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Case Report

Neck Lumps with Enlarged Lymph Nodes: Papillary Thyroid Cancer and Hodgkin Lymphoma

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Abstract

We describe a clinical common symptom, as the title suggest, growing rapidly neck lumps and multiple enlarged lymph nodes in a patient. The neck ultrasound and computed tomography revealed thyroid solid nodules with neck multiple enlarged lymph nodes. By cytopathology, right papillary thyroid cancer and left nodular goiter were diagnosed, lymphatic metastasis was considered, because some atypical cells were found. Which is your first consideration for it? We report a very rare case: synchronous papillary thyroid cancer and Hodgkin lymphoma that is a challenging case for clinical diagnosis before surgical pathology practice.

Keywords: Hodgkin Lymphoma; Lymphatic Metastasis; Neck Lumps; Neck Enlarged Lymph Nodes, Papillary Thyroid Cancer

Introduction

Papillary Thyroid Cancer (PTC) is a common malignant neck tumor with peak incidence in the female under 40 years of age. Papillary thyroid cancer grows slowly, but with a high ratio for lymphatic metastasis. The preoperative examination usually depends on images and cytopathology. Hodgkin Lymphoma (HL) usually occur at the male of 15-27 years old, supraclavicular or neck multiple indolent and progressive enlarged lymph nodes is the common clinical sign and followed by the typical symptoms of low-grade fever, night sweat, weight loss sometimes. However, papillary thyroid cancer with concomitant Hodgkin lymphoma is very rare. For treatment and prognosis, there is huge difference between single papillary thyroid cancer with lymphatic metastasis and papillary thyroid cancer with concomitant Hodgkin lymphoma, so we should consider the possibility of papillary thyroid cancer with concomitant lymphoma for the cases of neck lump with multiple enlarged lymph nodes, especially in the cases of no low-grade fever, night sweat or weight loss, even though papillary thyroid cancer with lymphatic metastasis was supported by images and cytopathology. So, it is necessary to report the challenging case, neck lumps and neck multiple enlarged lymph nodes: thyroid cancer with concomitant lymphoma, a snake in grass for clinical diagnosis.

Case Report

A 50-year-old male was admitted to our hospital, because of rapidly growing neck lumps for one month. And neck multiple enlarged lymph nodes could move in pace with swallowing, no percussion pain. There were no other remarkable abnormal physical examinations. Whole body Computed Tomography (CT) revealed low density shadows of bilateral thyroid with neck multiple enlarged lymph nodes (Figure 1A). Ultrasound hinted right thyroid solid nodule (TI-RADS 4A classification) and left cystic nodule (TI-RADS 2 classification), neck hypoechoic nodules were explored, the size of largest one was 37×21mm (Figure 1B,1C).

