Clinical Case Report: Recurrence of CASTLE Thyroid Tumor

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Abstract

Background: CASTLE (Carcinoma showing thymus-like differentiation) in thyroid gland is a rare disease with favorable prognosis. Treating with surgery and adjuvant radiation therapy has been reported to be able to improve local controlling and long – term survival rates. In this report, we give an account of a clinical case of thyroid gland CASTLE and include relevant literature review in diagnosis and treatment of this disease.

Case presentation: A 60-year-old female patient diagnosed with Castle in 2015, had a total thyroidectomy and hormone maintenance. After 5 years, the patient was diagnosed with recurrence, late stage and incapable of surgery. Due to the refusal of radiation therapy, the patient is followed and is currently stable after 15 months.

Conclusions: CASTLE is a rare disease, diagnosis is based on postoperative pathology and immunohistochemistry analysis, especially upon CD5 marker. In the case of relapse, treatment includes surgery and radiation therapy. In some cases, follow-up is also an acceptable option for the patient.

Background

CASTLE is a rare and difficult-to-be-diagnosed disease due to lack of specific clinical characteristics. CASTLE normally invades neighbor organs and metastasizes to local lymph nodes[1]. CASTLE is a favorable prognosis disease, there is no standard treatment for this rare lesion although it appears that the first line treatment of choice is surgery with or without adjuvant radiotherapy. We report a clinical CASTLE thyroid tumor case, which is the first CASTLE case in our department. The patient was treated with total thyroidectomy and lymph node dissection, then CASTLE diagnosed by postoperative pathology. After 5 years of follow-up, the patient was admitted to our hospital again due to recurrence enlarged cervical lymph nodes.

Case Presentation

A 60-year-old woman, diagnosed as thyroid gland cancer in 2015, then was treated with total thyroid gland dissection, and postoperative pathology was carcinoma showing thymus-like differentiation (CASTLE). She was discharged and prescribed to take Levothyroxine 100mg/day. Then, she self-observed at home and did not follow up periodically. After 2 years, the patient found a left neck tumor. The tumor grew very slowly and did not cause any symptom; hence, she did not take health examination. In May 2020, about 3 years since the appearance of her left neck tumor, the patient was admitted to our hospital due to shortness of breath, which was then found to be due to the compression of the tumor upon the trachea. Clinical examination then found enlarged solid cervical lymph nodes level III, IV, stuck in a block size of 3x6 cm in diameter, and with no pain. No hypopharynx damage showed in the ENT, and her vocal cords were stable. Her neck's CT scan revealed a lesion size of 16x54mm compressed trachea, and many

local left cervical lymph nodes with the size of about 25mm (Fig. 1). Patient was directed to tracheostomy and tracheal stent before taking any particular examination.

PET/CT results revealed total thyroidectomy, no lesion recur in surgical bed, left cervical lymph nodes level III, IV, extranodal extension with sternocleidomastoid sizing 29x43x59 mm, SUV max 6.8. Her thymus sized 19x31x37mm, increased metabolism of FDG, SUV max 3.6. The anterior mediastinal on the left had a mass with the size of 33x39x49 mm, unidentified margin with neighbor organs surrounding trachea and thorax, SUV max 6.0. It also showed many nodes near the lower trachea, next to the superior vena cava, posterior thymus node and aortic loop nodes, the largest size was 26x40mm, increased metabolism of FDG, SUV max 7.9. The other organs were stable. No metastasis in other organs was found (Fig. 2).

Thyroid function test: TSH: 0.00726 mIU/L, FT4: 22.34 pmol/L and FT3: 4.0 pmol/L. We had a consultation of cervical lymph node specimen's pathology at that moment and thyroid specimen's pathology in the past 5 years (2015). The results showed that thyroid tumors appeared invasive cells which were poorly differentiated with squamous cell morphology, separated from conventional thyroid carcinoma. The immunohistochemistry (IHC) analysis showed to be positive with CK5, CK7, p63, C-kit, CD5 and negative with TTF-1, Thyroglobulin, GATA3, ER, CD99 and NKX2.2. The last result confirmed CASTLE pathology for both 2 specimens.

The patient was diagnosed with CASTLE thyroid gland recurrent in cervical lymph node. She was consulted with specialists in thoracic surgery, head and neck surgery to assess possibility of surgery to remove the maximum of recurrent tumors. However, it was assessed as a hard, high-risk work; her family refused to take surgery. Then, we decided to treat the patient with palliative radiotherapy. However, her family denied to have treatment and got the patient discharged from the hospital.

