Intrathyroid Thymic Carcinoma With Papillary Carcinoma Of Thyroid:A Case Report

Meng Wu
The First Affiliated Hospital of Gannan Medical University
Muyun Luo
The First Affiliated Hospital of Gannan Medical University
Yangyang Zhao
The First Affiliated Hospital of Gannan Medical University
Tao Sun
The First Affiliated Hospital of Gannan Medical University
Qiuxiang Xiao (xqx1812@163.com)
The First Affiliated Hospital of Gannan Medical University

Research Article

Keywords: intrathyroid thymic carcinoma(ITTC), Papillary thyroid carcinoma (PTC), pathological features, immunophenotype

Posted Date: May 5th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1616890/v1

Abstract

Intrathyroid thymic carcinoma (ITTC) is an inert malignant tumor, which often occurs in the neck or thyroid soft tissue. It is difficult to distinguish ITTC from other thyroid tumors. There is no specificity in clinical manifestations and imaging. In addition, there are few cases of ITTC combined with papillary thyroid carcinoma(PTC). Here we report a 44-year-old man with left neck mass admitted to the First Affiliated Hospital of Gannan Medical College in June 2017. Ultrasound showed thyroid nodules in bilateral lobes. The left lobe showed 48 × 55 mm hypoechoic signal, and the right lobe showed 5.6 × 4.2 mm hypoechoic signal. Because the right nodule was small, it was not treated. The left thyroid nodule was finally diagnosed as ITTC by pathological diagnosis. No special treatment was performed after left lobectomy. In June of the next year, due to physical examination found on the right thyroid tumor again in our hospital, the patient came to our hospital for treatment again. The pathological diagnosis was papillary thyroid carcinoma, and then the right lobe of the thyroid was resected. Combined with the history of patients, the patient suffered from left thyroid endothoracic adenocarcinoma with right thyroid papillary tumor. In this study, the clinical pathological characteristics, immune phenotype and differential diagnosis of thyroid endothoracic adenocarcinoma were analyzed and discussed, providing information and reference for the majority of medical researchers and clinical workers.

Introduction

Intrathyroid thymic carcinoma(ITTC) was first named by Chan and Rosai as carcinoma showing thymus like differentiation (CASTLE) in 1991(Delellis, et al. 2004), and was renamed as Intrathyroid thymic carcinoma in the WHO (2017) endocrine organ tumor classification (Lloyd, et al. 2017). This tumor often occurs in the soft tissue of the neck or thyroid, and is histologically similar to squamous cell carcinoma. It is difficult to distinguish it from thyroid undifferentiated carcinoma and thyroid squamous cell carcinoma because of its similar structure. At present, there is no report of ITTC with other thyroid cancer. Here we report a case of Intrathyroid thymic carcinoma with papillary thyroid carcinoma.

Case Description

A 44-year-old male first found a left neck mass in June 2017 for a week, without pain, no hoarseness, no dysphagia, mild breathing difficulties, normal daily activities. He came to our hospital for medical treatment. Physical examination found that tracheal position slightly right. A 40 × 50 mm mass was found in the left neck, and part of the mass broke into the suprasternal fossa. There was No pressing pain. The right neck did not touch obvious nodules, and the neck did not touch the enlarged lymph nodes. No visible lesions were found in the throat and nose. Ultrasound showed that the left lobe was 48 × 35 mm heterogeneous slightly hypoechoic, and the right lobe was 5.6 × 4.2 mm hypoechoic. The boundary was still clear. CT showed that the left lobe of the thyroid was enlarged, nodular low density shadow was seen, the edge was clear, and the trachea was compressed to the right(Fig. 1). The patients underwent resection of the left lobe of the thyroid in the same month.

