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CASE REPORT

Spindle epithelial tumor with thymus-like differentiation: A case report and literature review*

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Abstract

Spindle epithelial tumor with thymus-like differentiation (SETTLE) is a rare, low-grade malignant neoplasm that mainly occurs in the thyroid gland or its perimeter. Fewer than 10 cases of SETTLE have been reported in the Chinese literature, whereas approximately 50 cases have been reported in the international literature. We report a rare case of SETTLE that occurred in the soft tissues of the neck around the thyroid gland in a 41-year-old man. The neoplastic tissue, which mainly consisted of spindle epithelial components, included sporadically visible thymus-like structures. Immunohistochemistry demonstrated CK and CK19 positivity in the thymic epithelial components and CK, vimentin, and Bcl-2 positivity in the spindle cells. Surgical resection is the main treatment option for SETTLE. This patient underwent mass resection of the neck, and no recurrence or metastasis was observed even at 8 months postoperatively.

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Key words: spindle epithelial tumor; thymus-like differentiation; immunohistochemistry

Spindle epithelial tumor with thymus-like differentiation (SETTLE) is a rare, low-grade thymic malignancy. Histologically, SETTLE presents with a lobulate structure and a biphasic cellular association characterized by spindle epithelial cells mixed with thymic structures. It primarily occurs in or around the thyroid gland. In this paper, we report a case of SETTLE, which developed in the soft tissues of the neck around the thyroid gland and discuss its clinicopathological features and differential diagnoses to improve the understanding of this tumor.

Materials and methods

A 41-year-old man presented with an incidentally discovered mass on the right side of the neck one week ago. He did not experience any obvious discomfort. Physical examination revealed that the mass, located on the right anterior side of the neck above the clavicle, was palpable and measured approximately 4.0 cm in diameter. No tenderness or restriction of neck movement was evident. Computed tomography revealed a soft tissue shadow in the right parathyroid gland. An ultrasound B-scan showed a deep-seated subcutaneous hypo echoic nodule in the neck, not occupying the thyroid gland. Results of serology tests showed that levels of thyroglobulin, thyroglobulin antibodies, thyroxine, and other thyroid function parameters were within the reference range. The right cervical mass was resected clinically.

The surgical specimen was fixed with 10% neutral-buffered formalin solution, paraffin-embedded, and routinely sectioned for histological analysis. Immunohistochemical analysis was performed using a Roche automatic immunohistochemistry staining machine. CK, EMA, CK19, vimentin, SMA, desmin, STAT-6, Bcl-2, S-100, TTF-1, TG, calcitonin, Syn, CD5, TdT, HMB45, and Ki-67 antibodies were commercially obtained from Fuzhou Maxim Biotechnology Co., Ltd. Each antibody was validated with positive and negative controls.

Results

Macroscopic examination revealed a piece of gray–red irregular tissue that was 6.0 cm × 3.0 cm × 1.5 cm in size

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and characterized by a gray–white cut surface, tough texture, and intact envelope.

The neoplastic tissue was mainly composed of spindle-shaped cells (Fig. 1). The spindle-shaped cells were arranged in bundles and weaves with short spindle-shaped nuclei and fine chromatin. Nucleoli could not be discerned easily. Few nuclear fission images were evident. Scattered thymus-like structures, arranged in a cystic or cord-like pattern, were visible inside the tissue (Fig. 2). Immunohistochemical analysis of the neoplastic thymic epithelial components revealed positive staining for CK (Fig. 3) and CK19 and partially positive staining for CK7. Further, the tumor was positive for CK, Bcl-2, and vimentin (Fig. 4), partially positive for SMA, and negative for TTF-1, TG, calcitonin, CD5, TdT, CD5, CEA, HMB45, SATA-6, Syn, and desmin in spindle cells. The Ki-67 index was approximately 5%.

Discussion

SETTLE is believed to emanate from ectopic thymic tissue or the remnants of the branchial sac. It often develops in children, adolescents, and young adults with a mean age of onset of 19 (ranged, 4–59) years. However, SETTLE has also been reported in older adults, albeit rarely, and is more common in males. To the best of our knowledge, fewer than 10 cases have been reported in the Chinese literature, whereas approximately 50 cases have been reported in the international literature [1-5]. The youngest patient reported in the literature was a 2-year-old child [6, 7], whereas the oldest patient was a 75-year-old man [8]. A painlessly growing thyroid mass is the primary clinical sign. A rapidly enlarging mass in the neck, local tenderness, and tracheal compression are uncommon manifestations. Thyroid function is unaffected, and results of pathological investigations such as CEA and calcitonin levels do not show any abnormalities. No susceptibility factor (e.g., iodine deficiency, ionizing radiation, genetics, or environment) is associated with the development of SETTLE. It mainly occurs in the thyroid gland, but it can also occur in the soft tissues surrounding the thyroid gland. This case features a lesion occupying the soft tissues surrounding the thyroid gland.

