

## Case Report

# Primary thyroid Burkitt lymphoma in a 15-year-old boy

Hong Wu<sup>1</sup>, Meng-Lan Huang<sup>1</sup>, Lu Liang<sup>2</sup>, Xing-Huan Liang<sup>2</sup>, Zi-Li Lv<sup>1</sup>

Departments of <sup>1</sup>Pathology, <sup>2</sup>Endocrinology, First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous Region, P. R. China

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**Abstract:** In children, primary thyroid Burkitt lymphoma (PTBL) is an extremely rare pathologic entity of thyroid malignant tumor. Here we describe a case of PTBL in a 15-year-old boy, who developed a rapidly enlarging neck mass that showed signs of compression. The color Doppler ultrasound revealed diffuse swelling of the thyroid gland, with a solid and irregular mass from the left to the isthmus, which was about  $8 \times 7 \times 5$  cm in size. Computed tomography showed Irregular masses were seen in the left thyroid with a range of about  $7.1 \times 5.4 \times 8.0$  cm, and a beaded slightly enlarged lymph node with a maximum of  $1.6 \times 0.8$  cm was discovered in the left neck. Postoperative pathologic examination also found the specific starry-sky phenomenon of Burkitt lymphoma. Moreover, immunohistochemistry also indicated that the related cellular immunophenotypic expression was also positive or negative. In particular, the proliferation rate by ki67 was almost 100% and C-MYC was also positive. After thyroidectomy, patient underwent four cycles of CHOP regimen chemotherapy. Unfortunately, the patient died as a result of the deterioration of his condition. This report provides an opportunity to review an uncommon type of PTBL in children.

**Keywords:** Thyroid, Burkitt lymphoma, immunohistochemistry, children

## Introduction

PTBL is an extremely rare pathological entity of thyroid malignant tumor. It is reported that the proportion of primary thyroid lymphoma (PTL) is only 2-4% in all thyroid neoplasms [1, 2] and 2% in extranodal lymphomas [3]. It comes mainly from B lymphocytes and usually shows a fast growing neck mass and symptoms of compression. Although this highly aggressive malignancy occurs in a low percentage of thyroid tumors, its frequency is increasing [4]. Therefore, we should gain more comprehension this rare pathologic entity of thyroid malignant neoplasm. According to the results of the literature review, only a few of PTBL have been reported in the English literature. Here, we report another case of PTBL in a 15-year-old boy, and review systematically the etiology, clinical features and diagnosis of this unusual tumor in children.

