Primary Thyroid Lymphoma: A Clinicopathologic Study of 9 Cases and Review of the Literature

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Abstract

Background: Primary thyroid lymphoma (PTL) is extremely rare, thus the dilemma of diagnosis and treatment persists and prognosis remain incompletely understood.

Materials and methods: The clinicopathological characteristics, treatment outcomes and prognoses of 9 consecutive primary thyroid lymphoma patients were analyzed retrospectively. Data such as age, gender, presence of Hashimoto's thyroiditis (HT), treatment protocol, pathologic results and survival status were evaluated. Stage was determined according to the Ann Arbor staging system.

Results: They were mostly females with female to male ratio of 1.25:1. The 9 patients ranged in age from 15 to 77 years, with a median age of 63 year. Most of them (7/9) were older than 40 year. A previous history of Hashimoto's thyroiditis (HT) was observed in 4 patients. All of the nine patients were non-Hodgkin lymphoma (NHL), eight patients were B cell NHL and one patient was T cell NHL. All patients were treated with surgical excision and most patients received 5-7 cycle of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) based chemotherapy post-operation only.

Conclusions: The majority of them had good prognosis. Except two lost cases, 85% (6/7) of patients had a survival period of more than 5 years.

Introduction

Although thyroid cancer is a very common endocrine tumor, thyroid lymphoma is relatively uncommon, especially for the primary thyroid lymphoma (PTL). PTL is an extremely rare entity which representing 5% of thyroid malignancies and roughly 2% of extra-nodal lymphomas [1–3]. Owing to its rarity, few literatures that investigated the diseases has been published, thus the dilemma of diagnosis and treatment persists and prognosis remain incompletely understood. Here we analyzed the clinicopathological characteristics, treatment outcomes and prognosis of 9 consecutive PTL patients and review the relevant literature.

Materials And Methods

A retrospective review of clinicopathological database during a period (2002–2012) discovered 9 patients with PTL at surgery department in Wenzhou Central Hospital. Data such as age, gender, presence of Hashimoto's thyroiditis (HT), treatment protocol, pathologic results and survival status were evaluated. Stage was determined according to the Ann Arbor staging system as follows: stage I, disease localized to the thyroid; stage II, disease localized to the thyroid and regional lymph node basins; stage III, disease involvement on both sides of the diaphragm; and stage IV, disseminated disease.

Results

Nine patients referred to Wenzhou Central hospital between 2002 and 2012 with PTL were included in this study. As showed in Table 1, five patients were females and four were males with female to male ratio of 1.25: 1. Their age ranged from 15 to 77 years with a median age of 63 year. Most of them (7/9) were older than 40 year. No patient had B symptoms, such as fever, night sweats, weight loss. And only two of them had compression symptoms, one was performed as local pain and dyspnea, the other was with difficulty in swallowing. A previous history of HT was observed in four patients. According to the Ann Arbor staging system, five patients were in stage I—two patients were in stage II—and the rest two patients were in stage III and IV respectively. Of all the patients, five presented with a multinodular goiter and four had a solitary thyroid nodule.

Table 1

NO.	AGE/SEX	CLINICAL PRESENTATION			SIZE	STAGE
		BS	CS	HT		
1	77/F	N	N	Y	multinodular goiter	IV
2	15/F	N	Y with pain	N	solitary nodule	I
3	42/M	N	N	Y	solitary nodule	I
4	36/F	N	N	N	solitary nodule	I
5	59/F	N	N	Y	multinodular goiter	II
6	76/M	N	N	N	solitary nodule	III
7	63/M	N	N	Y	multinodular goiter	I
8	76/M	N	N	N	multinodular goiter	I
9	73/F	N	Y	N	multinodular goiter	II
(BS: B symptom; CS: compression symptom; HT: Hashimoto's thyroiditis; N: no; Y: yes)						