Microscopically(Fig. 2), the cancer cells were lobulated and island-like distribution, and there were obvious fibrous tissue separation around the tumor cells.Under high magnification, a large number of small lymphocytes and plasma cells were infiltrated in the stroma and around the tumor cells. The cancer cells were spindle-shaped, squamous-shaped, and syncytial.The nuclear enlargement was round, and the nucleolus was obvious. Some nuclei were vacuolated. Immunohistochemical results showed that tumor cells diffusely expressed CD5 and CD117, CK5/6 and P63 were focal positive, P53 tumor cell nucleus scattered positive,BRAF V600 E gene mutation was wild type,However, it is a common mutation type in papillary thyroid carcinoma. and thyroid transcription factor-1 (TTF-1), thyroglobulin (TG), calcitonin (CT), CD56, Syn, CgA and P40 were negative (Fig. 3). These results show that the tumor tissue does not originate from thyroid or parathyroid tissue, but from thymic epithelial tissue. The final pathological diagnosis is thymic differentiated carcinoma in thyroid.

In April 2018, the patient came to our hospital for further consultation. Ultrasound found that there were tiny solid nodules on the right thyroid, which was 4.0 × 3.1 mm in size. In June, the right lobe of the thyroid was resected. After operation, a grayish-white nodule with a diameter of 4 mm was found in the thyroid, which was tough. Papillary structure can be seen at low magnification, and nuclear enlargement, ground glass-like nuclei, nuclear inclusion bodies and nuclear grooves can be seen at high magnification, showing classic papillary thyroid carcinoma. The pathological diagnosis result is papillary thyroid carcinoma(Fig. 4).

The patient was combined with papillary thyroid carcinoma of the right lobe on the basis of thyroid endothoracic adenocarcinoma of the left lobe of the thyroid, and there was no fusion of lesions on both sides. Therefore, patients with thyroid endothoracic adenocarcinoma still had a certain risk of papillary thyroid carcinoma.The patients were followed up recently. The patients were healthy and no recurrence was found in regular physical examination.

Methods

Pathological examination was performed on the surgical specimens of the patients. The specimens were fixed with 10% neutral formalin fixative and routinely dehydrated, paraffin-embedded, sliced, HE staining, microscopic observation, and immunohistochemical staining. EnVision two-step immunohistochemical method was used. All the above were carried out in the author ’ s hospital.

Discussion

ITTC is a rare malignant tumor, which was first reported Intrathyroid intraepithelial thymoma by Miyauchi et al (Miyauchi, et al. 1985) in 1985. In 1991, Chan and Rosai divided this tumor into four categories : ectopic hamartoma thymoma, ectopic neck thymoma, spindle epithelial tumor with thymic differentiation of thymoma and intrathyroid thymoma (Chan and Rosai 1991). The 2017 edition of WHO endocrine organ tumor classification renamed it ITTC (Lloyd, et al. 2017). The tumor mainly involves the inferior pole of thyroid, which is often the location of ectopic thymus tissue or branchial remnant of thyroid(Gao,

et al. 2018). ITTC is similar to thymic squamous cell carcinoma, but its clinical invasiveness is lower than that of thymic carcinoma(Tahara, et al. 2020).Papillary thyroid carcinoma (PTC) is the most common thyroid cancer, accounting for about 80% of all thyroid cancer(Yamamoto, et al. 1990). It usually occurs in middle-aged women aged 30 to 40, with low malignant level and good prognosis. As far as we know, there is no case of patients with ITTC have PTL .

The pathogenesis of ITTC is still unclear, and some scholars believe that it is related to the mutation of telomerase reverse transcriptase (TERT) promoter (Tahara, et al. 2020,Qasem, et al. 2015). However, in Zhao L et al (2018), TERT promoter mutation was not found in ITTC cases, Since the patient sample size was relatively small, and the low numbers are underpowered to show any statistical significance.Therefore, further statistical studies are needed to investigate whether TERT is ITTC-specific gene change. The patient is 44 years old. The age of patients reported by ITTC is between 25 and 69 years old. Most patients are older than 40 years old. There is no obvious gender advantage due to the small number of existing cases. Most patients have no other special symptoms except neck mass, dyspnea and hoarseness caused by tumor compression of trachea or invasion of recurrent laryngeal nerve (Zhao, et al. 2018,Luo, et al. 2005). Gao R et al (Gao, et al. 2018,Reimann, et al. 2006)reported a high metastasis rate of ITTCs : 52% (32 / 62) with lymph node metastasis and 16% (7 / 45) with distant metastasis, but there was no reason that metastasis had an impact on prognosis .