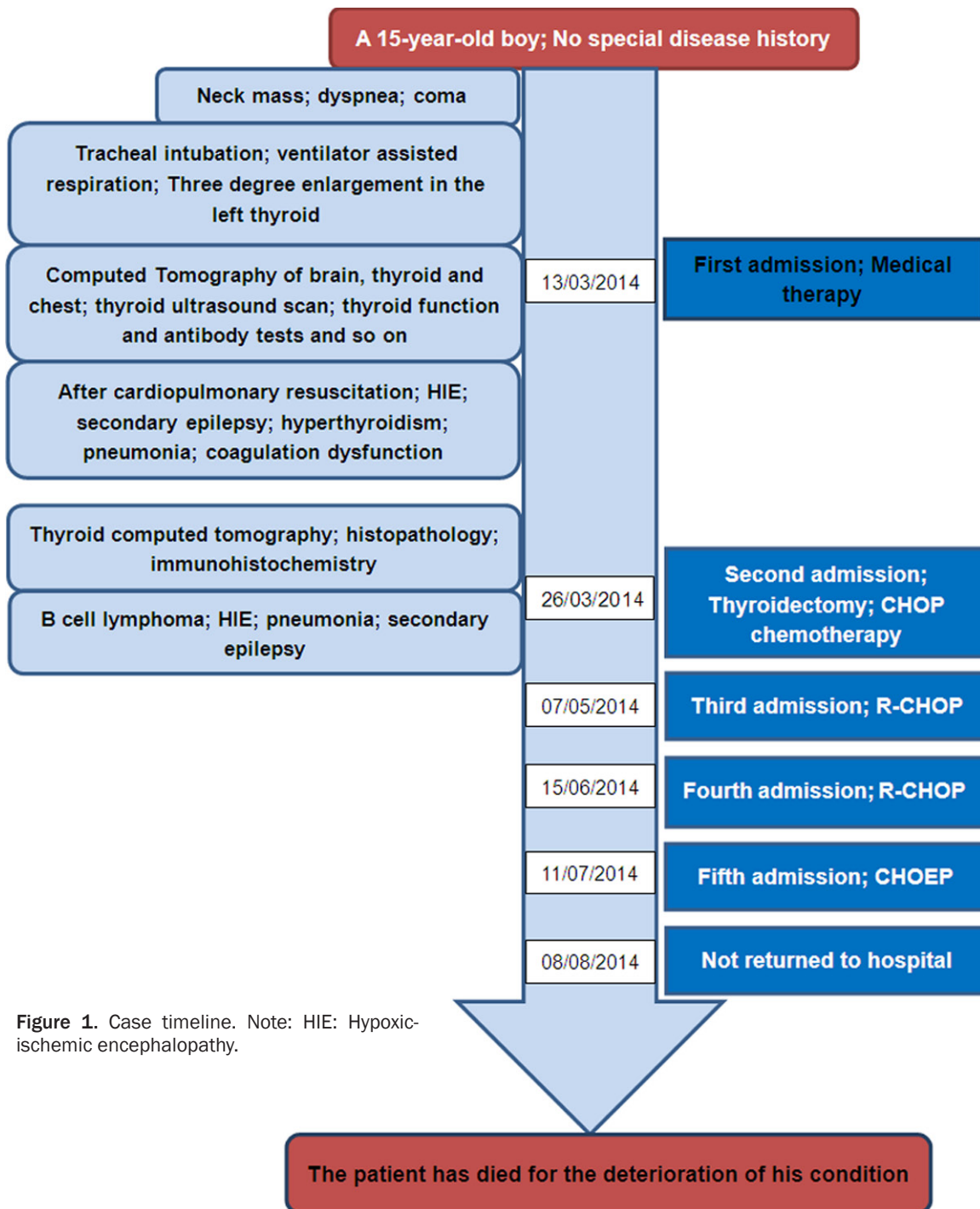
## Case presentation

On March 13, 2014, a 15-year-old boy was transferred to our hospital for the first time

(**Figure 1**). Six months ago, the boy presented with a cervical mass and the tumor was progressively enlarged without any other discomfort. Three months ago, the patient showed symptoms of eating more and becoming hungry, who was diagnosed as hyperthyroidism by local hospitals and was medically treated without any improvement. Yet, a week prior, the boy began to develop oppressive symptoms of dyspnea and dysphagia, so that he fell into a coma and was transferred to our hospital.

Thyroid color Doppler ultrasound indicated the thyroid gland had diffuse swelling, with a solid and irregular mass from the left to the isthmus, which was about  $8 \times 7 \times 5$  cm in size, and the diagnosis was thyroid carcinoma with lymph node metastasis. In addition, thyroid computed tomography and enhancement scan (**Figure 2**) showed the anterior part of the neck was protruded. Irregular masses were seen in the left lobe and isthmus of the thyroid, which were distinct from the surrounding tissues, and no abnormalities were on the other side of thyroid gland. The density inside the thyroid gland was not uniform and there were multiple flaky low

