TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2017) 47: 1322-1327
© TÜBİTAK
doi:10.3906/sag-1611-91

Eleven patients with primary thyroid lymphoma: a single center experience

Hasan BOSTANCI[1], Kürşat DİKMEN[1,*], Nalan AKYÜREK[2], Ahmet Çağrı BÜYÜKKASAP[1], Aydın YAVUZ[1], Mehmet Muhittin YALÇIN[3], Murat AKIN[1]

[1]Department of General Surgery, Faculty of Medicine, Gazi University, Ankara, Turkey
[2]Department of Pathology, Faculty of Medicine, Gazi University, Ankara, Turkey
[3]Department of Endocrinology, Faculty of Medicine, Gazi University, Ankara, Turkey

Received: 22.11.2016 • **Accepted/Published Online:** 23.02.2017 • **Final Version:** 13.11.2017

Background/aim: Primary thyroid lymphoma (PTL) is a very rare thyroid malignancy. It should be diagnosed and treated immediately and accurately. Our aim was to evaluate the diagnostic methods and treatment results for patients with PTL. **Materials and methods:** We retrospectively evaluated the records of 11 patients with PTL from 2009 to 2015, diagnosed at our institute. Age, sex, stage, histopathologic type, presence of Hashimoto's thyroiditis, diagnostic methods, treatment types, and recurrence were examined.

Results: Six patients were female, 5 were male, and the median age of the patients was 61 years (range: 15–76 years). All patients had a large palpable mass in the neck. Fine needle aspirate (FNA) biopsy was performed in all patients; however, it was useful only in the diagnosis of 7 patients. Excisional and surgical biopsy was performed in 4 patients. All patients had non-Hodgkin B-cell lymphoma, including 9 cases of diffuse large B-cell lymphoma (DLBCL), and 2 patients had mucosa-associated lymphoid tissue (MALT) lymphoma. Recurrence was observed in one patient. Median survival was 34 months.

Conclusions: The preferred option for the diagnosis of PTL should be FNA biopsy, and the treatment should be decided on according to whether the disease is limited to the thyroid gland or not, its histological type, and its stage.

Key words: Lymphoma, primary thyroid lymphoma, diagnostic methods, treatment

1. Introduction

Primary thyroid lymphoma (PTL) is quite a rare malignancy, constituting 1%–5% of all thyroid malignancies, and 2% of all extranodal lymphomas (1). It is seen more frequently in females with chronic Hashimoto's thyroiditis, with 3–4-fold higher incidence than in male patients. PTL incidence peaks in the mid-sixties; hence, half of PTL patients are between the age of 60 and 79 years (2,3).

The most frequent complaint is a large palpable swelling in the neck that resembles anaplastic thyroid cancers. Diagnosis must be performed rapidly due to differences in treatment. A large neck mass triggered by PTL also causes symptoms such as dysphagia, dyspnea, and hoarseness due to mass effect, which is typically associated with the disease. In addition to these symptoms, some patients may show B symptoms such as fever, night sweats, and weight loss of 10% and higher in the last 6 months.

Histopathologically, PTLs appear in the form of B-cell and T-cell type non-Hodgkin's lymphomas (4). B-cell non-Hodgkin lymphoma, which is the most frequent type of PTL, is classified as mucosa-associated lymphoid tissue (MALT) lymphoma, diffuse large B-cell lymphoma (DLCBL), and mixed type (5). In addition, it has histological subtypes that are less frequent such as follicular lymphoma, small lymphocytic lymphoma, Burkitt's lymphoma of the thyroid, primary thyroid mantle cell lymphoma, and primary thyroid T-cell lymphoma (6–10).