SETTLE is a spindle epithelial neoplasm. The tumor is commonly bifurcated and characterized by spindle-shaped epithelial cells mixed with thymus-like structures. However, rarely, it can be unidirectional and consist of spindle cells or thymus-like structures

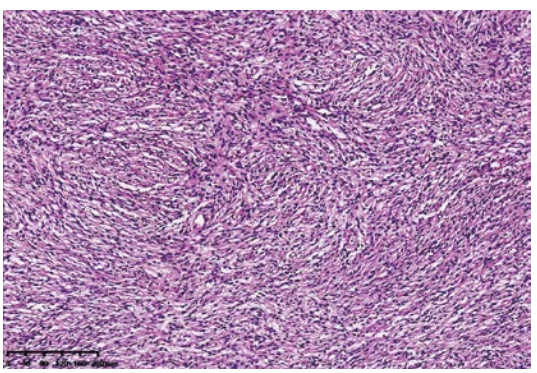

Fig. 1 The tumor predominantly spindle cells arranged in bundles or weaves (HE staining × 100)

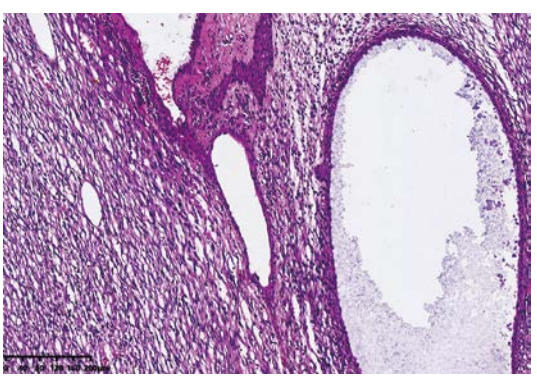

Fig. 2 Cystic thymic structures seen between the spindle cells (HE staining × 100)

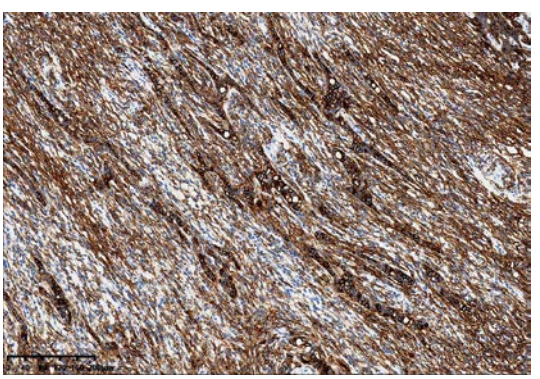

Fig. 3 CK positive in spindle cells and thymic epithelium, stained by automatic immunohistochemical staining machine (IHC × 100)

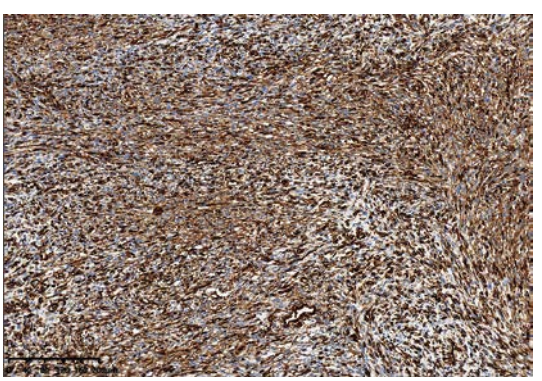

Fig. 4 Vimentin-positive spindle cells, stained by automatic immunohistochemical staining machine (IHC × 100)

only. Spindle cells are not distinctly anisotropic. Spindle cells are characterized by little cytoplasm, long nuclei, fine chromatin, inconspicuous nucleoli, and rare nuclear fission. Spindle cells sporadically exhibit hyper-disintegrative activity and focal necrosis. The thymus-like component may be tubular, papillary, or cord-like or comprise small islands of lightly stained cells or epithelium-lined cystic lumens, with cuboidal or columnar cells lining the thymic ducts. This component can also be mucinous or accompanied by cilia with some squamous metaplasia observed in a few cases. There is no obvious lymphocytic infiltration. Immunohistochemically, both neoplastic components of SETTLE have an epithelial phenotype, express broad-spectrum CK, and have spindle cells that are positive for vimentin. Spindle cells also express SMA, c-kit, and Bcl-2 but do not express TG, TTF-1, calcitonin, S-100, Syn, and CgA. The diagnosis of SETTLE relies primarily on histological features and immunohistochemical phenotypes, and accurate preoperative cytological diagnosis is difficult. Kijong Yi *et al.* [9] reviewed eight cases in the literature that were diagnosed using fine needle aspiration cytology. These cases were described only morphologically with respect to cytological diagnosis.

SETTLE should be differentiated from neoplasms with a spindle cell component.

