Tokai J Exp Clin Med., Vol. 45, No. 3, pp. 144-147, 2020

Incidentally Detected Microcarcinoma of Thyroid in Surgical Specimens of the Goiter in Pediatric Patient: A Case Report

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(Received March 24, 2020; Accepted June 30, 2020)

A 14 year-old girl with a previous medical history of cholecystic polyps was referred to our department with throat discomfort during swallowing. The cervical ultrasound and magnetic resonance imaging revealed a massive polycystic formation with a diameter of 45 × 24 × 31 mm consistent with a right lobe goiter. However, there were no findings for suspected malignancy. Hemithyroidectomy was performed and the specimen was sent for histopathological assessment. Hematoxylin-eosin staining of the right lower nodule showed variably-sized follicles consistent with adenomatous goiter. The right upper nodule showed a growth of relatively compact sized follicles with a thick fibrous capsule. A satellite nodule lying outside of the tumor capsule was consistent with minimally invasive follicular thyroid microcarcinoma. We observed her without any additional treatment and no recurrence is seen at present.

Key words: Follicular thyroid microcarcinoma, Pediatric thyroid microcarcinoma

INTRODUCTION

The incidence of thyroid cancer has been increasing in recent decades [1], most commonly in older people. Specifically, thyroid microcarcinoma (TMC) which is defined as thyroid cancer measuring less than 10mm at the greatest dimension according to the World Health Organization, tend to be detected with histopathological examination after surgery that has been performed for benign thyroid disease [2] or medical screening. TMC is also known to be found after lymph node biopsy or autopsy. There is no clear therapeutic approach for TMC. However, conservative follow-up has been suggested for TMC without any risk factors such as cervical lymph node metastasis or distant metastasis. In contrast, thyroid cancer is rare in the pediatric population, accounting for over 6% of all pediatric cancers [3]. Although the most common subtype of thyroid cancer in pediatric is papillary thyroid carcinoma, follicular thyroid carcinoma is also increasing [3]. However, the increased rate of thyroid cancer might be the result of increased use of medical imaging and increased imaging sensitivity [4]. The management of thyroid cancer in pediatric has been often followed by adult guidelines [5] although the characteristics of thyroid cancer in pediatric differs from adults [5–8]. Here, we present a case of pediatric patient that has incidentally detected microcarcinoma of thyroid in surgical specimens of the goiter.

CASE REPORT

A 14-year-old girl with a previous medical history of cholecystic polyps was referred to our department with throat discomfort during swallowing. Physical examination revealed a mass of the right lateral neck. The mass was soft and not tender and moved with deglutition. The ultrasound revealed a solid, hypoechoic thyroid nodules with a diameter of 45 × 24 × 31 mm located within the entire right lobe of the thyroid (Fig. 1). Magnetic resonance imaging (MRI) revealed a massive polycystic formation consistent with a right lobe goiter and also abnormal lymph nodes were not found (Fig. 2). Laboratory tests returned normal findings including thyroid functions and tumor marker (Table). Hemithyroidectomy was performed and the specimen was sent for histopathological assessment. Macroscopic appearance showed an encapsulated solid white nodule with areas of hemorrhage (30 × 20 mm) in the right lower area (Fig. 3B, dotted arrows) and a small well-circumscribed white nodule (3 × 3 mm) in the right upper area of the thyroid (Fig. 3B, arrows). Hematoxylin-eosin staining of the right lower nodule showed variably-sized follicles consistent with adenomatous goiter. The right upper nodule showed a growth of relatively compact sized follicles with a thick fibrous capsule (Fig. 3C). Although there were no clear mushroom-shaped images of capsular invasion, a satellite nodule lying outside of the tumor capsule was seen (Fig. 3C, arrows). Additionally, the abnormal mitoses were seen in the outside of the capsule area (Fig. 3D arrows). There was no evidence of vascular and