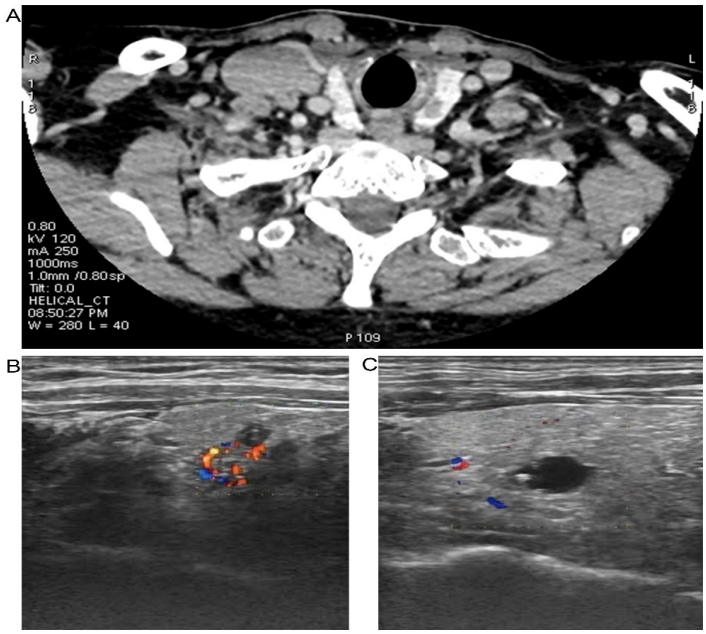

Figure 1: Imaging examinations: Computed tomography revealed **(A)** The low density shadows of bilateral thyroid and multiple enlarged lymph nodes. Neck Ultrasound revealed **(B)** Right thyroid solid nodule (TI-RADS 4A classification) and neck hypoechoic nodules, **(C)** Size of the largest one was 37×21mm.

The right papillary thyroid cancer (Figure 2A) and left nodular goiter were diagnosed by the cytopathology, and lymphatic metastasis was considered due to some atypical cells (Figure 2B) in lymphatic puncture liquid. Bilateral thyroidectomy and dissection of IV-VI areas of right neck were carried out subsequently. Macroscopically, an off-white nodule (0.3cm in diameter) of right thyroid was found. 6 lymph nodes were taken out, the biggest one was 4.5cm in diameter, it was surrounded by complete membrane, light yellow and weakly glistening, pliable in texture (Figure 2C). Microscopic diagnosis was right papillary thyroid cancer (Figure 2D), left nodular goiter and concomitant two sixths right neck lymphatic metastasis (Figure 2E). To our surprise, in the biggest lymph node, no cancer metastasis, but the lymphatic structure was destroyed, sporadic R-S cells (Figure 2F) were discovered in the background of asystematic hyperplastic lymphocytes, and the mitotic images (Figure 2G) were seized. The immunohistochemical examinations (Figure 2H,2I) were carried out for the biggest lymph node subsequently. CD30, PAX-5, Bob-1, EMA and Ki-67 were positive expression. CK5/6, CK-Pan, P40, P63, EBER, CD20, CD15, CD3, CD2, ALK, OCT-2 was negative expression.

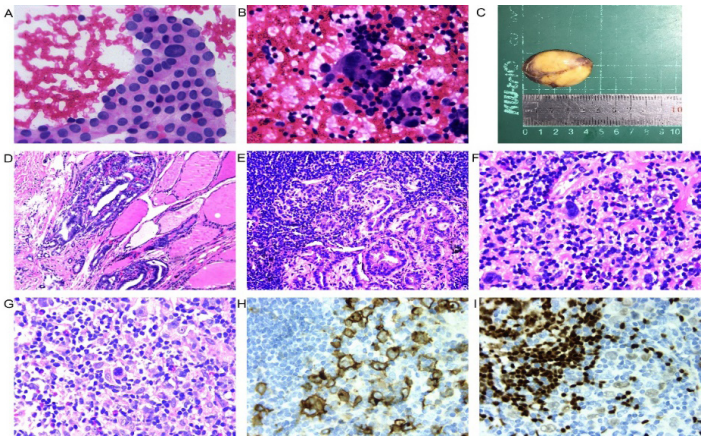

Figure 2: Pathological examinations: Cytopathology revealed **(A)** PTH of right thyroid, some atypical cells. **(B)** were found in puncture smear of the largest lymph node (HE, ×400). Macroscopically, **(C)** the largest lymph node was 4.5cm in diameter, light yellow, weakly glistening, whole membrane and pliable in texture. Microscopic diagnosis was **(D)** right papillary thyroid cancer and **(E)** lymphatic metastasis (HE, ×200). In the largest lymph node, normal lymphatic structure was destroyed, **(F)**sporadic R-S cells were found in the background of asystematic hyperplastic lymphocytes and **(G)** pathological mitotic images were seized (HE, ×400) and **(H)** CD30 and **(I)** PAX-5 were positive expression (IHC, ×400).