Table 2

revealed the imaging features, including computed tomography features and ultrasound features and pathologic types of the patients. Seven patients underwent computed tomography (CT) examination, and the majority of them (6/7) showed signs of adjacent organ compression—more than half of them showed decreased thyroid parenchymal density. All patients accepted ultrasound examination. Most cases had hypoechoic area and two cases showed cystic mass. The vast majority of them had blood flow signal inside the masses. By pathology, all of the nine patients were non-Hodgkin lymphoma (NHL). Among them—eight patients were B cell NHL and one patient was T cell NHL. The eight cases of B cell lymphoma can be subdivided into 3 cases of diffuse large B cell lymphoma (DLBCL), 1 case of mucosa-associated lymphoid tissue lymphoma (MATL), 1 case of MALT with DLBCL differentiation and 3 cases that cannot be subdivided.

NO.	CT features	Ultrasound features	Pathologic types
1	N/A	nodule with microcalcification: plaque-like low-echo area	MALT
2	uniform density, indistinct boundary—trachea and esophagus compressed and displaced	Cystic adenoma with hemorrhage: Cystic mass, uneven echo	T cell type NHL
3	significant decrease in density, distinct boundary, trachea compressed	hypoechoic areas, distinct boundary, fibrous cord-like echo and nodular hyperecho inside, abundant blood flow signal	B cell type NHL
4	low density, unevenly strengthen, indistinct boundary—no smooth edge—trachea compressed	Mixed echoic mass: indistinct boundary, blood flow signal inside	DLBCL
5	significant decrease in density with multiple low-density shadow (indistinct boundary); trachea compressed—DR	uneven parenchymal echo; a cystic anechoic area, distinct boundary—blood flow signal inside	B cell type NHL
6	parenchyma decrease in density, no calcification—no low-density area	hypoechoic mass: irregular shape, distinct boundary—uneven echo	DLBCL
7	parenchyma decrease in density evenly, the right lobe extending down to the back of the sternum and Adjacent organs compressed	no smooth envelope, uneven echo with multiple hypoechoic areas (blood flow signal inside)	B cell type NHL
8	decrease in density, distinct boundary—uniform density—trachea compressed	hypoechoic area, distinct boundary, uneven echo, no blood flow signal inside	DLBCL
9	N/A	hypoechoic mass: distinct boundary, uneven echo	Mixed MALT and DLBCL
(CT: computed tomography; N/A: not available; MATL: mucosa-associated lymphoid tissue lymphoma; NHL: non-Hodgkin's lymphoma; DLBCL: diffuse large B cell lymphoma)			

All patients were treated with surgical excision prior to pathological confirmation and eight patients received 5–7 cycle of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) based

chemotherapy post-operation only, as show in Table 3. One patient was discharged automatically after surgery and one was lost to follow-up after five sessions of chemotherapy. Duration of follow-up was from 2 months to 170 months, One patient died of a stroke and one died of a recurrence of the disease, the other patients were still alive. Six patients survived more than five years .

Table 3

NO.	Chemotherapy regimens	Overall survival duration(months)	Outcome	Cause of death
1	CHOP*7	94	Alive	
2	CHOP*5	2	N/A	N/A
3	CHOP*3 + COEP*3	168	Alive	
4	CHOP*6	72	Alive	
5	R-CHOP*6	70	Alive	
6	CHOP*6	50	Death	Disease progression
7	N/A	N/A	N/A	N/A
8	CHOP*6	170	Death	Stroke
9	COEP*6	75	Alive	
(CHOP: cyclophosphamide, doxorubicin, vincristine and prednisolone; COEP: cyclophosphamide, vincristine, etoposide and prednisolone; N/A: not available)				