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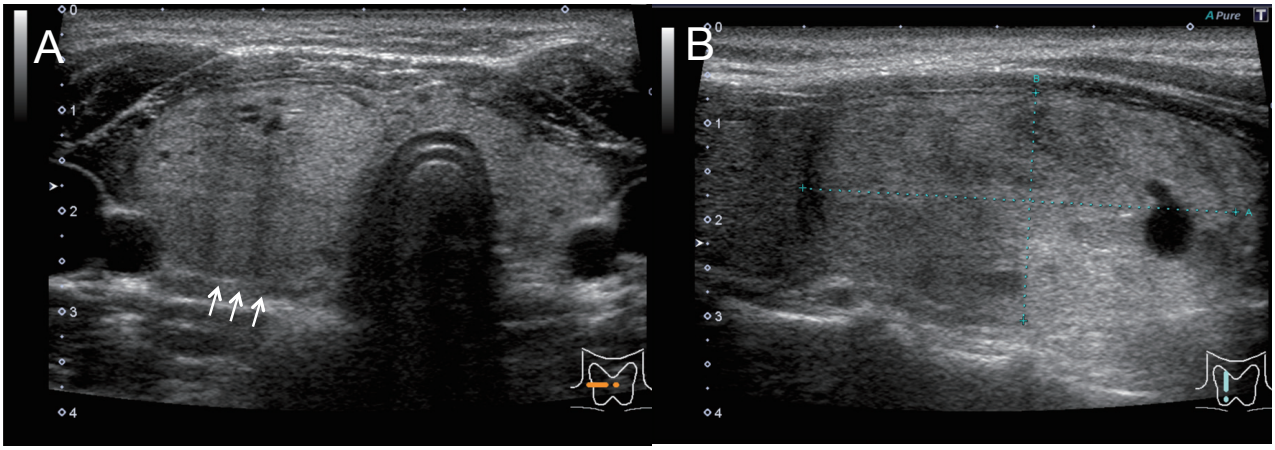

Fig. 1 (A, B) Ultrasound revealing a solid, hypoechoic thyroid nodules (arrows) with a diameter of 45 × 24 × 31 mm located within the entire right lobe of the thyroid.

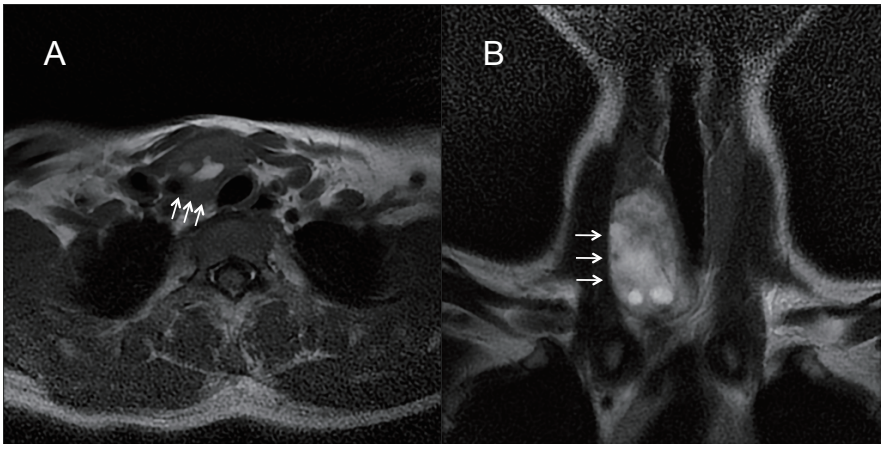

Fig. 2 Magnetic resonance imaging: T1 Axial (A) and T2 coronal (B) images revealing a massive polycystic formation in the right thyroid.

Table Laboratory findings

WBC	6100/μl	FSH	6.68 mIU/ml
RBC	4.64 10^6 /μl	TSH	0.732μlU/ml
Hb	13.2 g/dl	FreeT4	1.41 ng/dl
Ht	39.2 %	TSH-RAb	0.8 IU/LTg
Plt	33.7 10^4 /μl	Tg Ab	20 IU/ml
TP	7.8 g/dl	Calcitonin	0.7 pg/ml
AST	15 U/L	CEA	1.1 ng/ml
ALT	12 U/L		
BUN	12 mg/dl		
Cr	0.60 mg/dl		
Glu	85 mg/dl		
Na	145 mEq/L		
K	3.9 mEq/L		
Cl	107 mEq/L		

WBC, white blood cells; RBC, red blood cells; Hb, hemoglobin; Ht hematocrit; Plt, platelets; TP, total protein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; Glu, glucose; FSH, follicle-stimulating hormone; TSH, thyroid stimulating hormone; TSH-RAb, TSH receptor antibodies; TgAb, anti-thyroglobulin antibody; CEA, carcinoembryonic antigen

lymphatic invasion. We diagnosed her with minimally invasive follicular thyroid microcarcinoma and there were no findings of the cervical lymph node metastasis or distant metastasis with MRI imaging and abdominal ultrasound.

The postoperative course was uneventful and the patient remained free of recurrence during regular clinical follow ups for 10 months.

