CASE REPORT

Spindle Epithelial Tumor with Thymus-like Element (Settle): a Case Report

Cengiz Tavusbay¹ · Demet Arikan Etit² · Ercan Kadioglu³ · Mehmet Hacıyanli¹

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Abstract Spindle epithelial tumor with thymus-like element (SETTLE) is a very rare malignant neoplasm of the thyroid. It is generally encountered in children, adolescents, and young adults Objective: We aimed to present a patient with SETTLE and to review the clinical and pathologic features of this rare tumor. A 13-year-old male patient presented to our clinic with complaints of a rapidly growing lump on his neck. There was no evidence of distant metastases at time of presentation. A total thyroidectomy was performed. Lymph node dissection was not performed. On the first postoperative day, the patient was discharged uneventfully. Histopathological and immunohistochemical analysis revealed a SETTLE in our case. During 1 year of follow-up, the patient had no complaints or symptoms, without tumor recurrence on imaging studies. Although SETTLE is a very rare entity, it should be considered when diagnosing rapidly growing masses in the thyroid, especially in younger patients.

Keywords Immunocytochemistry · SETTLE · Thyroid

Introduction

Spindle epithelial tumor with thymus-like element or differentiation (SETTLE) is a rare neoplasm of the neck and it almost always originates from thyroid gland. It affects mostly children and adolescents [1–3]. Chan and Rosai described these tumors as SETTLE in 1991 [1]. The most authors suggested that SETTLE is developed from ectopic thymic tissue or remnants of branchial pouches, and histologically it is predominantly composed of spindle cells with gland-like epithelial structures without significant atypia. Although it is a slow growing tumor, it has a significant potential of metastases. Since it is very rare (It has been reported approximately 42 cases so far in the English literature), the optimal diagnostic and therapeutic algorithms have not been established [4].

Herein, we report a new case of SETTLE of the thyroid in a 13-year-old boy.

Case Report

A 13-year-old male patient was admitted to the hospital with a rapidly growing lump on his neck within 6 months. His past medical history and family history was unremarkable. A 3 × 3 cm, firm nodule was palpated on the right lobe of the thyroid gland. Serum thyroid hormone and thyroid antibody and calcitonin levels were within normal range. Any other complaint or abnormality was encountered. Ultrasonography of the neck showed a heterogeneous, hypoechoic nodule filling the right lobe, which was 23 × 25 × 33 cm in size and solid in nature. There was no pathologic lymphadenopathy in the neck. The fine needle aspiration (FNA) biopsy of the thyroid nodule was nondiagnostic.

The patient underwent thyroidectomy. On histopathological evaluation, a neoplastic proliferation with a well-defined

✉ Cengiz Tavusbay
tavusbay3@gmail.com

¹ Department of Surgery, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey

² Department of Pathology, Izmir Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey

³ Department of General Surgery, Hatay State Hospital, Hatay, Turkey

borders predominantly composed of spindle cells with gland-like epithelial structures and ductular formations without significant atypia was detected (Fig. 1). The immunohistochemistry panel was performed on the formalin-fixed, paraffin-embedded tissue using the antibodies for cytokeratin AE1/AE3 (Fig. 2), epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), vimentin, cytokeratin7 (CK7), p63, CD10, calponin, phospho-histone H3 (pHH3), and revealed strong and diffuse positivity for cytokeratin AE1/3, cytokeratin 8/18, vimentin, and smooth muscle actin in both spindle and glandular components, a focal positivity for cytokeratin 7, EMA, CD10, calponin, and P63 in the glandular component. It was negative for Desmin, CD34, thyroglobulin, CD117, S-100, TTF-1, calcitonin, and CEA. The Ki-67 proliferation index was 5–7%. Mucicarmine and alcian blue were positive in cytoplasm. Based on those findings, the final diagnosis of SETTLE was reported. Microscopically, the surgical margin was free of the tumor infiltration.

His postoperative course was uneventful. There were no postoperative complications and any adjuvant treatment was not given after operation. Our case is asymptomatic and free of disease 2 years after the surgery.