Fine needle aspirate (FNA) biopsy is frequently used to diagnose the disease, but is not always successful (11). Therefore, core needle biopsy or surgical biopsy is used in such cases (12,13). PTLs are typically sensitive to chemotherapy and radiotherapy and, hence, the role of surgery in treatment is restricted. The five-year survival rate of a PTL patient that is accurately diagnosed and treated is stated to be 90% (12). Therefore, accurate diagnosis and rapid targeted treatment are vital in these PTL cases. In this study, clinical and histopathological features of 11 patients with PTL were evaluated in terms of the means of preparative diagnosis and postoperative follow-up data.

* Correspondence: kursatdikmen@yahoo.com

2. Materials and methods

2.1. Inclusion criteria and collection of the demographic data

Eleven patients with PTL were evaluated retrospectively in our center between 2009 and 2015. During this time, we performed 1824 various thyroidectomy operations. Histopathological results of the 309 patients were malignant thyroid diseases, and for 11 of these patients the histopathological diagnosis was primary thyroid lymphoma. We included these 11 patients in our study. Age, sex, diagnostic modality, stage, histopathologic type, Hashimoto's thyroiditis existence, thyroid function tests, sedimentation values, ultrasonographic features of the mass, treatment protocols, recurrence, and overall survival status were evaluated. Hashimoto's thyroiditis was diagnosed when there was lymphocytic infiltration in the thyroid glands, according to the pathologic report, or the presence of antithyroglobulin or antimicrosomal antibody. FNA biopsy, core needle biopsy, and surgical biopsy were used for diagnosis. Ultrasonography (USG) findings were correlated with pathologic results. Patients who had systemic disease were excluded from the evaluation.

2.2. Histopathologic evaluation and staging of the patients

The diagnostic criteria of thyroid lymphoma and its subtypes are very well established, both histopathologically and immunohistochemically (14). B-cell type non-Hodgkin's lymphoma was classified into 3 subtypes, namely MALT lymphoma, DLBCL, and mixed type. Staging of the patients was performed according to the Ann Arbor staging system (15). According to this system, Stage I is regarded as disease localized to the thyroid, Stage II is characterized as disease localized to the thyroid and regional lymph node basins, Stage III is the disease involving both sides of the diaphragm, and Stage IV is regarded as disseminated disease.

2.3. Treatment

The treatment of thyroid lymphoma depended on histology, patient comorbidities, and performance status. Management included chemotherapy, radiotherapy, and a combination treatment of chemotherapy and radiotherapy. The most commonly used chemotherapy regimens were cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) and Rituximab with CHOP (R-CHOP).

2.4. Statistical evaluation

The evaluated parameters were computerized and evaluated with IBM SPSS 20.0 (IBM Co., Armonk, NY, USA). Descriptive statistics are presented as median, frequency, and percentage.

3. Results

3.1. Patient demographics

The median age of the 11 patients examined in this study was 61 years (range: 15–76 years). Six were female (54.5%), five were male (45.5%), and the female/male ratio was 1.2. The median age of females was 60 years (range: 36–76 years), and the median age of males was 54 years (range: 15–65 years). In our institute, the prevalence of PTL is about 3.5%. The mean follow-up period of the patients was 34 months (range: 19–70 months). Although all patients had a large palpable swelling in the neck, only five patients (45.5%) had symptoms of compression. One patient (9.1%) had type B symptoms, including fever, night sweats, and weight loss. Although FNA biopsy was performed in all patients, only 7 (63.6%) could be diagnosed as having PTL. Two patients (18.2%) were diagnosed by excisional biopsy, and 2 (18.2%) were diagnosed by surgical excision (Table 1). All patients were euthyroid.

3.2. Histopathologic evaluation and staging of the patients

Histopathologic evaluation revealed DLBCL [n = 9 (81.8%)], and two other patients had MALT lymphoma (18.2%). Five (45.5%) were at Stage IE, 4 (36.4%) were at IIE, 1 (9.1%) was at IIIE, and 1 (9.1%) was at IVE (Table 1).