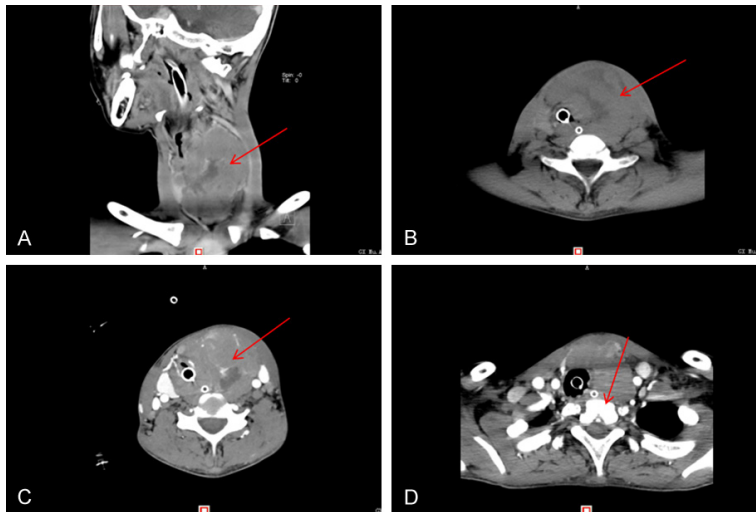
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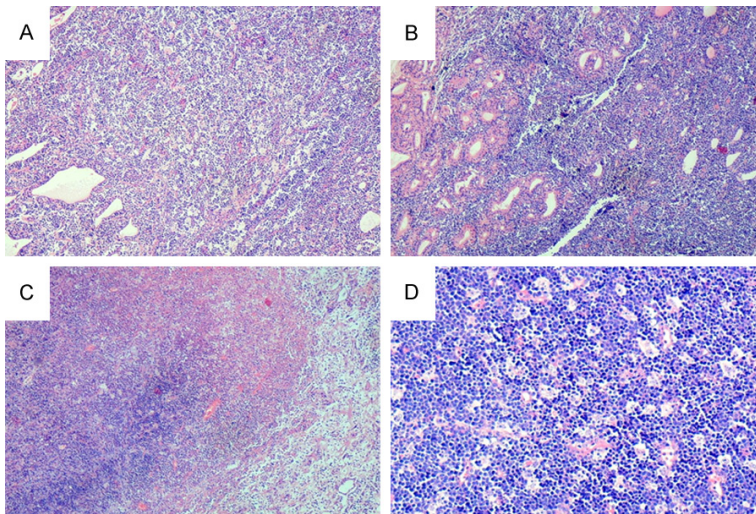
**Figure 1.** Case timeline. Note: HIE: Hypoxic-ischemic encephalopathy.

density areas with a range of about  $7.1 \times 5.4 \times 8.0$  cm, and the lower margin reached the level of the sternoclavicular joint. Enhancement scan revealed slight uneven enhancement. The trachea was displaced to the right and the lumen was narrow; the esophagus was also compressed. A beaded slightly enlarged lymph node with maximum dimensions of  $1.6 \times 0.8$  cm

was discovered in the left neck. Tracheal intubation was found in cervical trachea and intubation shadow was noticed in esophagus. The diagnosis was a tumor of the left thyroid, considering thyroid carcinoma with cervical lymph node metastasis. Besides, thyroid function test indicated hyperthyroidism and thyroid antibody detection was normal. Therefore, surgical



**Figure 2.** Computed tomography showed the anterior part of the neck was protruded (A) and Irregular masses were seen in the left thyroid (B). Enhancement scan revealed slight uneven enhancement (C). A beaded slightly enlarged lymph node with a maximum of  $1.6 \times 0.8$  cm was discovered in the left neck (D).



**Figure 3.** Histopathologic examination. A diffuse distribution of medium size cells was observed and these cells invaded the thyroid tissue (A: Hematoxylin & eosin staining,  $\times 100$ ) with residual thyroid tissue and large areas of necrosis (B and C: Hematoxylin & eosin staining,  $\times 100$ ). The starry sky phenomenon was noticed for the presence of multiple visible body macrophages (D: Hematoxylin & eosin staining,  $\times 1,000$ ).

resection based on clinical diagnosis of thyroid cancer was performed on April 18, 2014.

