patients, with a mean of 1.0–1.2 cm (range 0.8–2.5 cm). The submaxillary groups were involved bilaterally in 5 patients, and unilaterally in 3 patients with a mean of 1.3 cm (range 0.9–2.0 cm). The submental groups were involved in 2 patients, with the shorter diameter of 0.9–1.2 cm. The posterior cervical triangle groups were involved in 3 patients, with the shorter diameter of 0.5–1.1 cm. The parapharyngeal, retropharyngeal, and parotid lymph nodes were involved in 1 case, with shorter diameters of 0.8 cm and 1.0 cm.

Of the 19 patients that underwent enhanced CT scan, lymph nodes appeared as homogeneously enhanced in 11 patients, and the density was slightly higher than that of muscle. Heterogeneous enhancement with necrosis and cystic changes appeared in 6 patients (Figure 5). Ring-like enhancement appeared in 2 patients. Homogeneous density was apparent in the 3 patients that underwent non-contrast scan and was similar to muscle (Figure 4). Solitary lymph nodes were apparent in 17 patients, the unilateral amount was less than 5 on each scan slice, and one of them invaded the sternocleidomastoid muscle.

Parts of lymph nodes fused into a clump in 5 patients, and 4 of them invasion into the sternocleidomastoid muscle (Figure 2). Lymph nodes with shorter diameters of less than 1.0 cm were confirmed to have obviously shrink or disappeared after treatment on follow-up CT.

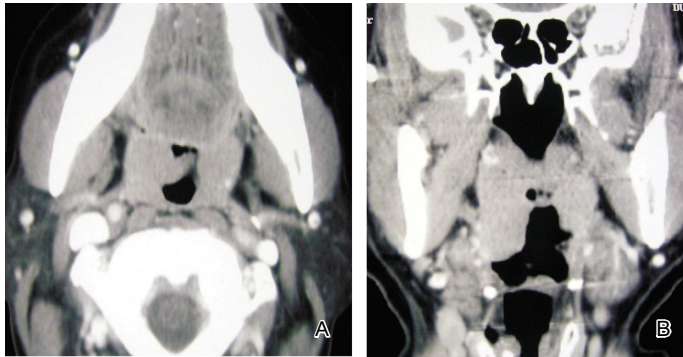


Figure 1 A 50-year-old woman with diffuse large B-cell lymphoma
Bilateral tonsil enlargement is enhanced slightly and homogeneously by contrast-enhanced axial CT scan (A) and coronal MPR (B).

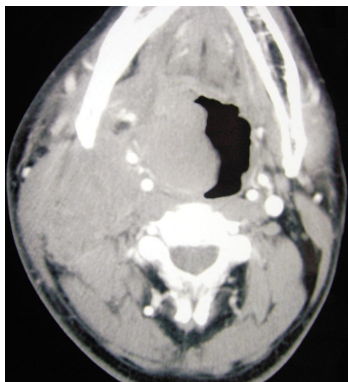


Figure 2 A 53-year-old man with lymphoma deriving from cells of the follicular center (Follicular grade II)
Right tonsil has enlargement, lobular contour, and slightly homogeneous enhancement, with confluent lymph node lesions enhanced heterogeneously in ipsilateral upper-middle neck, by contrast-enhanced CT scan.

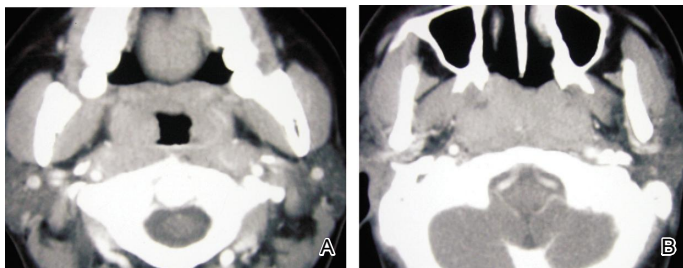


Figure 3 A 25-year-old woman with diffuse large B-cell lymphoma
Bilateral tonsils have symmetrical enlargement with slight and homogeneous enhancement by contrast-enhanced CT scan (A) and with involvement of the nasopharynx and parapharynx (B)