So, the final diagnosis was made as classical Hodgkin lymphoma (lymphocyte rich) and right papillary thyroid cancer with two sixths right neck lymphatic metastasis and left nodular goiter. The molecular pathological examination revealed that the genetic mutation of BRAF V600E was positive in papillary thyroid cancer tissues (Figure 3A). Subsequently, bone marrow aspiration revealed that lymphoma invaded bone marrow. The chemotherapy protocol of ABVD is executed fortnightly. 10 weeks later, PET-CT showed that the activity of lymphoma was inhibited, in 14 weeks, the patient is alive and in continuous chemotherapy.

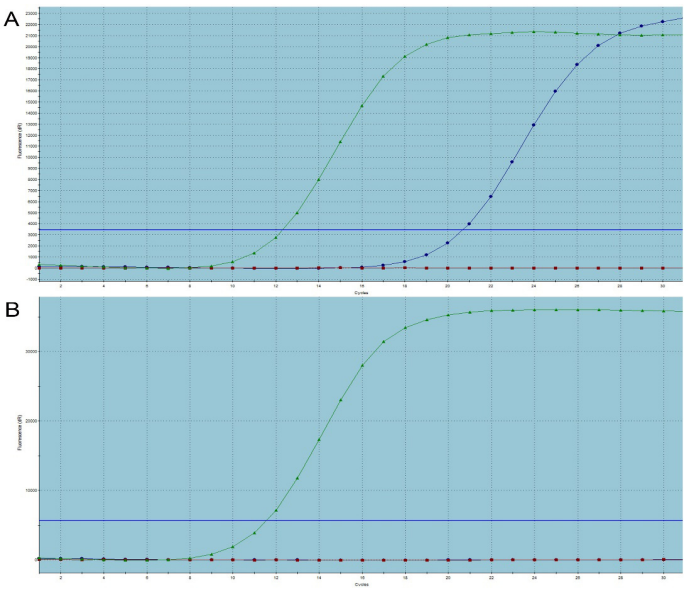

Figure 3: The ARMS fluorescent quantitation PCR revealed that there was genetic mutation of BRAF V600E in PTC tissues **(A)**, but not in CHL tissues **(B)** for this case (CT=19.08; green curve, positive QC; red curve, negative QC; blue curve, sample; QC, quality control).

Discussion

Neck lump with multiple enlarged lymph nodes, no clinical symptoms of low-grade fever, night sweat and weight loss, it is very difficult for us to consider the occurrence of synchronous thyroid cancer and lymphoma firstly, even if preoperative examinations of CT and ultrasound have been carried out. For cytopathology, it is not easy to make a precise differential diagnosis between neck lymphatic cancerometastasis and lymphoma in a patient of definite papillary thyroid cancer. There are three main reasons: Firstly, the obtaining of diseased tissue is limited. Secondly, some clinical manifestations should usually be explained by a kind of disease, it is also called monism of disease. Thirdly, the condition of synchronous PTC with lymphatic metastasis and lymphoma is very rare [1,2]. Neck lump with multiple enlarged lymph nodes is also a challenging clinical case for surgeons and radiologists because of the possibility of the neck malignancy with concomitant hematological malignancy as the case. For treatment and prognosis, there are huge different between single papillary thyroid cancer and PTC with concomitant lymphoma. So it is necessary to make a precise differential diagnosis. In order to prevent the inadequate diagnosis to occur again like this case, we summarized the differential diagnosis experience of common examinations (Table 1) to make a more accurate clinical decision for the cases of thyroid lump with multiple enlarged lymph nodes.

Examinations and Diagnosis	Clinical Signs and Symptoms	Neck Ultrasound	Whole Body CT
Consideration for thyroid cancer with lymphatic metastasis	Ipsilateral enlarged lymph nodes, no typical symptoms of lymphoma	Unilateral neck hypoechoic nodes with PBF and the highest RI, PI	Enlarged lymph nodes in ipsilateral neck with obvious intensification and necrosis
Consideration for thyroid cancer with concomitant lymphoma	Enlarged lymph nodes of many parts with typical symptoms of lymphoma	Bilateral neck hypoechoic nodes and inner reticulum with mixed type bloodstream and a higher RI, PI	Enlarged lymph nodes in many parts of body with a trend of fusion, uniformity, a few necrosis
RI, Resistance index (normal ＜0.7); PI, Pulsatility index (normal ＜1.5); PBF, Peripheral blood flow.			