Gross pathologic examination showed that the size of thyroid tumor was about  $11.5 \times 6.5 \times 4$  cm, and necrosis could be seen. A diffuse distribution of medium sized cells was observed under the microscope, which invaded the thy-

roid tissue (**Figure 3A**). In addition, residual thyroid tissue and large areas of necrosis could also be found (**Figure 3B, 3C**). In particular, the starry sky phenomenon that characterizes Burkitt lymphoma was noted (**Figure 3D**).

Additionally, the immunohistochemical investigation was conducted. On the immunohistochemical study, TG presented residual thyroid tissue (**Figure 4A**). The tumor cells stained positive for CD20 (**Figure 4B**), PAX-5 (**Figure 4C**), BCL-6 (**Figure 4D**), CD10 (**Figure 4E**) and MUM-1 (**Figure 4F**) and negative for CD21 (**Figure 4G**), CD5 (**Figure 4H**), CD43 (**Figure 4I**), CD38 (**Figure 4J**) and TDT (**Figure 4K**). Moreover, the proliferation rate ki67 was almost 100% (**Figure 4L**). Furthermore, C-MYC was also positive (**Figure 4M**) and CYCLIND1 was negative (**Figure 4N**). Based on these pathological results, the diagnosis was Burkitt lymphoma of the thyroid.

After thyroidectomy, the patient received chemotherapy with CHOP regimen. However, after four cycles, the boy did not return to the hospital to continue chemotherapy, and there was no note of outpatient follow-up records. Therefore, we considered that the patient was in poor condition, with repeated infections. Finally, we learned that the patient had died as a result of the

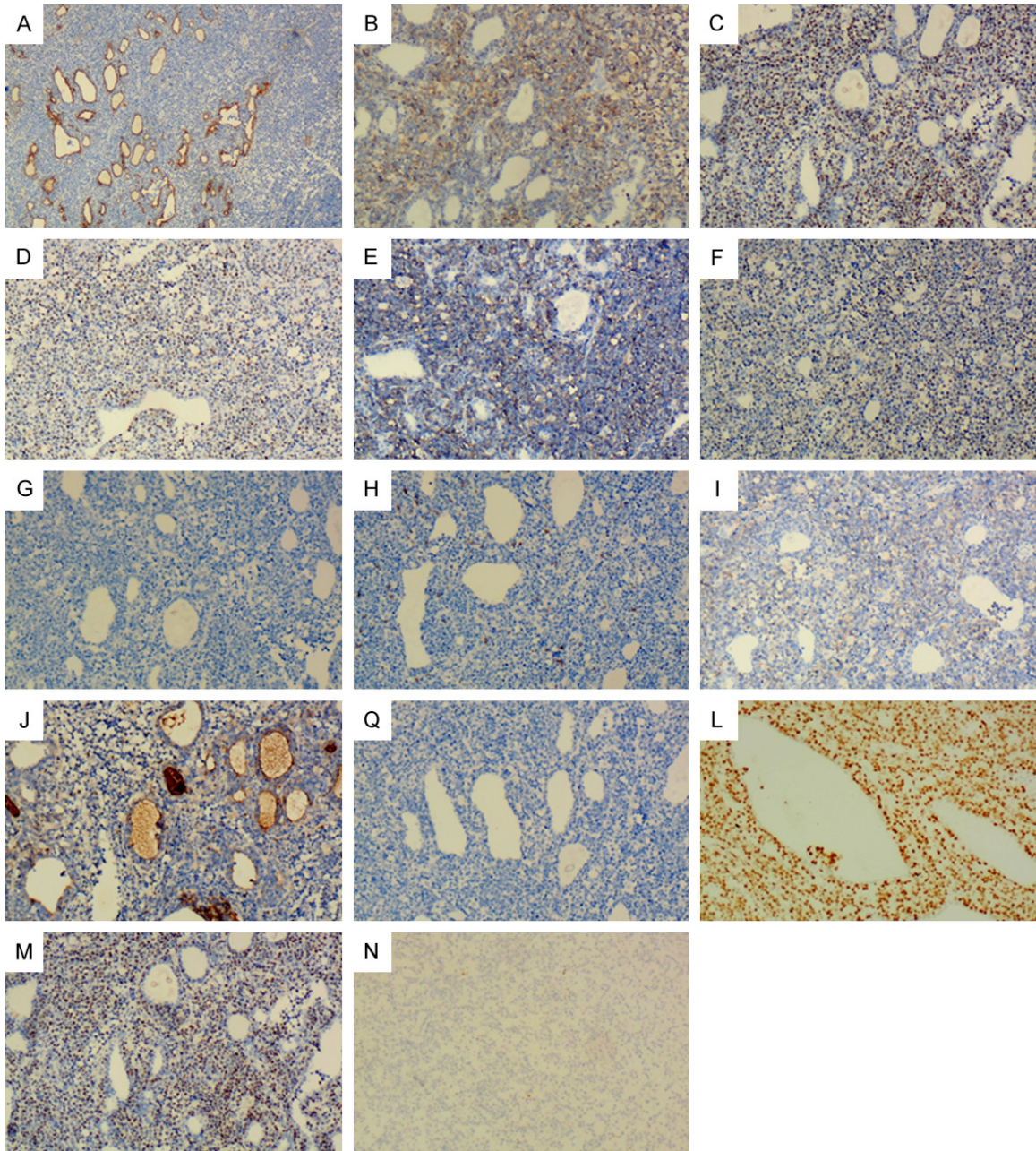
deterioration of his condition. But regrettably, the family refused to follow up further in November 2018.