3.3. Evaluation of research parameters

Ultrasonographic examination of the masses revealed that lesions were hypoechoic for 6 (54.5%) patients and isoechoic for 5 (45.5%) (Table 1).

Seven (63.6%) patients received only chemotherapy. On the other hand, four (36.4%) underwent both chemotherapy and radiotherapy. Average length follow-up of the patients was 34 (19–70) months. Only one patient (9.1%) with histologic subtype DLBCL had recurrence, observed after a 20-month follow-up period (Table 1).

The clinical and radiologic features of the patients are summarized in Table 2. Five (55.6%) of the nine patients with DLBCL were female and four (44.4%) were male. All patients had a large palpable swelling in the neck. Furthermore, three patients (33.3%) had dyspnea, one patient (11.1%) had dysphonia, and one patient (11.1%) had both dyspnea and dysphonia as associated symptoms. Three patients (33.3%) with DLBCL had a history of Hashimoto's thyroiditis.

Two patients (one female, 50%) with a histologic subtype of MALT lymphoma presented with cervical mass as the primary complaint. One female (50% of the patients) had Hashimoto's thyroiditis history. Biopsy was used for definitive diagnosis in both, and the stages of the disease in these patients were Stages IE and IIE, respectively. MALT lymphoma lesions appeared to be hypoechoic on the ultrasonographic examination. One patient (50%) received chemotherapy as the primary therapy. On the

Table 1. Summary of demographic, histopathologic, and diagnostic parameters of the patients.

	n (%)
Age (years)	54 (36–66)
Sex	
Female	6 (54.5)
Male	5 (45.5)
Symptom	
Sudden neck swelling	6 (54.5)
Dyspnea + sudden neck swelling	3 (27.3)
Dysphonia + sudden neck swelling	1 (9.1)
Dyspnea + dysphonia + neck swelling	1 (9.1)
Concomitant Hashimoto's thyroiditis	
No	7 (63.6)
Yes	4 (36.4)
Diagnostic method	
Surgical excision	2 (18.2)
Excisional biopsy	2 (18.2)
FNA	7 (63.6)
Histologic type	
DLCLL	9 (81.8)
MALT lymphoma	2 (18.2)
Stage	
IE	5 (45.5)
IIE	4 (36.3)
IIIE	1 (9.1)
IVE Low-grade malignancy Intermediate-grade malignancy High-grade malignancy	1 (9.1) 2 (18.2) 3 (27.3) 6 (54.5)
Ultrasonographic findings	
Hypoechoic	6 (54.5)
Isoechoic	5 (45.5)
Treatment	
Chemotherapy only	7 (63.6)
Chemotherapy + radiotherapy	4 (36.4)
Recurrence	
No	10 (90.9)
Yes	1 (9.1)
Follow-up period (months)	34 (19–70)

other hand, the other patient (50%) received a combination of chemotherapy and radiotherapy. During the median follow-up period, recurrence did not develop in these patients.

4. Discussion

PTL is a rare disease entity that is frequently seen in females with chronic Hashimoto's thyroiditis (16). PTL is seen to occur on average between the ages of 59 and 71 years (16). Its female/male ratio is 3–4/1, and it has been reported to appear 10 years earlier in men than in women (3,6,17). Females constituted 54.5% of all patients in our study, and female/male ratio was 6/5. This female dominance can be due to autoimmune thyroid diseases occurring more commonly in women. It is thought that there may be a link between PTL and Hashimoto's thyroiditis (lymphocytic thyroiditis). The risk for PTL is increased by 67%–80% in patients with Hashimoto's thyroiditis (18,19). Our study has indicated that Hashimoto's thyroiditis is commonly associated with PTL.

The most frequent symptoms are dyspnea and hoarseness, related to the large palpable mass in the neck leading to compression symptoms and/or infiltration of the surrounding neck tissues (16,20). In 10% of patients, type B symptoms can be seen such as fever, night sweat, and weight loss (21). Symptoms of hypothyroidism can be seen at a rate of 10%; however, most patients are reported to be euthyroid (22). In our study, the clinical symptoms of the patients were similar to those in the literature.