Results of follow-up

Of the 18 follow-up cases, lesions of the tonsils of 17 patients appeared to obviously shrink after treatment, and the invaded cervical lymph nodes also shrink or disappeared. For the 1 patient with stage-IVA diffuse B-cell derived (small cleaved cell) lymphoma complicated by chronic lymphocytic leukemia and invaded bilateral axillary lymph nodes, lesions on the tonsils showed no obvious change after treatment, the cervical lymph nodes were slightly enlarged, the bilateral axillary lymph nodes presented no obvious change. Of the 17 patients that showed improvement, 1 patient with stage-IVBS T precursor T lymphoblastic lymphoma complicated by invasion to the bone marrow, mediastinum, left hilar lymph nodes, left pleural fluid, spleen, and bilateral kidneys, the follow-up results showed that the mediastinal mass, left hilar lymph nodes, spleen, and bilateral kidneys shrink after treatment for 3 months. One patient with stage-IIA NK/T-cell lymphoma showed invasion in the groin, bilateral iliac vessel areas, and lymph nodes around the rectum and the spleen was also enlarged after 2 years. After treatment for 4 months, lesions of pelvic lymph nodes shrink and spleen showed no change. One patient with stage-IIIEA diffuse large B-cell lymphoma presented with an enlarged spleen, so it was

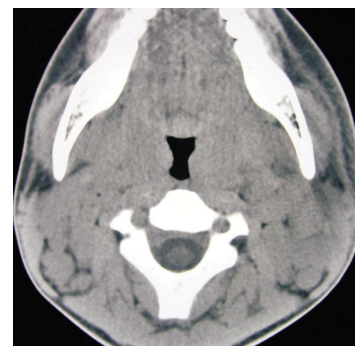


Figure 4 A 53-year-old woman with T-cell lymphoblastic lymphoma
Symmetrical enlargement of bilateral tonsils is shown with enlarged lymph nodes on bilateral sides of the neck. The density of both tonsils and nodes is homogeneous and similar to muscle by nonenhanced CT scan.

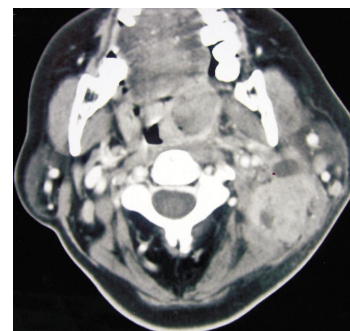


Figure 5 A 53-year-old woman with diffuse large B-cell lymphoma
Enlargement of the left tonsil is heterogeneously enhanced with low-density cystic changes by contrast-enhanced CT scan, having lymph node lesions with cystic necrosis and confluence changes in the left upper-middle neck and the submandibular region.

considered that the spleen was invaded, then the liver appeared to have probably invasive lesions and the splenic hilar lymph nodes were enlarged after 10 months.

Discussion

Large-cell lymphoma is the most common pathologic classification of non-Hodgkin's lymphoma occurring in the Waldeyer's ring. According to the 2001 classification of malignant lymphoma by the World Health Organization (WHO), about 66%–75% lymphomas occurring in the Waldeyer's ring are the diffuse large B-cell type^[9], while other pathologic classifications, such as small lymphocytic, follicular large-cell, lymphoblastic, Bunkitt's lymphoma, and peripheral T-cell types are rare. Diffuse large B-cell lymphomas were dominant in the patients included in our research (accounting for 64%), which was consistent with most reports. Pathologic classification is considered as an important prognostic factor. Different pathologic classifications lead to great differences in prognosis. Generally, T-cell derived NHL occurring in the Waldeyer's ring has a poorer prognosis than that of B-cell derived lesions^[6-7]. The International Lymphoma Study Group (ILSG) asserts that, compared with B-cell derived lesions at the same histologic grade, T-cell derived lesions present more multiple morphologic features and have more vascular infiltration and focal necrosis^[7]. The number of T-cell derived lesions was very small in our research and no such regularity was presented.