Discussion

SETTLE is a very rare primary tumor of the thyroid, and is seen mostly in young adults with a mean age of 17 years (range, 2–59 years) at presentation [4]. The male to female ratio is 1.4/1 [4].

It has been reported that a slow-growing, painless cervical mass is the most common presentation. However, the neoplasm can grow quickly within a short period of time in some similar to our patient. The prognostic importance of such a rapid growth is unknown. Sometimes, it can be painful. Commonly, the mass is placed in the right lobe of the thyroid

Fig. 1 Uniform spindle-shaped cells proliferation with a well defined border (hematoxylin and eosin staining; original magnification, $\times 10$)

Fig. 2 The spindle cells showed strong immunopositivity with cytokeratin AE1/AE3 (original magnification, $\times 10$)

[4, 5]. Nonetheless, upon presentation of a patient with a mass, (such as sarcomatoid anaplastic carcinoma, medullary carcinoma can have spindle cells and gland-like structures), immunocytochemistry is very useful in distinguishing other thyroid tumors such as medullary carcinoma and synovial sarcoma.

As it presents a thyroid nodule or mass, physicians must consider thyroid neoplasms especially medullary and papillary cancer pertaining to those age groups or thyroglossal cyst, immature teratoma, and synovial sarcoma in the differential diagnosis. FNAB is the logical first line method for preoperative diagnosis. Kaur et al. described that FNA showing a biphasic round and spindle cell population may suggest the diagnosis in an appropriate clinical setting, although the diagnosis of SETTLE is challenging using FNA [6].

The exact diagnosis is usually established after the surgical excision of the mass. Macroscopically, SETTLE is usually noted to be smooth, white-tan, well circumscribed tumor surrounded by a capsule, varying in size from 1.8 to 12 cm [7]. It may be well-circumscribed, solitary, round mass or a lobular mass, and sometimes it can also include cysts and mucous-containing focal areas [7]. Examination in the light microscope, spindle cells have elongated nuclei with fine chromatin, small nucleoli, with abundant and eosinophilic cytoplasm and may show prominent mucinous and squamous differentiation. The epithelial cells are columnar, cubic, or plane, and generally lack atypia. The increased mitotic index (10–20/10 high power field) and focal necrosis may be showed. Generally, tumor shows biphasic pattern but rare cases may be predominantly monophasic [7]. Thyroid gland invasion are rare phenomena [4]. Our case had no atypia, high mitotic index, or necrosis. No thyroid invasion was detected.

Immunopathology is very important in the diagnosis of SETTLE and different immunohistochemical methods are used by a number of authors. The most important feature of epithelial cells is the presence of positive expression of high-molecular-weight cytokeratins (HMWCKs) and cytokeratin 7.

In contrast, expression of low-molecular-weight cytokeratins (LMWCKs) and epithelial membrane antigen (EMA) is frequently focally positive [5].

Surgery is mainstay of the diagnosis and the treatment of the primary tumor. Recondo et al. review the all 42 cases in the English literature in details in contact with the all authors [4]. Twenty patients were metastatic at diagnosis (28.5%) and distant metastases reach 46% at 10-year follow-up. The lungs and mediastinum were the most common sites for metastases (83%). The extent of surgery was not described in detail, but resection with tumor free margin and cervical lymph node dissections in metastatic disease were emphasized.

Most authors reported that SETTLE is a distinct low grade malignant tumor with a favorable prognosis after surgery, but more aggressive course has been recognized in some cases [4]. Another characteristic feature of SETTLE is long survival for many years despite development of metastasis [4, 6].

Although the 5-year survival rate was approximately 83%, it has been reported that 50% of patients followed for more than 5 years had late metastasis [4]. Additionally, long-term follow-up (>10 years) is necessary. The effect of chemotherapy and radiotherapy is unknown, but radical resection of metastases and primary tumor can provide a long-term survival results as expected for all slowly growing tumors [4].

As a result, evaluating a thyroid mass in pediatric and adolescent group, one should kept in mind SETTLE in the pre-operative differential diagnosis. Because of the rarity, the clear algorithm for the treatment are not exactly known, but surgery

is the mainstay of treatment and long-term follow-up is essential in clinical management due to late metastases in patients having SETTLE.

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