In histological manifestations,Intrathyroid thymic carcinoma is usually more similar to thymic carcinoma(Tai, et al. 2003).In this case,the cancer cells were lobulated, surrounded by fibrous tissue intervals, and lymphocytes and plasma cells infiltrated. The microscopic manifestations of cancer cells are diverse, mostly spindle-shaped, squamous, round, polygonal or combined. The cell boundary is unclear, and the cytoplasm is rich. The nucleus is oval, vacuolar, visible nucleolus, and mitotic figures are rare. These manifestations are also extremely similar to thyroid-derived squamous cell carcinoma and thyroid undifferentiated carcinoma, which are easy to be misdiagnosed.

The disease has a unique immunophenotype. Recent studies have found that CD5 and CD117 can be expressed in ITTC (Reimann, et al. 2006,Dorfman, et al. 1998,Nakagawa, et al. 2005). The patient was positive for CD5. D. M. DORFMAN et al found that squamous differentiated thyroid cancer had no CD5 immune response, a few typical thyroid cancer cases showed weak CD5 immune response, other head and neck cancer had no CD5 immune response(Dorfman, et al. 1998). Moreover, most studies have shown that CD5 is expressed in most thoracic adenocarcinomas, but not in thymomas and other malignant tumors, which can be used as a marker for the identification of thoracic adenocarcinoma (Tai, et al. 2003). Therefore, ITTC can be diagnosed by immunohistochemistry.

PTC originates from the follicular epithelial cells derived from the endoderm. Usually, the disease progresses slowly and the prognosis is relatively good. In recent years, some scholars believe that the occurrence of PTC is related to, in which TERT promoter mutation and PAX8 / PPARr rearrangement are also reflected in the study of ITTC occurrence (Tahara, et al. 2020,Qasem, et al. 2015,Suzuki, et al.

2018,Nikiforov and Nikiforova 2011), which may be related to the occurrence of papillary thyroid carcinoma in the second year after patient in this study suffered from Intrathyroid thymic carcinoma.

Conclusion

ITTC is less invasive than other malignant tumors in the thyroid, so radical thyroidectomy is the main treatment. Some studies (Sun, et al. 2011)have found that patients with ITTC have a good prognosis after radical thyroidectomy and postoperative radiotherapy. Even patients with local recurrence also benefit from subsequent surgery or radiotherapy. In summary, the occurrence of ITTC combined with PTC is extremely rare, and there are great differences in histological morphology between the two.The identification of ITTC and other malignant tumors of the thyroid needs to rely on immunohistochemical staining, and CD5 and CD117 are important immune markers. In recent years, the number of patients with Hashimoto ' s thyroiditis complicated with PTC has gradually increased. However, this patient has no history of Hashimoto ' s thyroiditis, and there is a certain correlation between ITTC and PTC from the perspective of gene. Therefore, the possibility of combined recurrence of PTC should be considered in the diagnosis of ITTC, and patients should be followed up and reviewed regularly.

Declarations

Acknowledgements

We thank all the participants for the intensive studies of this challenging case.

Ethics Statement

Patient has provided informed consent for publication of the case.

Author contributions

M Wu, QX Xiao, MY Luo, YY Zhao, T Sun were major contributors in conceiving and writing the manuscript; M Wu and QX Xiao were responsible for preparation of the draft; M Wu and QX Xiao performed the histological staining and analysis. M Wu and QX Xiao contributed to the information acquisition. all authors contributed to the critical revision of the manuscript.