Ultrasonography is usually the first imaging modality performed of a thyroid mass. PTL generally appears as heterogeneous, intense hypoechoic areas, but these findings are not specific (23), since they overlap with anaplastic thyroid cancer. Furthermore, the diagnostic accuracy of imaging methods, such as computerized tomography, MR, and scintigraphy, is low. In this study, the radiologic findings were similar to other study results (24,25).

After imaging, the next diagnostic step accepted for most thyroid masses is FNA biopsy. Although the sensitivity of FNA biopsy for definitive diagnosis was low in previous years due to certain limitations, the value of FNA biopsy has increased in recent years, thanks to the advances in immunohistochemical and flow cytometric methods. However, an expert pathologist is needed for the diagnosis of PTL with FNA biopsy, and it is absolutely necessary to share with the pathologist that there may be a PTL, because the ability of FNA biopsy in differentiating between Hashimoto's thyroiditis and PTL is unreliable (25,26). Furthermore, differentiation between undifferentiated thyroid carcinomas and PTL cannot always be made by FNA biopsy, due to the existence of low-grade malignancy. In the study by Matzuka et al. involving 119 patients, it

Table 2. Clinical and radiologic characteristics of the patients according to the histologic subtype of the primary thyroid lymphomas.

	MALT lymphoma (n = 2)	DLCLL (n = 9)
	n (%)	n (%)
Sex		
Female	1 (50.0)	5 (55.6)
Male	1 (50.0)	4 (44.4)
Symptom		
Sudden neck swelling	2 (100)	4 (44.4)
Dyspnea + sudden neck swelling	0	3 (33.3)
Dysphonia + sudden neck swelling	0	1 (11.1)
Dyspnea + dysphonia + neck swelling	0	1 (11.1)
Hashimoto's thyroiditis		
No	1 (50.0)	3 (33.3)
Yes	1 (50.0)	6 (66.7)
Diagnostic method		
Surgical excision	0	2 (22.3)
Excisional biopsy	2 (100)	0
FNA	0	7 (77.7)
Stage		
IE	1 (50.0)	4 (44.4)
IIE	1 (50.0)	3 (33.3)
IIIE	0	1 (11.1)
IVE	0	1 (11.1)
Ultrasonographic findings		
Hypoechoic	2 (100)	4 (44.4)
Isoechoic	0	5 (55.6)
Treatment		
Chemotherapy only	1 (50.0)	6 (66.7)
Chemotherapy + radiotherapy	1 (50.0)	3 (33.3)
Recurrence		
No	2 (100)	8 (88.9)
Yes	0	1 (11.1)

was reported that the diagnoses of 78% of patients were confirmed with FNA biopsy (27). The study by Matzuka et al. reported intermediate and high-grade malignancy in 77% of the patients. In our study, only 7 cases (63.6%) were diagnosed by FNA biopsy alone. In the present study, 2 patients (18.2%) had low-grade malignancy, 3 patients (27.2%) had intermediate malignancy, and 6 patients (54.5%) had high-grade malignancy. Additionally, there were 3 patients who were assessed as suspicious for thyroid lymphoma with FNA biopsy. Large needle or excisional biopsy are recommended as other methods for diagnosis (22). The study by Sharma et al. suggested core needle biopsy as the first diagnostic step when thyroid lymphoma is suspected (23). However, we selected excisional biopsy, because it provides clearer histopathological information and shows the exact degree of malignancy. In addition, this would likely decrease the repeat biopsy interventions.

