

## RESEARCH ARTICLE

# Primary Thyroid Lymphoma: Multi-Slice Computed Tomography Findings

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### Abstract

**Background:** The objective of this study was to investigate the MSCT characteristics of PTL in order to enhance the awareness of this uncommon entity among both clinicians and radiologists. **Materials and Methods:** The clinicopathological data and MSCT images of 27 patients with PTL were retrospectively reviewed. The MSCT appearances were classified into three types: type 1, solitary nodule surrounded by normal thyroid tissue; type 2, multiple nodules in the thyroid, and type 3, enlarged thyroid glands with a reduced attenuation with or without peripheral thin hyperattenuating thyroid tissue. **Results:** The patients were enrolled in the study with a mean age of 68 years (range, 51-86years) and compression symptoms or enlarged cervical lymph nodes at diagnosis. Hashimoto's thyroiditis was in 20 patients. All patients had non-Hodgkin lymphoma of B-cell in origin, including 22 cases of diffuse large B-cell lymphoma (DLBCL) and 5 of low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT). For MSCT appearance, type 1 pattern was observed in 2 patients, type 2 in 8, and seventeen type 3 in 17. The lesions occurred in more than one lobe with a mean maximal transverse diameter of 6.9 cm and an ill-defined margin. Most tumors showed a homogeneous attenuation equal to that of surrounding muscles before contrast and obvious enhancement after contrast. Cervical lymph node involvement and invasion of the trachea and (or) esophagus were mainly observed in patients with DLBCL. **Conclusions:** PTL should be clinically considered in elder patients presenting with a history of Hashimoto's thyroiditis and cervical lymphadenopathy. The MSCT characteristics of PTL includes a mass diffusely affecting more than one thyroid lobe, isointense to muscle and obvious enhancement before and after contrast. DLBCL, the most common histological subtype of PTL, is associated with a higher invasive tendency.

**Keywords:** Thyroid - neoplasms - X-ray - computed tomography - Lymphoma

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### Introduction

Primary thyroid lymphoma (PTL) is an uncommon neoplasm, accounting for <5% of all thyroid malignancies and approximately 2% of all malignant extranodal lymphomas (Pedersen et al., 1996; Stein et al., 2013). Preoperative diagnosis of PTL is important since the disease confined to the neck may be adequately and effectively controlled with radiation therapy and chemotherapy. Imaging plays an important role in accurate tumor staging and evaluating treatment response, which is crucial for treatment decisions.

Ultrasonography is the initial diagnostic modality used in the workup of thyroid diseases. Although nonspecific, there are certain characteristics that suggest PTL (Nam et al., 2012). Ultrasound imaging, however, depends on the skill of operators and is limited in depicting lymph nodes in the retropharyngeal space, mediastinum, and low level VI and depiction of tumor extension to adjacent structures (Loevner et al., 2008). Compared to ultrasound, multi-slice computed tomography (MSCT) is a superior method for

staging of thyroid neoplasms, because it can show the location and extent of the primary tumor and invasion of adjacent structures, including the esophagus and trachea (Soler et al., 2008). Due to PTL's low prevalence, the previous literatures specifically addressing MSCT findings of PTL are limited by the facts that they are case reports or small case series (Takashima et al., 1995; Kim et al., 2003). The distinct MSCT features of PTL have not been well described. Therefore, the objective of this study was to investigate the MSCT characteristics of PTL in a relatively larger case series in order to enhance the awareness of this uncommon entity among both clinicians and radiologists.

### Materials and Methods

#### Patients

This retrospective study was approved by the institutional review boards of our hospital, wherein the requirements for informed consent were waived. PTL is defined as a lymphoma that only involves the thyroid gland or the thyroid gland and adjacent cervical lymph

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nodes (Ansell et al., 1999). Twenty-seven patients with histology-confirmed PTL from our medical records between October 2007 and March 2014 were enrolled in this study. All patients underwent neck plain MSCT scanning and contrast MCT scanning was also performed in 15 patients at the same time in order to further find and evaluate the enlarged lymph node and invasion of adjacent structures after ultrasound examinations. Their clinical presentations and histological diagnosis were extracted from the medical records.