Synovial sarcoma is a mesenchymal-derived spindle cell tumor with some degree of epithelial differentiation, including gland formation. It can affect any site, and approximately 5% of these tumors occur on the head and neck. Bidirectional synovial sarcoma has components of both epithelial and spindle cells, and the two components are present in variable proportions. The spindle-shaped tumor cells are distinctly anisotropic and relatively small and are characterized by oval nuclei; lightly stained, inconspicuous nucleoli; minimal cytoplasm; and poorly defined cells. The epithelial cells contain oval nuclei and abundant cytoplasm, forming thymus-like lumens containing epithelial mucus, which may also be papillary in structure. The interstitial collagen fibers are sparse and may become focally mucinous or focally calcified. The tumors may contain large numbers of mast cells. The tumors express cytokeratin CK, EMA, vimentin, CD99, BCL-2, and calponin, but not desmin or CD34. Furthermore, t(X; 18) (p11; q11) is a specific cytogenetic marker for this neoplasm and can be ascertained by molecular biology testing for cases in which differentiation of SETTLE seems difficult.

Ectopic malformed thymoma is a benign tumor arising from the superficial or deep soft tissues of the neck. It has both ectopic and neoplastic features and is most commonly observed in males. This tumor is similar in origin to SETTLE, and it is considered to be one of the tumors of the neck that is associated with parotid or gill bursal derivatives. The tumor consists of a mixture of spindle cells, islands of epithelial cells, and adipose tissue. The spindle cells were predominantly arranged in bundles but may also be of woven or matted shapes, containing fat spindle-shaped or elongated nuclei, fine chromatin or vacuole-like, small nucleoli, and non-isomorphic nuclei. Epithelial cells often appear as islands, small nests, or dilated cysts, and epithelial cells often show squamous epithelial differentiation, which may be accompanied by the formation of a varying number of thymic ducts. Immunohistochemistry revealed the myoepithelial differentiation of spindle cells, signifying that neoplasms or tumor cells are a mixture of epithelial cells and myoepithelial cells. Immunohistochemically, epithelial cells express epithelial markers, such as CK, CK5, CK6, CK7, CK8, and EMA, whereas spindle cells express epithelial markers, CD34, and CD10, with some of them expressing MSA, a-SMA, and calponin.

Carcinoma with thymus-like differentiation usually occurs in the lower end of the thyroid gland and, rarely, in the soft tissues surrounding the thyroid gland. Morphologically similar to thymic carcinoma, the tumor is characterized by squamous cell-like or syncytial cells and a pale eosinophilic cytoplasm. The tumor cells are short, and are spindle-shaped or polygonal, containing a poorly defined cell contour and a mild-to-moderate atypical, large, ovoid, or vesicular nucleus with a mitotic count of 1–2/10 HPF. Tumor cells may be associated with squamous differentiation, and lymphocytic infiltration of intercellular substances may be noted. Immunohistochemistry revealed the expression of CD5 and CD117 in addition to that of Bcl-2, Mcl-1, CK, EMA, and CEA. TTF-1 expression was absent.

Sarcomatous undifferentiated carcinoma is a highly malignant, extensively invasive tumor consisting of a mixture of spindle cells, pleomorphic giant cells, and epithelioid cells. When the tumor is predominantly composed of spindle cells, it often exhibits a sarcomatous form, featuring a fascicular or matted arrangement of cells as well as marked anisotropy and pleomorphism. Immunohistochemistry revealed strong positivity for CK and TP53 with minimal or no TG and TTF-1 expression.

Medullary thyroid carcinomas are a group of malignant neoplasms that emanate from parafollicular cells of the thyroid gland and exhibit varied histological patterns. Some medullary carcinomas may consist mainly of spindle-shaped cells arranged in bundles, which are known as spindle cell medullary carcinomas. Although this form is uncommon, it is important to differentiate it from SETTLE. Amyloid deposits are often noted in medullary carcinomas, and immunohistochemistry showed positivity for calcitonin and some neuroendocrine markers, such as CD56 and Syn.

Other tumors with a spindle cell component, such as

isolated fibrous tumors, malignant fibrous histiocytoma, and malignant melanoma, can be accurately identified using the knowledge of SETTLE histological patterns and assistance from differential immunohistochemical markers.

Although SETTLE is a low-grade malignancy, distant metastasis is possible, with the lung being the most common site of metastasis. In some cases, SETTLE lesions also metastasize to the lymph nodes, bones, and kidneys. Distant SETTLE metastases generally occur at a late stage, up to 25 years after the initial diagnosis [10]. Even in the presence of metastatic lesions, the patient can still survive for a long time after treatment. However, there have been some reports on short-term metastases and even patient death [11]. The treatment of SETTLE primarily involves surgical resection. Chemotherapy and radiotherapy may represent a feasible approach for patients with advanced disease to control tumor growth, local infiltration, and bloodstream metastasis. Since late metastases may occur, long-term follow-up is recommended to detect such cases [12]. In our patient, no tumor recurrence or metastasis was observed even at postoperative 8-month follow-up.

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Conflicts of interest

The authors indicated no potential conflicts of interest.

Author contributions

All authors contributed to data acquisition, data interpretation, and reviewed and approved the final version of this manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethical approval

Not applicable.

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