In the last three decades, the role of surgery in thyroid lymphomas has changed. While previously, surgery was thought to be the primary treatment, today the primary

treatments are chemotherapy and radiotherapy (28–30). Despite this regression of surgical treatment, 61% of patients with thyroid lymphoma are reported to have undergone surgery for various reasons between 1997 and 2005, according to the SEER database analysis (6). Due to providing quick decompression in MALT lymphoma, in patients with thyroid-localized diseases or life-threatening compression symptoms, surgical treatment is still performed today (3,9,31–34). In fact, according to the SEER database analysis, the long-term results of patients treated only with surgery or with surgery and radiotherapy are reported to be better than those treated only with chemotherapy (6). In our study, a thyroidectomy was performed in one patient, whose FNA biopsy diagnosis was reported as suspicious for anaplastic carcinoma.

Histopathologic type and stage are the most important factors that determine prognosis for PTL patients. DLBCL is more aggressive than MALT lymphoma, and according to other studies, the five-year disease survival rate is approximately 75% (3,9,32). MALT lymphoma is frequently restricted to the thyroid and is determined at an early stage (5). Disease-specific survival rate is 96% (3,6). The mixed type has a similar clinical course to DLBCL (12). Stage is one of the factors that affects PTL prognosis. Generally, as the stage progresses, the possibility of survival decreases. According to a population-based study, five-year survival rate is 86% at Stage IE, 81% at Stage IIE, and decreases to 64% at Stages IIIE and IVE (12). In this study, 9 patients (81.8%) are at Stages IE and IIE. Recurrence occurred in one patient (9.1%), who was at Stage IIIE.

Thyroid lymphomas are tumors that are responsive to radiotherapy and chemotherapy; these should be given prior consideration in primary treatment. If the tumor is localized to the thyroid gland, external beam radiation can be preferred for primary treatment. Response to radiotherapy is dramatic and enables quick shrinkage of the tumor. However, relapses have been reported in about 30% of patients, even if the disease was at Stage IE or IIE (29). For this reason, the dominant view is that even if it appears to be a localized disease, there is a need for combination chemotherapy regimens. Chemotherapy is used as a primary treatment in advanced diseases or in combination with radiotherapy in localized diseases. The combination chemotherapy regimen usually consists of CHOP and R-CHOP. Rituximab is a monoclonal antibody that selectively binds to the CD20 antigen found on the surface of pre-B and mature B lymphocytes (35). Meta-analysis of published reports on primary nodal lymphoma patients verifies the superiority of adding rituximab to combination chemotherapy (36). Several other monoclonal antibody drugs are entering clinical practice (e.g., obinutuzumab, ofatumumab, and ibritumomab) (37). In our study, 5 patients with DLBCL received R-CHOP chemotherapy regimen, and 1 received only CHOP regimen therapy. One patient with MALT lymphoma received R-CHOP chemotherapy regimen. Prospective randomized studies are still needed to determine the best method of diagnosis and treatment. However, the fact that it is a very rare disease and that the number of patients is limited makes it almost impossible for such studies to be conducted.

In conclusion, PTL is a disease with good prognosis after treatment, performed according to whether it is limited to the thyroid gland, low grade, Stage IE, or according to its histological type. PTL is very similar to anaplastic thyroid carcinomas in terms of symptoms. Therefore, rapid accurate diagnosis and initiation of prompt therapy are important. The FNA biopsy can be used initially; however, if pathologic diagnosis is suspicious and PTL diagnosis is supported by clinical features, other diagnostic tools can be used. Creating a standardized diagnosis protocol and effective treatment modality for PTL requires further studies with a larger number of patients.