Discussion

Malignant lymphoma primarily arising in the thyroid gland,Primary thyroid lymphoma(PTL), is defined as a lymphomatous process involving the thyroid gland without contiguous spread or distant metastases at diagnosis [1]. It is a very rare disease and few literatures that investigated the diseases has been published. PTL is more prevalent in female patients than man with a reported predominance of 3–4: 1 [4,5]. In our study, this predominance was significantly reduced, which may be related to the insufficient number of patients we included. PTL always occurs in the age ranges from 40–80 years, predominantly in the seventh decade of life and few under the age of 40 [3,4]. It usually present as a rapidly growing anterior cervical mass, which tend to cause compression signs and symptoms such as neck pain, dysphagia, hoarseness, and dyspnea [6]. Thus prompt diagnosis and appropriate treatment is necessary for an excellent prognosis. B symptoms are uncommon—only 10–20% of patients have B symptoms at diagnosis [1,3,7]. In our study, no patients had B symptoms, in agreement with the literature. HT has been associated with an increased risk of thyroid lymphoma. In patients with HT—the risk of PTL is at least 60 times higher than in patients without thyroiditis [8]. Therefor PTL pathogenesis is probably related to

chronic inflammation that provides the lymphocytes in which lymphoma can develop or predisposes to the malignant transformation of the lymphocytes [4,9].

PTL can be divided into NHL and Hodgkin's lymphoma. most of them are of B cell origin, which mainly include mucosa-associated lymphoid tissue lymphoma (MALT) and diffuse large B cell lymphoma (DLBCL) [10]. Few of them are of T cells origin [11]. In our study eight cases were B cell lymphomas, only one case was T cell lymphomas. In addition, the eight cases of B cell lymphomas can be subdivided into three cases of DLBCL, one case of MATL, one case of mixed MATL and DLBCL, and three cases of non-subdivided B cell lymphoma.

The diagnosis of thyroid lymphoma depends on pathological results. How to obtain the appropriate tissue for the pathology? In the past, Open biopsy or surgery was the most common method for diagnosis. But it was gradually withdrawn from the diagnostic strategy, only for whom had local compressive and invasive symptoms [12], Instead, ultrasonography-guided fine-needle aspiration biopsy (FNA) is a widely accepted technique for the diagnosis of thyroid nodules now, due to its cost-effectiveness and safety. However, PTL can be difficult to diagnose with FNA alone. Core needle biopsy, though not considered a first-line method for the diagnosis of lymphomas, has been reported to have a higher diagnostic yield [13,14]. As a method for diagnostic confirmation, core needle biopsy would be an alternative with a high priority along with FNA. in our study, all patients were treated with surgical excision prior to pathological confirmation. because most of them had symptoms or imaging showed that the airway or esophagus were compressed.

Treatments included chemotherapy, with or without surgery, and radiotherapy, but no consensus has been reached. The main regimen for chemotherapy is chop, which including cyclophosphamide, doxorubicin, vincristine and prednisolone. Most patients in our research underwent surgery and chemotherapy. All of them had a relatively good prognosis. Except two lost cases, 85%(6/7) of patients had a survival period of more than 5 years which is consistent with the literature [15]. The optimal treatment modality for PTL remains yet to be defined. The benefits of surgical treatment in PTL still remain in debate.

Conclusions

Although the best treatment for primary thyroid lymphoma is still unknown, all the patients in this study were treated with the combination of surgery and chemotherapy, they obtained a good prognosis.

Abbreviations

PTL: primary thyroid lymphoma; HT: Hashimoto's thyroiditis; NHL: non-Hodgkin lymphoma; CT: computed tomography; CHOP: cyclophosphamide, doxorubicin, vincristine, prednisolone; MATL: mucosa-associated lymphoid tissue lymphoma; DLBCL: diffuse large B cell lymphoma; FNA: fine-needle aspiration biopsy; COEP: cyclophosphamide, vincristine, etoposide,

prednisolone

Declarations

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Authors' contributions

WWW performed literature review, drafted and revised manuscript. SWL and XCZ participated in the design of the study and revised the manuscript for intellectual content. LJP evaluated the histopathological features and contributed to the histopathological section of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Wenzhou Central Hospital, Wenzhou, Zhejiang, P.R.China. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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