Discussion

CASTLE is a rare disease of unknown etiology, accounting for 0.1–0.15% of all thyroid gland cancer. It commonly occurs among around 40 to 50 years old, and had a slight female predominance. It was first described by Miyauchi et al. in 1985 named "thymus carcinoma in the thyroid". In 1991, Chan and Rosai separated the concept of this type of tumor into four groups: ectopic hamartomatous thymoma, ectopic cervical thymoma, spindle epithelia tumors with thymic-like differentiation – SETTLE and Carcinoma showing thymus-like elements – CASTLE. SETTLE and CASTLE show characteristics of malignant tumors, the other two pathologies were considered as benign tumors. SETTLE commonly occurs among the young, while CASTLE is more common at the ages of 50 [2,3].

The histopathology and immunohistochemistry of tumor show features similar to thymus carcinoma cancer and possibly initial origins in thymus gland or branchial pouch. Immunohistochemical test showed CD5-positive characteristics in most cases, and negative with thyroid gland markers such as thyroglobulin and calcitonin. Molecular analysis shows p63-positive on most tumors of thymus origin, but negative results were found on cystic carcinoma and poorly differentiated form in thyroid gland[4].

CASTLE is clinical indolent growth and favorable prognosis. Most patient came with a painless, slowly-growing mass in neck (especially the lower lobe of thyroid gland). Some patients may also experience hoarseness or swallowing due to the tumor's invasion of neighboring soft tissue and regional lymph node. Other symptoms include dry cough and short of breath[5]. Our patient after initial total thyroidectomy and following up, until the recurrence of slowing growing cervical lymph node; the lymph node enlarged gradually over 3 years, making a compression at the time of recurrence. It has been reported that CASTLE can metastasize to the brain, liver and lungs at a very low rate[6].

CASTLE arises in thyroid gland or the soft tissue of the neck. It is necessary to differentiate CASTLE from the other tumors such as primary or metastatic head and neck squamous cell or carcinoma of thyroid gland, because the prognosis and treatment therapy are different. Diagnostic imaging methods include neck ultrasound, head and neck CT scans and MRI. CASTLE tumors on head and neck CT scans often show an unclear boundary and no calcification lesion. Fine needle aspiration plays an important role in the diagnosis of thyroid cancer, especially papillary thyroid cancer, with the specific and sensitive rates of more than 90%. However, cytology cannot differentiate CASTLE from less differentiated thyroid cancer such as squamous carcinoma or undifferentiated thyroid carcinoma[4,7]. A needle biopsy can obtain a tissue samples with the appropriate size for immunohistochemistry. The IHC analysis shows a tumor that is strongly positive with CD5, p63, and cyto-keratin as well as negative with thyroglobulin, TTF1, and calcitonin[5,8]. Positiveness with CD5 marker helps to differentiate CASTLE from other tumors of the thyroid or respiratory tract – upper gastrointestinal tract[9]. Our case also showed similar results on pathology and IHC analyses: lesion positive with CK5, CK7, p63, C-kit and CD5 but negative with TTF-1, Thyroglobulin, GATA3, ER, CD99 and NKX2.2 (Fig. 3).

Due to the rarity of the disease, there are currently no standard treatment guidelines, but surgery is usually the first choice. According to the reports, the rates of extracellular invasive tumors and lymph node metastases are relatively high, at 50–60% and 50% respectively[1,10,11]. It í also reported that patients receiving curative surgery including total thyroidectomy and cervical lymph node dissection had favorable results, with regional recurrence rates of 14%, and 5 years and 10 years survival rates of 90% and 82% respectively[12]. Therefore, complete resection of the tumor, including removal of invasive organs, is essential to reduce rates of local recurrence and improve survival rates. CASTLE is considered as a disease that has good response to radiotherapy[7]. In one of Hidemitsu's literatures, one patient refused surgery and was treated with radiotherapy only; after that, the tumor got a complete response, the following up for 7 years on CT scan did not show any recurrence. In addition, according to a study of 10 CASTLE patients undergoing surgeries (of that, 9 patients with a breaking thyroid tumor) and adjuvant radiotherapy, only 4 patients were witnessed recurrence and all of them were outside the irradiation areas[10]. It was suggested that patient with CASTLE should undergo surgery to completely remove tumors following by adjuvant radiotherapy. Also, some authors suggested that postoperative radiotherapy should be considered for patients possessing or suspecting positive lymph node. As reported by Roka and Piacentini, surgery was sufficient for patients who did not have lymph node metastases, as none of those patients had relapsed[1,13]. In Hidemitsu's study, 2 patients who had no lymph node metastases and did

not take postoperative radiotherapy, were followed up for 5 years and 10 years with no recurrence. According to the study of Sun et al., it rarely recurred after lymph node removal at initial surgery with negative pathology results[11]. For patients recurring after the initial treatment, surgery and radiotherapy still play an important role than chemotherapy. Some reports indicated the lower rates of local recurrence in the group of patients who had locally invasive widespread tumors and cervical lymph node metastases treated with radiotherapy[10]. Base on data reported, through multi – specialist consultation, maximal tumor removed surgery and adjuvant radiotherapy were chosen.