References

1. Widder S, Pasieka JL. Primary thyroid lymphomas. Curr Treat Options Oncol 2004; 5: 307-313.
2. Cheng V, Brainard J, Nasr C. Co-occurrence of papillary thyroid carcinoma and primary lymphoma of the thyroid in a patient with long-standing Hashimoto's thyroiditis. Thyroid 2012; 22: 647-650.
3. Derringer GA, Thompson LD, Frommelt RA, Bijwaard KE, Heffess CS, Abbondanzo SL. Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. Am J Surg Pathol 2000; 24: 623-639.
4. Vigliar E, Caleo A, Vitale M, DiCrescenzo V, Garzi A, Zeppa P. Early cytological diagnosis of extranodal stage I, primary thyroid non-Hodgkin lymphoma in elderly patients. Report of two cases and review of the literature. BMC Surg 2013; 13: 49.
5. Chai YJ, Hong JH, Koodo H, Yu HW, Lee JH, Kwon H, Kim SJ, Choi JY, Lee KE. Clinicopathological characteristics and treatment outcomes of 38 cases of primary thyroid lymphoma: a multicenter study. Ann Surg Treat Res 2015; 89: 295-299.
6. Graff-Baker A, Roman SA, Thomas DC, Udelsman R, Sosa JA. Prognosis of primary thyroid lymphoma: demographic, clinical, and pathologic predictors of survival in 1,408 cases. Surgery 2009; 146: 1105-1115.
7. Guastafierro S, Falcone U, Celentano M, Ferrara MG, Sica A, Carbone A, Rossiello R. Primary mantle cell lymphoma of the thyroid. Leuk Res 2010; 34: 548-550.