Table 1: The differential diagnosis experience of common examinations.

The synchronous PTC and classical Hodgkin lymphoma is very rare, there is no any authoritative elucidation for the producing mechanisms. Maybe their occurrences are stimulated by some identical molecular incident. Genetic mutation of BRAF V600E usually hint poor prognosis for PTC, and the research of BRAF V600E is mature in colorectal cancer, thyroid cancer and melanoma, and BRAF mutation is very significant for proliferation, invasion and metastasis of these tumors. For hematological malignancy, Tiacci [3] reported the universal phenomena of mutation of BRAF in hairy-cell leukemia in 2011. Another study showed that BRAF play an important role in occurrence and development of peripheral T-cell lymphoma. We supposed that the genetic mutation of BRAF V600E is the identical molecular mechanism [4,5] of papillary thyroid cancer and classical Hodgkin lymphoma. If that is true, BRAF V600E will probably be a new therapeutic target for classical Hodgkin lymphoma and have potential applications in diagnosis and prognosis for classical Hodgkin lymphoma, so we used the ARMS fluorescent quantitation PCR skill to examine the genetic mutation of BRAF V600E in classical Hodgkin lymphoma tissues of the case, but the result was negative (Figure 3B).

We analyzed that PTC and CHL of the patient may be two kinds of different primary tumor. Or the mutation point was not V600E, but other sites of BRAF. So further study remains to be needed. Another theory is that thyroid disease is associated with an increased

ailing risk for hematological malignancy, which came from 6,386 subjects cross-sectional research [6]. In this case, lymphoid cells of neck lymph nodes were activated and proliferated abnormally due to the excessive immunologic mechanism to PTC, it's not impossible. Because we lack experience for synchronous papillary thyroid cancer and classical Hodgkin lymphoma, which may be in significant diagnostic and treatment predicament. Up to now, there was no any standardized approach to deal with this condition world widely, but most scholars approved of individualized joint radiotherapy and chemotherapy, and the five-year survival rate is more than 80 percent according to reports, [7,8] however, surgical treatment is not the first approach. In this way, not only is surgical risk reduced, but also oncological benefit is increased. In our case, not synchronous thyroid cancer and lymphoma, but thyroid cancer with lymphatic cancerometastasis was considered firstly, therefore, bilateral thyroidectomy and dissection of IV-VI areas of right neck were carried out. After operation, bone marrow aspiration revealed that lymphoma invaded bone marrow.

The chemotherapy protocol of ABVD (Epirubicin 70mg d1+Bleomycin 15mg d1+Vincristine 2mg d1+Dacarbazine 600mg d1) is executed fortnightly. 10 weeks later, PET-CT showed that enlarged neck lymph nodes shrank and the activity of lymphoma was inhibited, glycometabolism of bone marrow was normal. And remarkable toxic side effects did not appear. In 14 weeks, the patient is alive and in continuous chemotherapy.

Conclusion

In this case, the genetic mutation of BRAF V600E is not the identical molecular incident of PTC and HL. For the case of neck lump with multiple enlarged lymph nodes, CT and neck ultrasound reveal thyroid nodules with neck multiple enlarged lymph nodes, PTC with lymphatic metastasis is in the majority, but the possibility of synchronous thyroid cancer and lymphoma should not be ignored, only in this way can the most appropriate treatment be formulated for patients and get the best benefit. The cases of PTC with concomitant lymphoma are poorly reported and yet relevant molecular mechanisms and treatment remain to be explored.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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