## Discussion

Thyroid neoplasms are very infrequent in children and adolescents, having a different clini-



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**Figure 4.** Immunohistochemical study. TG presented residual thyroid tissue (A). Immunohistochemical staining revealed the negative expression of CD20 (B), PAX-5 (C), BCL-6 (D), CD10 (E), MUM-1 (F) and C-MYC (M) and the negative expression of CD21 (G), CD5 (H), CD43 (I), CD38 (J), TDT (K) and CYCLIND1 (N) by the neoplastic cells. The proliferation rate ki67 was almost 100% (L).

cal presentation and course from adults, in particular a high rate of malignancy [5], and about 0.4% of the total number of malignant tumors in children in Great Britain [6]. PTL is even rarer comprising 2-4% of all thyroid malignant tumor, accounting for about 2% of all malignant extranodal lymphomas, but accounting for 2-3% of pediatric thyroid tumors [6,

7]. One of the largest retrospective reports on thyroid lymphoma was published by Graff-Baker et al., which reviewed 1048 patients and showed that the incidence of Burkitt lymphoma was <1% [8]. PTL is usually associated with Hashimoto's thyroiditis and is generally more common in the elderly, with a gender ratio of 3:1 [9]. However, children suffering from PTL is

rare accounting for predominantly 1% of all lymphomas and Burkitt lymphoma is even less common still [10, 11].

PTL is more frequent among older children [12], mainly non-Hodgkin's lymphomas (NHL), including Burkitt lymphoma (BL), aggressive diffuse large B-cell lymphoma, mucosa-associated lymphoid tissue and follicular lymphoma [2, 13]. Both the lymphoma and anaplastic cancer of the thyroid have similar rapid growth clinical characteristics, such as compression symptoms, pain, hoarseness, dyspnea and dysphagia, which often lead to clinical confusion [2, 14-17]. Ultrasonography is usually used as a preliminary diagnostic method for thyroid masses and nodules. Although not specific, some certain features of internal echo, boundary echo and post-echo found by ultrasound can suggest PTL, such as enhanced post-echo, can help distinguish lymphoma from other types of thyroid disease. Also, because PTBL and Hashimoto's thyroiditis exist simultaneously, the diagnostic sensitivity and positive predictive value of core needle biopsy for thyroid lymphoma are higher than that of FNA, which reduces the accuracy of FNA [18, 19]. The histological features of BL are specific, including basophilic cytoplasm and small nucleoli, medium size and consistent atypical cells, and the starry sky phenomenon transmitted by a large number of benign macrophages phagocytosis of apoptotic tumor cells [20]. Tumor cells stain positive for B-cell associated antigens (CD19, CD20 and CD22) and have a distinctive atypical cellular immunophenotype (IgM, CD10, CD38, CD43 and Bcl-6) and usually are negative for TDT and Bcl-2 [14], with a Ki-67 proliferation index of almost 100% [21].