Competing interests

The authors declare no competing interests.

References

1. Delellis RA, Lloyd RV, Heitz PU, et al. (2004) World Health Organization Classification Classification of Tumours: Pathology and Genetics of Tumours of Endocrine Organs. Lyon: IARC Press, pp 96–97.

2. Lloyd RV, Osamura RY, Klöppel G, et al. (2017) WHO classification of tumours of endocrine organs, 4th ed. Lyon: IARC Press, pp 125–126.
3. Miyauchi A, Kuma K, Matsuzuka F, et al. (1985) Intrathyroidal epithelial thymoma: an entity distinct from squamous cell carcinoma of the thyroid. World J Surg;9(1):128–135 http://dx.doi.org/10.1007/bf01656263
4. Chan JK, Rosai J (1991) Tumors of the neck showing thymic or related branchial pouch differentiation: a unifying concept. Hum Pathol;22(4):349–367 http://dx.doi.org/10.1016/0046-8177(91)90083-2
5. Gao R, Jia X, Ji T, et al. (2018) Management and Prognostic Factors for Thyroid Carcinoma Showing Thymus-Like Elements (CASTLE): A Case Series Study. Front Oncol;8:477 http://dx.doi.org/10.3389/fonc.2018.00477
6. Tahara I, Oishi N, Mochizuki K, et al. (2020) Identification of Recurrent TERT Promoter Mutations in Intrathyroid Thymic Carcinomas. Endocr Pathol;31(3):274–282 http://dx.doi.org/10.1007/s12022-020-09635-0
7. Yamamoto Y, Maeda T, Izumi K, et al. (1990) Occult papillary carcinoma of the thyroid. A study of 408 autopsy cases. Cancer;65(5):1173–1179 http://dx.doi.org/10.1002/1097-0142(19900301)65:5<1173::aid-cncr2820650524>3.0.co;2-2
8. Qasem E, Murugan AK, Al-Hindi H, et al. (2015) TERT promoter mutations in thyroid cancer: a report from a Middle Eastern population. Endocr Relat Cancer;22(6):901–908 http://dx.doi.org/10.1530/erc-15-0396
9. Zhao L, Gao RL, Liu Q (2018) Clinicopathological analysis of five cases of intrathyroid thymic carcinoma. Journal of Shanghai Jiaotong University:1272–1276
10. Luo CM, Hsueh C, Chen TM (2005) Extrathyroid carcinoma showing thymus-like differentiation (CASTLE) tumor–a new case report and review of literature. Head Neck;27(10):927–933 http://dx.doi.org/10.1002/hed.20237
11. Reimann JD, Dorfman DM, Nosé V (2006) Carcinoma showing thymus-like differentiation of the thyroid (CASTLE): a comparative study: evidence of thymic differentiation and solid cell nest origin. Am J Surg Pathol;30(8):994–1001 http://dx.doi.org/10.1097/00000478-200608000-00010
12. Tai CM, Liang CW, Chang TC (2003) Intrathyroidal thymic carcinoma: a case report. J Formos Med Assoc;102(2):109–112
13. Dorfman DM, Shahsafaei A, Miyauchi A (1998) Intrathyroidal epithelial thymoma (ITET)/carcinoma showing thymus-like differentiation (CASTLE) exhibits CD5 immunoreactivity: new evidence for thymic differentiation. Histopathology;32(2):104–109 http://dx.doi.org/10.1046/j.1365-2559.1998.00318.x
14. Nakagawa K, Matsuno Y, Kunitoh H, et al. (2005) Immunohistochemical KIT (CD117) expression in thymic epithelial tumors. Chest;128(1):140–144 http://dx.doi.org/10.1378/chest.128.1.140
15. Suzuki A, Hirokawa M, Takada N, et al. (2018) Utility of monoclonal PAX8 antibody for distinguishing intrathyroid thymic carcinoma from follicular cell-derived thyroid carcinoma. Endocr J;65(12):1171–