#### MSCT protocols

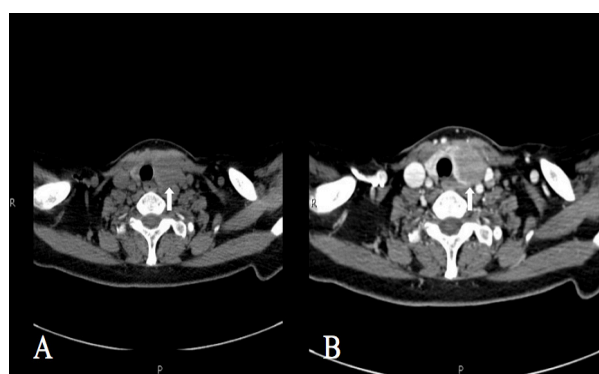
The thyroid function of all patients was checked before MSCT scan, which was never hyperthyroid. MSCT examinations were performed with a Light Speed VCT 64 Slice CT scanner (GE Healthcare, Milwaukee, WI, USA) through the neck. The images were acquired with 1.25 mm contiguous section thickness, a field of view of 260×260 mm, a peak voltage of 120 kVp, a tube current of 200 mA and a matrix of 512×512. For contrast-enhanced imaging, a bolus intravenous dose of 80-90 mL of nonionic iodinated contrast agent (Ultravist 300; Schering, Berlin, Germany) was administered using a power injector (Multilevel CT; Medrad, Pittsburgh, PA, USA), through an 18-gauge intravenous catheter placed in the antecubital vein at a rate of 2.5 ml/s. After the contrast material injection, 20 ml of normal saline was administered immediately. The scan was initiated 40-45 seconds after the onset of contrast injection. The axial images were reconstructed in both sagittal and coronal planes with a section thickness of 3 mm.

#### Image analysis

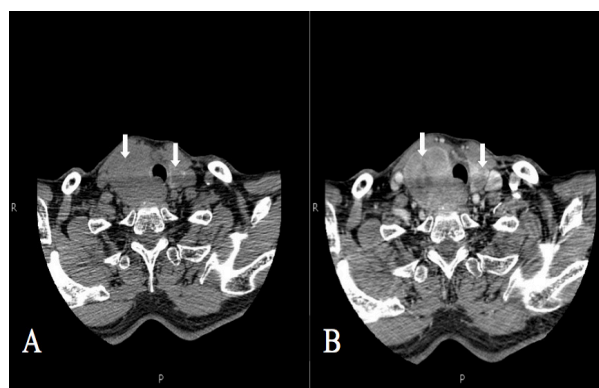
Two radiologists in head and neck imaging evaluated all images retrospectively for a consensus opinion. The pattern of the lesion was classified into three types based on MSCT findings (Kim et al., 2003): type 1, solitary nodule or mass surrounded by normal thyroid tissue; type 2, multiple nodules or masses in the thyroid; type 3, enlarged thyroid glands with a reduced attenuation with or without peripheral thin hyperattenuating thyroid tissue. The following morphologic features were carefully evaluated: (a) location; (b) maximal transverse diameter of the largest lesion; (c) margin (well defined, or ill defined); (d) calcification; (e) the attenuation of the lesion; (f) enhancement pattern of the tumor; and (g) the secondary manifestations (lymphadenopathy, invasion of surrounding structures and tracheal compression). The attenuation of the lesion was recorded in relation to that of the sternocleidomastoid muscle (hypoattenuation, hyperattenuation, or isoattenuation). Lymph nodes with a minimal axial diameter 10 mm were considered to be lymphomatous involvement (Sumi et al., 2001). Invasion of the cervical vessels, trachea or esophagus was diagnosed if the tumor was in contact with one half or more of the circumference of such organs and if the fat plane between them was lost (Takashima et al., 1990). The enhancement patterns of the tumors were divided into homogeneous and heterogeneous enhancements.