Stage of lymphoma directly affects the choice of treatment protocols. Radiotherapy alone or combined therapy are the primary treatment methods for stages I and II NHL occurring in the Waldeyer's ring^[8], and the target regions for radiotherapy in stages I and II NHL include the nasopharynx, the bilateral tonsils, the root of the tongue, the soft palate, the hard palate, all cervical lymph nodes, supraclavicular lymph nodes, and subclavicular lymph nodes. The nasal cavity is also included if it is invaded. For primary nasopharyngeal cavity lymphomas complicated by cranial nerve symptoms, the target regions should also include the area 2 cm above the base of the skull^[1]. Combined therapy could improve the 5-year tumor-free survival for patients with stage-II tonsillar NHL, and chemotherapy is the dominant treatment for patients with stage-III and -IV disease^[9-10]. However, results of long-term follow-up suggest that the therapeutic effects of lesions with different pathologic classifications are obviously different^[11-12]. Patients with low-grade malignant NHL occurring in the Waldeyer's ring can achieve a better therapeutic effect, however the majority of recurrent cases in patients with intermediate- or high-grade malignant lesions recur beyond the target region of radiotherapy. Recent studies demonstrate that the combined therapy of radiotherapy and chemotherapy is universally adopted in the treatment of patients with intermediate- and high-grade malignant lesions. Besides detecting the positions of the primary lesions, CT scans could also detect the deep structural invasion of the above positions, providing a basis for tumor stage, evaluation of therapeutic effect, and restaging in the follow-up after treatment.

Tumor size and the involved area of the primary tumor of

NHL primarily occurring in the Waldeyer's ring affect prognosis as reports. The prognosis would be different according to different lesion positions, and the rate of complete remission after treatment for patients with primary tonsil lesions is significantly higher than that of patients with primary lesions of the nasopharynx and the root of the tongue^[2,7]. For lesions at stages I and II, patients with bulky unilateral masses or enlarged bilateral cervical lymph nodes have a poorer prognosis than patients without these factors^[7]. Patients with bilateral tonsil invasion were dominant in our research (accounting for 59%), with a mean of 2.5 cm, and 2 patients presented with diffuse thickening of the oropharynx wall. In our research, 8 patients had unilateral stage-I and -II tonsil lesions and the lump was larger than 3 cm. Of them, 5 improved after treatment, with no recurrence after 3–20 months' follow-up (average 10 months), and 3 patients were lost to follow-up. Of the other 11 patients with stage-I and -II lesions, 10 improved after treatment, and no recurrence was found after 2–31 months (average follow-up 12 months), and 1 was lost to follow-up. There were 5 patients with simultaneously nasopharynx invaded, 2 with soft palate invaded, 1 with epiglottis invaded. All improved after treatment, and no recurrence was found after 2–31 months (average 12 months). Because of the small number of cases and limited follow-up time in our research, no previously reported regulations were found.

Most of the preliminarily diagnosed CT features of lymphoma invading the tonsils are bilateral invasion, and the homogeneous density and slightly enhanced mass-like presentations are characteristic. Of the 19 patients in our research, 15 (79%) had slightly homogeneous enhancement, and the density was slightly higher than that of muscle. Of the four patients (21%) with crannied or a patch of low density, 3 had diffuse large B-cell lymphoma, and 1 had the diffuse B-cell derived (mixed cellularity) type. The density of the lesions of the 3 patients that underwent non-contrast scans was homogeneous and similar to muscle. This is considerably different from squamous cell carcinoma of the tonsils, which presents as unilaterally enlarged tonsils and obvious heterogeneous enhancement with necrosis and most invasion to adjacent organs along the pharyngeal wall on the same side. The inflammatory enlargement of the tonsils could also bilaterally invade the tonsils, and the lesion primarily presents diffuse slight enlargement, and homogeneous enhancement, while some lesions present as abscesses with low density and edge enhancement, with edema of adjacent structures. This would be differentiated by the clinical history and remission after anti-biotics treatment.