However, in our case, patient and her family later decided not to receive treatment and was discharged. At present, after 15 months follow-up the patient was stable, mainly discomfort because of tumor compression and palliative care after tracheostomy and tracheal stent.

Conclusion

CASTLE is a rare disease, which has no specific signs and symptoms. Diagnosis of this disease is based on postoperative pathology and immunohistochemistry analysis, especially upon CD5 marker. Treatment for the disease includes surgery and radiation therapy. Curative surgery including total thyroidectomy and lymphadenectomy helps reduce recurrence rate and improve survival possibility. Adjuvant radiotherapy should be used with patients who have lymph node metastases and for recurrent tumors that are incapable of resection. In some cases, follow-up is also an option for the patient.

List Of Abbreviations

CASTLE (Carcinoma showing thymus-like differentiation); ENT (Ear, Nose and Throat); CT (Computed Tomography); PET CT (Positron Emission Tomography - Computed Tomography); MRI (Magnetic resonance imaging); FDG (Fluodeoxyglucose); SUV (Standardized Uptake Value); IHC (Immunohistochemistry); SETTLE (Spindle epithelial tumor with thymus-like differentiation).

Declarations

- Ethics approval and consent to participate: The study was approved by our research committee, Hanoi Medical University, Hanoi, Vietnam and Vietnam National Cancer Hospital, Hanoi, Vietnam.
- Consent for publication: The publication of this study has been consented by patient.
- Availability of data and materials: The datasets used during the current study are available from the corresponding author on reasonable request.
- Competing interests: Not applicable
- Funding: Not applicable
- Authors' contributions:

Dang NV: Radiation Oncologist, treated the patient, wrote manuscript.

Son LX: Resident of Oncology, wrote manuscript.

Hong NTT: Medical Physic, revised manuscript.

Nhung NTT: Radiation Oncologist, revised manuscript.

Tung NT: Professor, revised manuscript.

Quang LV: Professor, revised manuscript.