## Results

The patients enrolled in the present study included 11 male and 16 female with a mean age of 68 years (range, 51-86 years) at diagnosis. Sixteen patients were admitted to the hospital due to cervical or supraclavicular lymphadenopathy with firm, painless and fixed to surrounding tissues and eleven due to the rapidly enlarging thyroid volume. Most patients (24/27) clinically presented compression symptoms, including dysphagia, dyspnea, or hoarseness. The complaints were present for three months to one year. Tests for serum antithyroid antibodies were positive in all the patients. Pathological specimens were obtained by total thyroidectomy in 8 patients, lobectomy in 7 and core needle biopsy in 12. All patients had non-Hodgkin lymphoma of B-cell in origin. There were 22 cases of diffuse large B-cell lymphoma (DLBCL) and



**Figure 1. A 57-year-old Woman with Primary Thyroid lymphoma (low-grade B-cell Lymphoma Of Mucosa-Associated Lymphoid Tissue, MALT).** A, Axial plain MSCT scan demonstrates solitary nodule in the left lobe of the thyroid gland with a homogeneous attenuation equal to that of surrounding muscles (arrow). B, Contrast-enhanced axial MSCT image reveals the obvious enhancement of the lesion (arrow) with a partly ill-defined margin



**Figure 2. A 83-year-old Man with Primary Thyroid Lymphoma (Diffuse Large B-cell Lymphoma, DLBCL) and Hoarseness.** A, Axial plain MSCT image demonstrates the lesions in both lobes of the thyroid gland with a homogeneous attenuation equal to that of surrounding muscles (arrow). B, Contrast-enhanced axial MSCT image reveals the obvious heterogeneous enhancement of the lesions (arrow) with a partly ill-defined margin and the invasion of the esophagus



**Figure 3. A 77-year-old Woman with Primary Thyroid Lymphoma (Diffuse Large B-cell Lymphoma, DLBCL).** A, Axial plain MSCT image demonstrates the diffuse enlargement of the thyroid with a homogeneous attenuation equal to that of surrounding muscles (arrow) and the enlarged cervical lymph nodes (arrow head). B, Contrast-enhanced axial MSCT image reveals the obvious heterogeneous enhancement of the lesion (arrow) with a partly ill-defined margin

5 of low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT). Hashimoto's thyroiditis was in 20 patients.

For MSCT appearance, type 1 pattern was observed in 2 patients (Figure 1), eight type 2 in 8 (Figure 2), and type 3 in 17 (Figure 3). Type 1 pattern was only observed in patients with DLBCL. For type 2, 7 cases were DLBCLs, except one was MALT. For type 3, four cases were MALTs while thirteen were DLBCLs. The lesions occurred in left lobe of the thyroid in 4 cases and in right lobe in 3. More than one thyroid lobe were involved in 20. The mean maximal transverse diameter of the largest lesions was 6.9 cm (range, 1.7- 11.0 cm), with an ill-defined margin. On plain MSCT images, 22 patients had tumors of homogeneous attenuation equal to that of surrounding muscles. Five patients had both solid isoattenuation area and low attenuation area suggesting necrosis. No calcifications were seen in all the tumors. The plain CT value of the tumors ranged from 31.0 Hu to 52.0 Hu with a mean value of 42.8 Hu. After contrast enhancement in 15 patients, the CT value of the tumors ranged from 71.0 Hu to 136.0 Hu with a mean value of 92.4 Hu and 10 cases showed heterogeneous enhancement. Cervical lymph node involvement was observed in 12 cases of DLBCL and 3 of MALT. Invasion of the cervical vessel, trachea and esophagus was diagnosed in 11 cases including 8 of DLBCL, only invasion of the trachea in 3 cases with DLBCL, only invasion of the esophagus in 1 case with DLBCL, and only compression of the trachea in 9 cases including 7 of DLBCL.

## Discussion

PTL is an uncommon disease, occurring with a slight female predominance and involving individuals with ages between 50 and 80 years and an incidence peak in the sixth decade of life (Matsuzuka et al., 1993) and common clinical presentations (Aiken et al., 2008). In our

case series, the enrolled patients showed a slight female predominance, with a mean age of 68 years (range, 51-86 years) at diagnosis. Most patients presented various compression symptoms with cervical lymphadenopathy including dysphagia, hoarseness, choking or the rapid thyroid enlargement, which was in accordance with those previous literatures. In our case series, tests for serum antithyroid antibodies were positive in all the patients and Hashimoto's thyroiditis (chronic lymphocytic thyroiditis) was in 20 patients, which indicates that there is a strong relationship between Hashimoto's thyroiditis and PTL. It has been reported that the patients with Hashimoto's thyroiditis have an overall 67~80-fold higher risk of developing thyroid lymphoma compared to the general population (Arabi et al., 2011).