8. Koida S, Tsukasaki K, Tsuchiya T, Harasawa H, Fukushima T, Yamada Y, Ohshima K, Kamihira S, Kikuchi S, Tomonage M. Primary T-cell lymphoma of the thyroid gland with chemokine receptors of Th1 phenotype complicating autoimmune thyroiditis. Haematologica 2007; 92: 37-40.
9. Thieblemont C, Mayer A, Dumontet C, Barbier Y, Callet-Bauchu E, Felman P, Berger F, Ducottet X, Martin C, Salles G et al. Primary thyroid lymphoma is a heterogeneous disease. J Clin Endocrinol Metab 2002; 87: 105-111.
10. Yang H, Li J, Shen T. Primary T-cell lymphoma of the thyroid: case report and review of the literature. Med Oncol 2008; 25: 462-466.
11. Yang L, Wang A, Zhang Y, Mu Y. 12 cases of primary thyroid lymphoma in China. J Endocrinol Invest 2015; 38: 739-744.
12. Alzouebi M, Goepel JR, Horsman JM, Hancock BW. Primary thyroid lymphoma: the 40 year experience of a UK lymphoma treatment centre. Int J Oncol 2012; 40: 2075-2080.
13. Matsuda M, Sone H, Koyama H, Ishiguro S. Fine-needle aspiration cytology of malignant lymphoma of the thyroid. Diagn Cytopathol 1987; 3: 244-249.
14. Walsh S, Lowery AJ, Evoy D, McDermott EW, Prichard R. Thyroid lymphoma: recent advances in diagnosis and optimal management strategies. Oncologist 2013; 18: 994-1003.
15. Carbone PP, Kaplan HS, Musshoff K, Smithers DW, Tubiana M. Report of the Committee on Hodgkin's disease staging classification. Cancer Res 1971; 31: 1860-1861.
16. Fujita A, Tomita N, Fujita H, Motohashi K, Hyo R, Yamasaki E, Hattori M, Fujisawa S, Kanamori H, Ogawa et al. Features of primary extranodal lymphoma in Kanagawa, a human T-cell leukemia virus type 1 nonendemic area in Japan. Med Oncol 2009; 26: 49-54.
17. Pedersen RK, Pedersen NT. Primary non-Hodgkin's lymphoma of the thyroid gland: a population based study. Histopathology 1996; 28: 25-32.
18. Holm LE, Blomgren H, Lowhagen T. Cancer risks in patients with chronic lymphocytic thyroiditis. N Engl J Med 1985; 312: 601-604.
19. Kato I, Tajima K, Suchi T, Aozasa K, Matsuzuka K, Kuma K, Tominaga S. Chronic thyroiditis as a risk factor of B-cell lymphoma in the thyroid gland. Jpn J Cancer Res 1985; 76: 1085-1090.
20. Stein SA, Wartofsky L. Primary thyroid lymphoma: a clinical review. J Clin Endocrinol Metab 2013; 98: 3131-3138.
21. Kumar R, Khosla D, Kumar N, Ghoshal S, Bera A, Das A, Sharma SC. Survival and failure outcomes in primary thyroid lymphomas: a single centre experience of combined modality approach. J Thyroid Res 2013; 2013: 269034.
22. Pasieka J. Hashimoto's disease and thyroid lymphoma: role of the surgeon. World J Surg 2000; 24: 966-970.
23. Sharma A, Jasim S, Reading CC, Ristow KM, Villasboas Bisneto JC, Habermann TM, Fatourechi V, Stan M. Clinical presentation and diagnostic challenges of thyroid lymphoma: a cohort study. Thyroid 2016; 26: 1061-1067.
24. Hoang JK, Lee WK, Lee M, Johnson D, Farrell S. US features of thyroid malignancy: pearls and pitfalls. Radiographics 2007; 27: 847-860.
25. Triantafillou E, Papadakis G, Tzaida O, Papazian M, Megalakaki A, Moustakas K, Keramidas I, Kaltzidou V, Tertipi A, Pappas A. Primary thyroid lymphoma: the two ends of the spectrum. J BUON 2015; 20: 1164-1168.
26. Mack LA, Pasieka JL. An evidence-based approach to the treatment of thyroid lymphoma. World J Surg 2007; 31: 978-986.
27. Matsuzuka F, Miyauchi A, Katayama S, Narabayashi I, Ikeda H, Kuma K, Suguwara M. Clinical aspects of primary thyroid lymphoma: diagnosis and treatment based on our experience of 119 cases. Thyroid 1993; 3: 93-99.
28. DiBiase SJ, Grigsby PW, Guo C, Lin HS, Wasserman TH. Outcome analysis for stage IE and IIE thyroid lymphoma. Am J Clin Oncol 2004; 27: 178-184.
29. Doria R, Jekel JF, Cooper DL. Thyroid lymphoma: the case for combined modality therapy. Cancer 1994; 73: 200-206.
30. Udelsman R, Chen H. The current management of thyroid cancer. Adv Surg 1999; 33: 1-27.
31. Pyke CM, Grant CS, Habermann TM, Kurtin PJ, van Heerden JA, Bergstralh EJ, Kunselman A, Hay ID. Non-Hodgkin's lymphoma of the thyroid: is more than biopsy necessary? World J Surg 1992; 16: 604-609.
32. Sippel RS, Gauger PG, Angelos P, Thompson NW, Mack E, Chen H. Palliative thyroidectomy for malignant lymphoma of the thyroid. Ann Surg Oncol 2002; 9: 907-911.
33. Skarsgard ED, Connors JM, Robins RE. A current analysis of primary lymphoma of the thyroid. Arch Surg 1999; 126: 1199-1204.
34. Wirtzfeld DA, Winston JS, Hicks WLJ, Loree TR. Clinical presentation and treatment of non-Hodgkin's lymphoma of the thyroid gland. Ann Surg Oncol 2001; 8: 338-341.
35. Keating GM. Rituximab: a review of its use in chronic lymphocytic leukaemia, low-grade or follicular lymphoma and diffuse large B-cell lymphoma. Drugs 2010; 70: 1445-1476.
36. Gao G, Liang X, Jiang J, Zhou X, Huang R, Chu Z, Zhan Q. A systematic review and meta-analysis of immunochemotherapy with rituximab for B-cell non-Hodgkin's lymphoma. Acta Oncologica 2010; 49: 3-12.
37. Stathis A, Ghielmini M. New agents for the treatment of lymphoma. Ann Oncol 2012; 23 Suppl 10: x92-x98.