DISCUSSION

According to the systematic literature search, reasonable suspicion of malignancy and compression

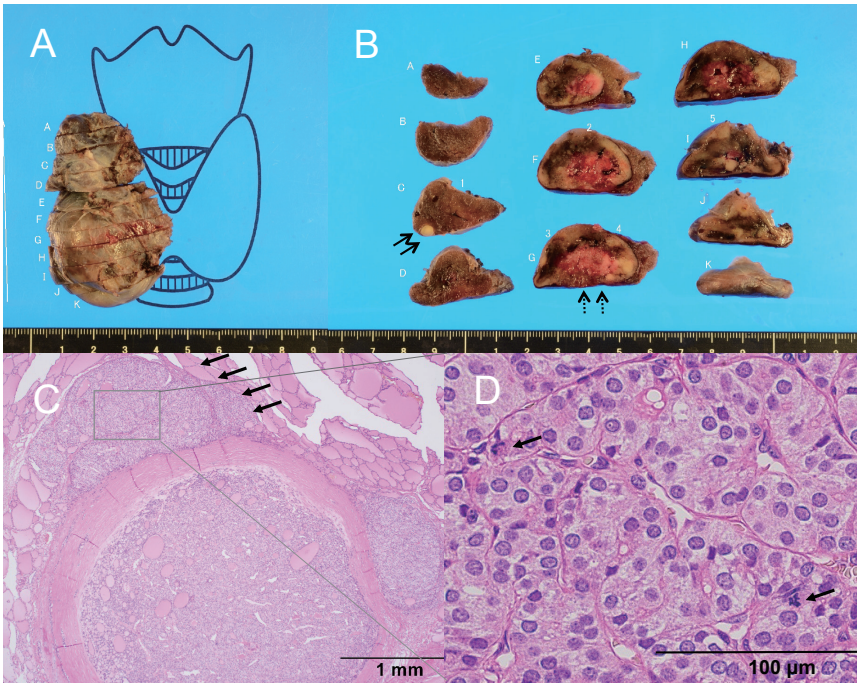

Fig. 3 Macroscopic appearance revealing an encapsulated solid white nodule with areas of hemorrhage (30 × 20 mm) in the right lower area (B, dotted arrows) and a small well-circumscribed white nodule (3 × 3 mm) in the right upper area of the thyroid (B, arrows). Hematoxylin-eosin staining (C, D) revealing a growth of relatively compact sized follicles with a thick fibrous capsule. A satellite nodule (C, arrows) lying outside of the tumor capsule could be seen (C). The abnormal mitoses are seen in the outside of the capsule area (D, arrows).

were indication for surgical management of benign goiter [9]. This report case suggested the possibility of existing occult TMC in pediatrics with thyroid benign tumor. Incidental thyroid cancer has been increasing in the adult population as the result of increased use of medical imaging and increased imaging sensitivity. Clinically, fine needle aspiration biopsy is also utilized to detect TMC in patients without palpable thyroid nodes. The prevalence of thyroid cancer with ultrasound screening is about 0.5% in adults [10]. The prevalence of incidental TMC is 4.5% in adult population [11]. These results are proposing that there might have been more occult pediatric patients if they were exposed to medical imaging screening.

Thyroid cancer is rare in children, accounting for over 6% of all pediatric cancers [3]. Children are more likely to present with advanced stage compared to adults. Specifically, papillary thyroid carcinoma which accounts for 90% of pediatric thyroid cancer has a high ratio of gene fusions [12]. This type of carcinoma is associated with more extensive extrathyroidal disease, and refers to targeted medical therapies [13–15]. Non-papillary pediatric thyroid tumors are not well studied due to their rareness. However, differences are seen in pediatric follicular thyroid carcinoma and medullary carcinoma. Lerner J *et al* previously reviewed 1825 cases of differentiated thyroid cancer in children. These authors reported 8.4% of them were TMC. They were treated with a partial thyroidectomy and not receiving radioiodine, and have an excellent overall survival (257.97 months) and disease-specific survival (256.38 months) [17].

In adult patients, the previous study showed that male sex, age 45 years and over, tumor size larger than 6mm, presence of bilateralism, and extrathyroidal extension were all independent risk factors for central lymph node metastasis for TMC [18]. Moreover, larger primary tumor, extrathyroidal extension, multifocality, bilateralism, and central lymph node metastasis were factors that conferred an increased risk of lateral lymph node metastasis. Notably, tumor location had an important factor of lymph node metastasis. Specifically, tumor location in the lower third of the thyroid gland and the isthmus was related with a higher risk of lymph node metastasis [18–20]. The majority of TMC is papillary TMC, which accounts for 65–99% of all cases. The follicular TMC has been found in 0.3–23.6% of all cases [21]. Previous study showed that there is not much difference of risk factor between papillary TMC and follicular TMC [21–22]. In our case, since none of those risk factors were seen, we observed her without any additional treatment and no recurrence is seen at present.

In the past the management of TMC in pediatrics has been informed by adult guidelines, and at this point those strategies do not seem to indicate that a new approach is necessary. Although our case was incidentally discovered in surgical specimens, we assume those cases will increase in the near future with increased use of medical imaging. More data is needed to determine the alternative therapeutic strategies for pediatrics.