1175 http://dx.doi.org/10.1507/endocrj.EJ18-0282

16. Nikiforov YE, Nikiforova MN (2011) Molecular genetics and diagnosis of thyroid cancer. Nat Rev Endocrinol;7(10):569–580 http://dx.doi.org/10.1038/nrendo.2011.142
17. Sun T, Wang Z, Wang J, et al. (2011) Outcome of radical resection and postoperative radiotherapy for thyroid carcinoma showing thymus-like differentiation. World J Surg;35(8):1840–1846 http://dx.doi.org/10.1007/s00268-011-1151-2

Figures

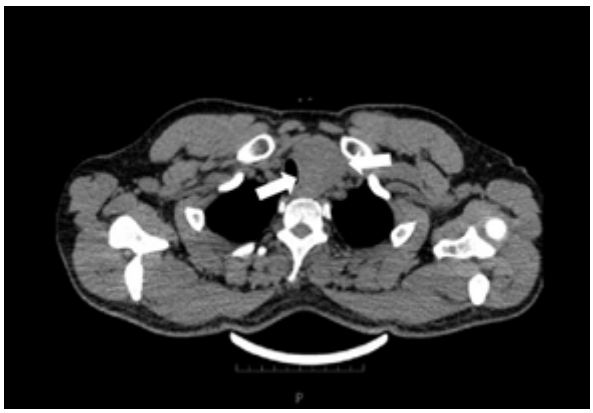

Figure 1

The left lobe of the thyroid has mass soft tissue density shadow size about 45×46mm into the upper mediastinum，the trachea was shifted to the right due to compression (white arrow).