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Figures

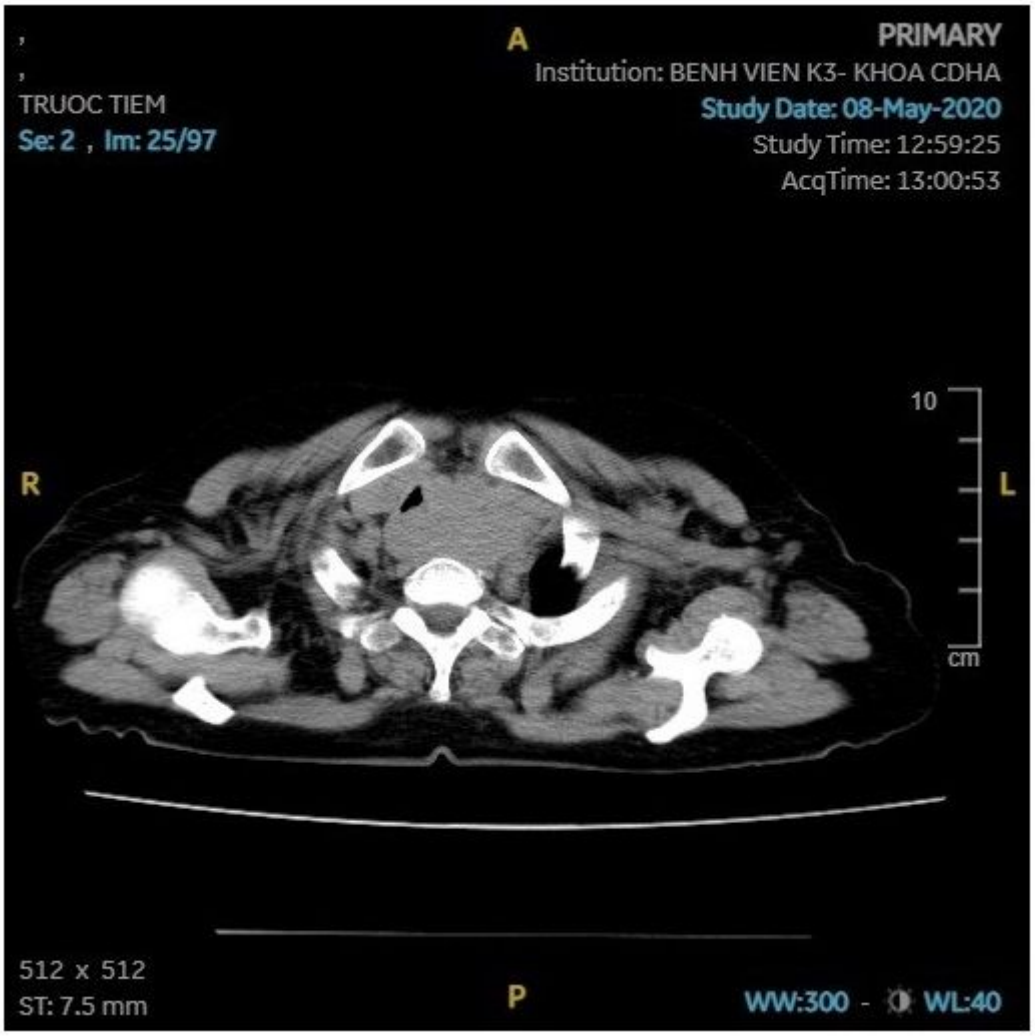

Figure 1

CT scan.