Most patients with primary or initially diagnosed with non-Hodgkin's lymphoma of the tonsils have the involvement of the bilateral deep cervical lymph nodes, especially the upper groups of cervical lymph nodes. In our research the invasion rate of the upper groups is 100%, and bilateral invasion accounts for 59%. The invasion rate of the middle groups is 77%, and bilateral invasion accounts for 32%. The invasion rate of the lower groups is 32%, and bilateral invasion accounts for 9%. The invaded lymph nodes are either very large or in a cluster with a diameter less than 1 cm in each lymph node. The maximum

shorter diameter in our study was 4.8 cm, with a mean of 1.5 cm.

Among numerous CT-enhanced features of cervical lymph node lesions in malignant lymphomas the most common one is enlarged lymph node with homogeneous density similar to muscle. Contral low-density with peripheral enhancement are not specific in lymph node metastasis of squamous cell carcinoma, and it is found in 37.5% malignant lymphomas. Central soft tissue density with a very thin enhanced capsule is observed in 26.8% lymphomas, but they are rare in lymph node metastasis of squamous cell carcinoma, only accounting for 1.5%^[13]. Most enhancement patterns of invaded lymph nodes in our research were slightly homogeneous enhancement (58%), necrosis, and cystic changes were observed in 6 patients (31%), and ring-like edge enhancement was observed in 2 patients (11%). In all the invaded lymph nodes, 77% of patients had solitary lymph nodes, 23% showed partial lymph node fusion, and part of the fused lymph nodes were more likely to invade the sternocleidomastoid muscle. Except for 1 patient with stage IVA lesions complicated by chronic lymphocytic leukemia, all invaded lymph nodes shrunk after treatment, and no recurrence was found after 2–31 months.

For differential diagnosis, deep cervical lymph nodes, the posterior cervical triangle, and superficial lymph nodes are frequently involved in NHL, which is different from squamous cell carcinoma of the tonsils, since the latter frequently invades the submaxillary groups and the deep upper groups of cervical lymph nodes, and the metastatic lymph nodes of squamous cell carcinoma of the tonsils often present with heterogeneous enhancement, combined with necrosis in the center and are prone to invade the capsule and fuse into a clump^[14]. When tonsil inflammation is associated with inflamed or enlarged cervical lymph nodes, the bilateral upper cervical and submaxillary lymph nodes could also be enlarged, the lymph nodes could present as round or oval, with a few fused into a clump, and slightly homogeneous enhanced. It can be differentiated by the shrink or the disappearance after anti-biotics treatment.

In summary, the lesions of both the tonsils and invaded cervical lymph nodes in patients with primary or initially NHL of the tonsils have some CT features. Understanding these CT features is essential for the diagnosis and differential diagnosis of the lesions. Besides detecting tonsils lesions and providing help for diagnoses, the main purpose of CT scanning also includes

detecting the invasion of deep structures, such as the nasopharynx, the nasal cavity, accessory nasal cavities, the soft and hard palates, the epiglottis, and parapharyngeal tissue. The tumor stage can then be determined for selecting a proper treatment protocol.

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勘误说明

发表于《癌症》杂志 2010 第 3 期第 290 页的《肿瘤干细胞异染色质对人结直肠癌放射敏感性的影响及探究》一文的作者陈婷、张瑜、郭文浩、孟茂斌等 4 人的单位有误,应为四川大学华西医院肿瘤中心胸部肿瘤科。特此更正。

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