Previous study has reported that diffuse large B-cell lymphoma (DLBCL) and low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) are the common histological sub-types of thyroid lymphoma (representing 70% and 15~30% of all primary non-Hodgkin PTLs, respectively) (Sakorafas et al., 2010). The present study demonstrated that PTL was almost exclusively of the non-Hodgkin's, B-cell type, including DLBCL in 22 patients and MALT in 5.

Accurate diagnosis of PTL is very important in order to provide suitable therapy and improve prognosis. Therefore, it is clinically useful to define radiological characteristics of PTL that can help distinguish PTL from other thyroid masses. Ultrasound is the initial diagnostic modality used in the workup of thyroid diseases. Ultrasound is useful for the narrowing down the differential diagnosis of PTL from other thyroid diseases, especially those associated with rapid thyroid enlargement, such as anaplastic carcinoma, hemorrhage into an adenoma or cyst, and subacute thyroiditis (King et al., 1997; Takashima et al., 1997). However, as is well known, ultrasound has limitations in evaluating the extent of malignant thyroid diseases, and in particular involvement of adjacent organs and lymph nodes in the retropharyngeal space, mediastinum, and low level VI. Compared to ultrasound, MSCT may play a critical role in the detection of metastatic lymph nodes in occult areas that are poorly assessed with ultrasound and in the evaluation of tumor extension into adjacent structures, including the esophagus and trachea (Soler et al., 2008).

Similar to the study reported by Kim et al. (2003), the MSCT appearances of PTL in our study could be also divided into three types: solitary nodule (mass), multiple nodules (masses) and diffuse enlargement types. Diffuse enlargement was the most common type. The lesions tend to involve more than one thyroid lobe with a larger diameter and an ill-defined margin. It has been reported that PTL tends to be more homogeneous than thyroid carcinoma on MSCT image and calcifications or cystic degeneration/necrosis is rare, distinguishing it from goiter with this modality (Widder et al., 2004). Our study indicated that most lesions showed homogeneous attenuation equal to that of surrounding muscles on plain MSCT images. No calcifications were observed in all the tumors. However, low attenuating areas suggesting necrosis were observed in 5 patients on plain MSCT images and 10 cases showed heterogeneous enhancement in our series. The reason is

probably that DLBCL, which is considered to have the most aggressive clinical course (Widder et al., 2004), is the most common immunophenotype and accounts for 81.5% of all cases in our series.

Previous research reported that PTL had a strong tendency to compress normal remnant thyroid and the surrounding structure without invasion (Kim et al., 2003). However, cervical lymph node involvement was observed in 12 of DLBCL and 3 of MALT in our series. Invasion of the cervical vessel, trachea and esophagus was diagnosed in 11 cases including 8 of DLBCL, only invasion of the trachea in 3 cases with DLBCL, only invasion of the esophagus in 1 case with DLBCL, and only compression of the trachea in 9 cases including 7 of DLBCL. The differences between our results and previous reports could depend on the time of imaging, the number of the sample and the proportion of DLBCL. It has been well known that DLBCL has the most aggressive clinical course; indeed, about 60% of these lymphomas are diagnosed at an advanced stage with disseminated disease, while MALT has usually a relatively benign biological behavior (Thieblemont et al., 2002; Widder et al., 2004). Our results also suggested that DLBCL could be differentiated from MALT because the former tends to have MSCT features suggestive of the highly aggressive nature of this tumor.

There are several limitations to the present study. First, the major limitation of our study is the retrospective study design. We do not have data on intraobserver and interobserver variability. Second, the number of patients with MALT in our study was too small to analyze and compare the relevant MSCT features to DLBCL. Further investigation with a larger number of patients of various subtypes of PTL is necessary. Last, we were unable to obtain both pre- and post-contrast MSCT images in all patients. Therefore, it was not possible to evaluate the degree of enhancement by calculating the difference in the mean attenuation values between pre- and post-contrast MSCT scans. However, we believe that our study adds to the existing knowledge about the clinical and imaging features of PTL.

In general, PTL should be considered in elder patients presenting with a history of Hashimoto's thyroiditis and cervical lymphadenopathy or a rapid thyroid enlargement. On MSCT scanning, PTL tends to appear as a mass diffusely affecting more than one thyroid lobe, iso-intense to muscle and obvious enhancement before and after contrast. DLBCL, the most common histological subtype of PTL, is associated with a higher invasive tendency.

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