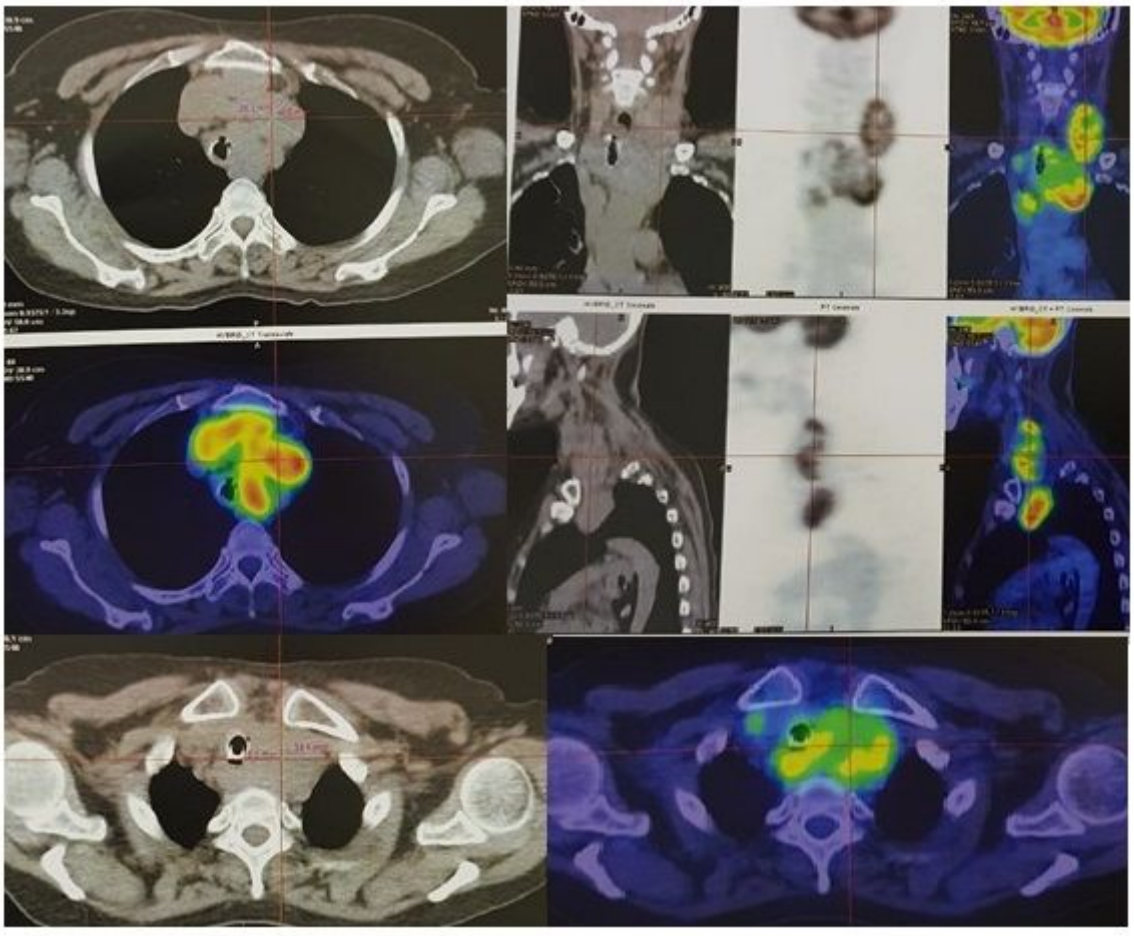

Figure 2

PET/CT

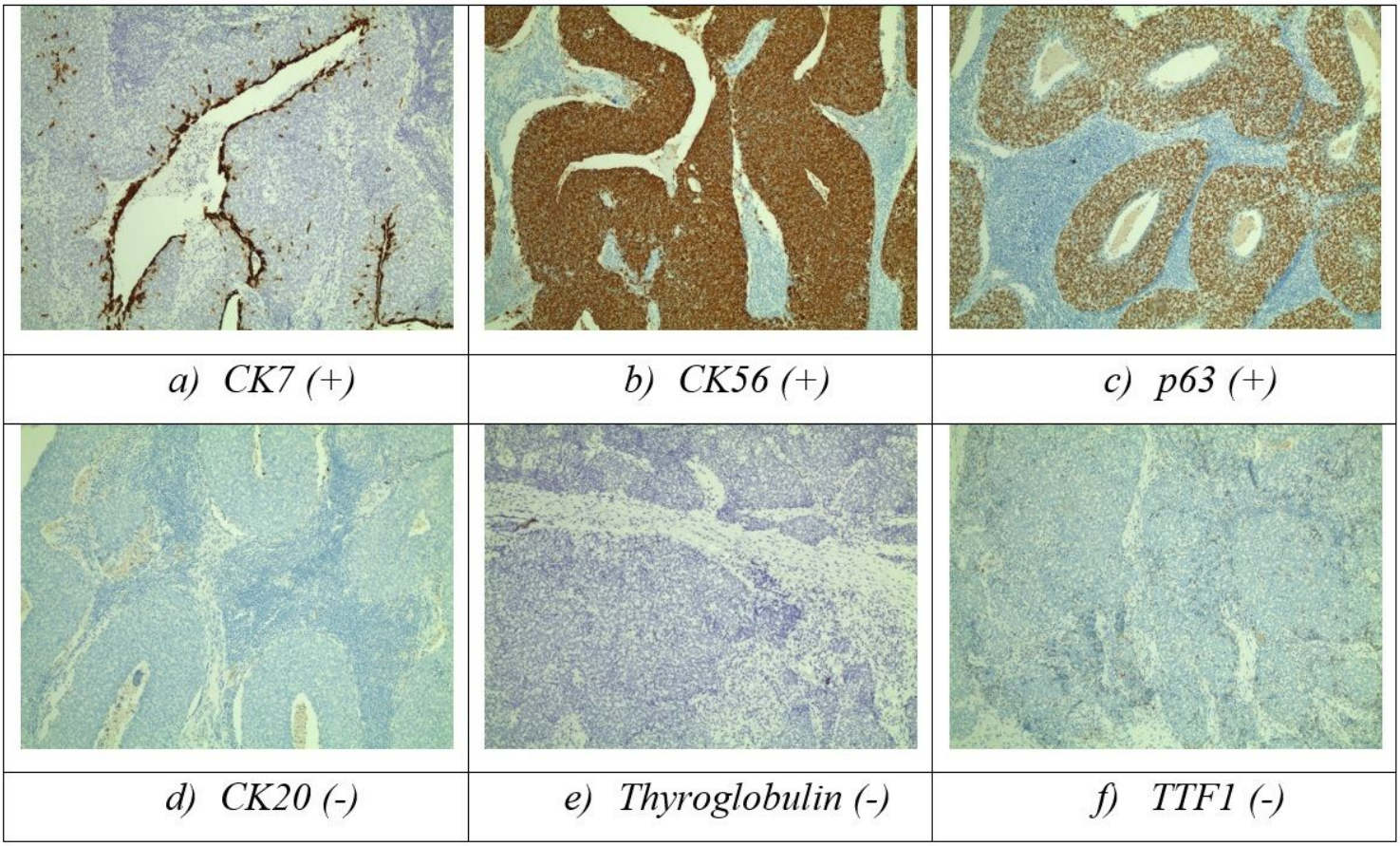

Figure 3

Immunohistochemistry