We know that the thyroid gland does not contain natural lymphoid tissue, so the endolymphatic tissue of the thyroid that causes thyroid lymphoma is derived from the migration of lymphoid tissue into the thyroid gland in the course of inflammation or immunity [22, 23]. Hashimoto's thyroiditis, the most common cause of thyroid disease in children and adolescents, is due to the migration of lymphoid tissue, which may be accompanied by correlative structural alterations of the thyroid in children and then benign thyroid nodules, cancer and, rarely PTBL can happen over time [24-27]. The occurrence of BL has been confirmed to be related to viral

infection, especially EBV infection. Even so, the detection rate of EBV in diverse subtypes of BL is same different and the detection of EBV infection accounted for 30% in sporadic BL and most of endemic BL [28]. In this report, the patient was a 15-year-old boy with BL stemming from the thyroid and developed a rapidly increasing mass in the neck, which caused specific compression symptoms, including pressure sense, hoarseness, dysphagia and dyspnea, even coma. Postoperative pathological examination also found the specific starry-sky phenomenon of Burkitt lymphoma. Moreover, immunohistochemistry also showed that the related cellular immunophenotypic expression was also positive or negative. In particular, the proliferation rate ki67 was almost 100% and C-MYC was also positive. But the cause of thyroid Burkitt lymphoma in this patient is still unknown, whether it is related to EB virus infection, to mutations in the C-MYC gene, or to other factors. Since the cellular immunophenotypic expression of C-MYC is positive, we speculate that the etiology of the patient is more associated with C-MYC mutation. Immunohistochemically, Burkitt lymphoma is characterized to have achromosomal translocation that activates an oncogene (C-MYC), located at 8q24, which gets involved in transcriptional regulation, cell proliferation, differentiation, metabolism, programmed cell death or apoptosis and angiogenesis, and has been related to the occurrence and development of multiple tumors [17, 29, 30]. A translocation between C-MYC and IgH genes takes place in about 80% of cases in despite of the clinical environment (t[8;14]) or differences between C-MYC and the gene for the kappa (t[2;8]) or lambda light chain (t[8;22]) are noted in the rest of 20% [9, 19]. The high expression of C-MYC gene leads to prolonged cell cycle progression and genetic instability, which explains the high cell proliferation rate and loss of cellular adhesion of tumor cells [17]. Dave *et al.* also believed that the abnormal expression of the MYC gene is a marker of BL, which is of great significance for its clinical diagnosis of BL [14]. Although the molecular mechanism of this gene in BL has been studied by many scholars, there are still many problems worthy of further study. New biologic markers and therapeutic targets for Burkitt lymphoma need to be explored in the near future.



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Overall, this article reports an extremely rare PTBL that occurs in children. To the best of the author's knowledge, BL of the thyroid gland in children and adolescence used to be considered incurable as a result of the high proliferative rate of tumors. Therefore, in the absence of evidence of common causes, Burkitt lymphoma should be taken into account because of its therapy that differs from other thyroid pathologies when doctors are dealing with thyroid masses in the clinical process, and the timely diagnosis and immediate treatment have important effects on prognosis. In addition, C-MYC gene testing is also necessary and should be performed, which will provide a theoretical basis for the diagnosis and treatment of BL, particularly in children.

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### Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Zi-Li Lv, Department of Pathology, First Affiliated Hospital of Guangxi Medical University, 6 Shuangyong Road, Nanning 530021, Guangxi Zhuang Autonomous Region, P. R. China. Tel: +86-15907817634; E-mail: 15907817634@163.com

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