REFERENCES

1) Chen AY, Jemel A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1998–2005. Cancer. 2009; 115: 3801–3807.
2) Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, *et al*. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer. 2007;

111: 508–516.
3) Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, *et al*. SEER Cancer Statistics Review, 1975–2016, National Cancer Institute; Bethesda, MD,USA: 2019.
4) Chen,A.Y Davies L. Children and thyroid cancer: Interpreting troubling trends. Cancer. 2019; 125: 2359–2361.
5) Paulson VA, Rudzinski ER, Hawkins DS. Thyroid Cancer in the Pediatric Population. Genes. 2019; 10: 723.
6) Stefan AI, Piciu A, Mester A, Apostu D, Badan M, Badulescu CI. Pediatric Thyroid Cancer in Europe: An Overdiagnosed Condition? A Literature Review. Diagnostics. 2020; 10: 112.
7) Collini P, Massimino M, Leite SF Papillary thyroid carcinoma of childhood and adolescence: a 30-year experience at the Istituto Nazionale Tumori in Milan. Pediatr Blood Cancer. 2006; 46: 300–306.
8) Collini P, Mattavelli F, Pellegrinelli A, Barisella M, Ferrari A, Massimino M. Papillary carcinoma of the thyroid gland of childhood and adolescence: Morphologic subtypes, biologic behavior and prognosis: a clinicopathologic study of 42 sporadic cases treated at a single institution during a 30-year period. Am J Surg Pathol. 2006; 30: 1420–1426.
9) Reinisch A, Malkomes P, Habbe N, Bojunga J, Grünwald F, Badenhoop K, *et al*. Guideline Compliance in Surgery for Thyroid Nodules - A Retrospective Study. Exp Clin Endocrinol Diabetes. 2017; 125: 327–334.
10) Fukunaga FH, Yatani R. Geographic pathology of occult thyroid carcinomas. Cancer. 1975; 36: 1095–1099.
11) Lim DJ, Baek KH, Lee YS, Park WC, Kim MK, Kang MI, *et al*. Clinical, histopathological, and molecular characteristics of papillary thyroid microcarcinoma.Thyroid. 2007; 17: 883–888.
12) Vera A, Erin R, Douglas S. Thyroid cancer in the pediatric population. Genes. 2019; 100: 723.
13) Francis GL, Waguespack SG, Bauer AJ, Angelos P, Benvenga S, Cerutti JM. Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer. Thyroid. 2015; 25: 716–759.
14) Parisi MT, Eslamy H, Mankoff D. Management of Differentiated Thyroid Cancer in Children: Focus on the American Thyroid Association Pediatric Guidelines. Semin Nucl Med. 2016; 46: 147–164.
15) Collini P, Mattavelli F, Pellegrinelli A, Barisella M, Ferrari A, Massimino M. Papillary carcinoma of the thyroid gland of childhood and adolescence: Morphologic subtypes, biologic behavior and prognosis: a clinicopathologic study of 42 sporadic cases treated at a single institution during a 30-year period. Am J Surg Pathol. 2006; 30: 1420–1426.
16) Chuk MK, Widemann BC, Minard CG, Liu X, Kim A, Bernhardt MB. A phase 1 study of cabozantinib in children and adolescents with recurrent or refractory solid tumors, including CNS tumors: Trial ADVL1211, a report from the Children's Oncology Group. Pediatr Blood Cancer. 2018; 65: e27077.
17) Lerner J, Goldfarb M. Pediatric Thyroid Microcarcinoma. Ann Surg Oncol. 2015; 22: 4187–4192.
18) Qu N[1], Zhang L, Ji QH, Chen JY, Zhu YX, Cao YM. Risk Factors for Central Compartment Lymph Node Metastasis in Papillary Thyroid Microcarcinoma: A Meta-Analysis. World J Surg. 2015; 39: 2459–2470.
19) Liu L, Liang J, Li J, Liu X, Jiang L, Long JX, *et al*. The Incidence and Risk Factors for Central Lymph Node Metastasis in cN0 Papillary Thyroid Microcarcinoma: A Meta-Analysis. Eur Arch Otorhinolaryngol. 2017; 274: 1327–1338.
20) Zheng X, Peng C, Gao M, Zhi J, Hou X, Zhao J, *et al*. Risk Factors for Cervical Lymph Node Metastasis in Papillary Thyroid Microcarcinoma: A Study of 1,587 Patients. Cancer Biol Med. 2019; 16: 121–130.
21) Pisello F, Geraci G, Sciumè C, Li Volsi F, Modica G. Total thyroidectomy of choice in papillary microcarcinoma]. G Chir. 2007; 28: 13–19.
22) Kaliszewski K, Wojtczak B, Strutyńska-Karpińska M, Łukieńczuk T, Forkasiewicz Z, Domosławski P. Incidental and non-incidental thyroid microcarcinoma. Oncol Lett. 2016; 12: 734–740.