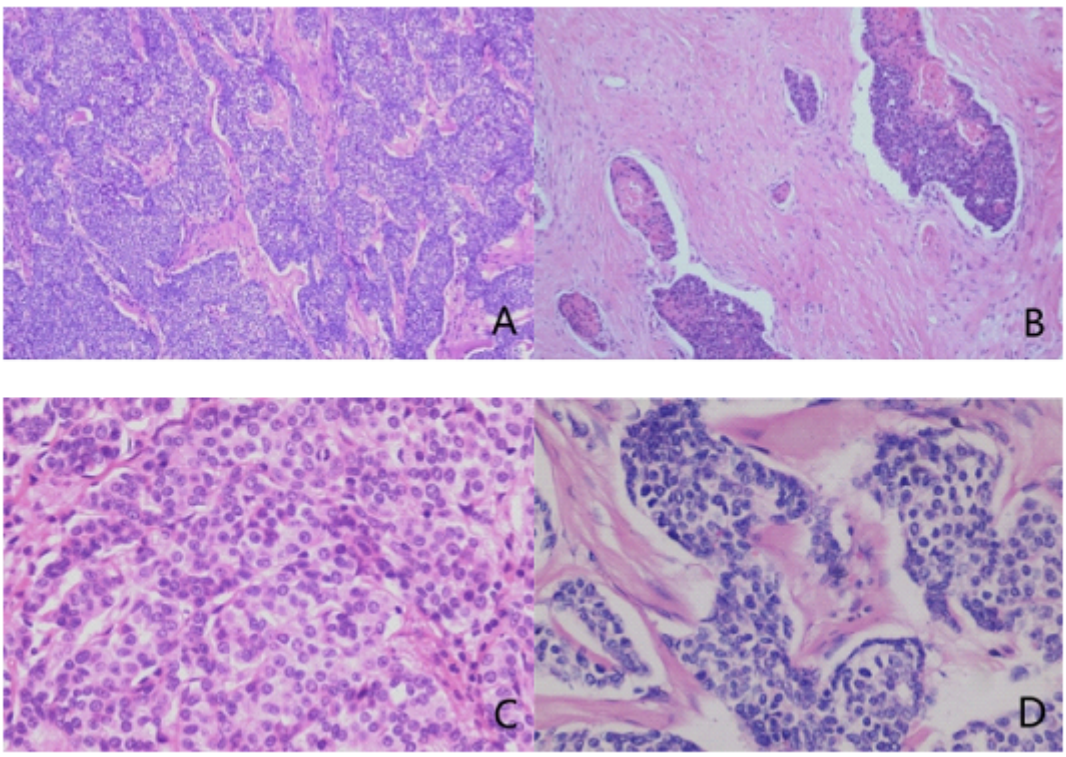

Figure 2

Microscopic morphology of ITTC. (**A)** Insular distribution of tumor cells surrounded by fibrous septa(H&E, ×100);(**B)** Tumor focal keratin bead formation(H&E, ×100);(**C)** Tumor cells fusiform, squamous, round nuclei, individual cells with vacuoles(H&E, ×400);(**D)** Dendritic epithelial cells in fibrous stroma(H&E, ×400).

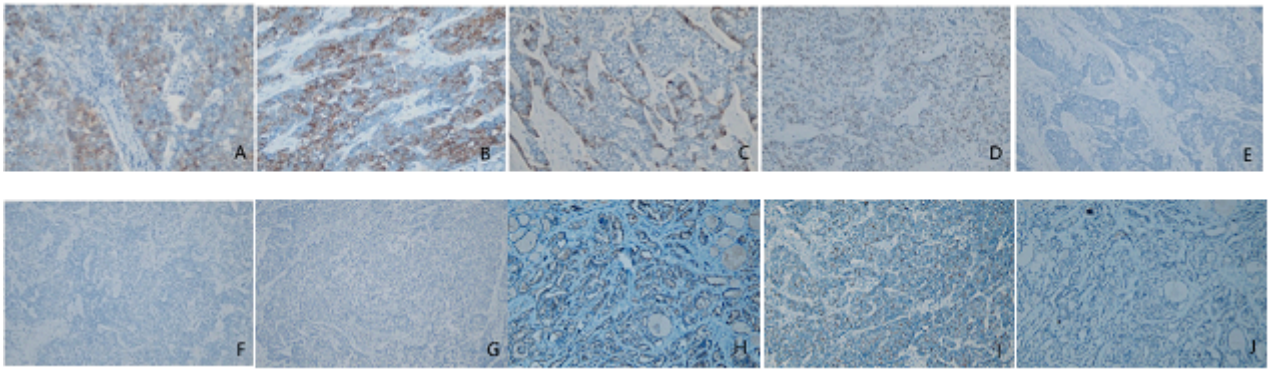

Figure 3

Immunohistochemical staining results of ITTC. The tumor cell membrane expressed CD5 **(A)** and CD117 **(B)** (EnVision, ×200); **(C)** CK5 / 6 were facal positive (EnVision, ×200); **(D)** Diffuse positive for P63 (EnVision, ×200); CT **(E)** and TG **(F)** were negative in tumor cells(EnVision, ×100); **(G)** BRAF of tumor cells was wild type, but BRAF was mutant in PTC **(H)** (EnVision, ×100); **(I)** P53 is mutant in ITTC tumor cells and wild type in PTC **(J)** (EnVision, ×100).

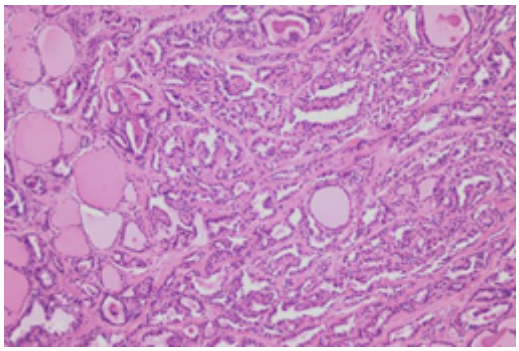

Figure 4

Microscopic observation of papillary thyroid carcinoma shows typical papillary tumor structure(H&E, ×100).