Case Report

Review of the touch preparation cytology of spindle epithelial tumor with thymus-like differentiation

ABSTRACT

We experienced a case of spindle epithelial tumor with thymus-like differentiation (SETTLE) with touch preparation cytology performed during the intraoperative frozen section diagnosis in a 22-year-old woman. The tumor was partially encapsulated by fibrous capsule. It was a highly cellular biphasic tumor characterized by fasciculated spindle cells with streaming pattern and tubulopapillary epithelial component. The tumor cells were positive for cytokeratin, vimentin, c-kit, epithelial membrane antigen (EMA), and thyroid transcription factor-1 (TTF-1). However, the tumor cells were negative for thyroglobulin, calcitonin, CD99, S-100 protein, CD34, smooth muscle actin, HBME-1, and galectin-3. The reviewed touch smears showed tight clusters with high cellularity. Most cellular clusters showed papillary configuration. However, some clusters showed spindle cells with streaming pattern. The spindle tumor cells showed elongated and cigar-shaped nuclei. Although the incidence is very rare, SETTLE should be included in the differential diagnosis when a spindle cell neoplasm is encountered in touch preparation cytology in young patients with a thyroid mass.

Key words: Cytology; spindle epithelial tumor with thymus-like differentiation (SETTLE); thyroid; touch preparation

Introduction

Spindle epithelial tumor with thymus-like differentiation (SETTLE) is a malignant tumor of the thyroid gland, which shows thymic or related branchial pouch differentiation.[1] This tumor is believed to be derived from the third or fourth branchial pouch and thymic remnants.[2] SETTLE is regarded as a low-grade malignant neoplasm because of its slow-growing nature and protracted clinical behavior.[1,2] To the best of our knowledge, there have been 42 published cases of SETTLE till now. The cytologic features of SETTLE have been rarely described in only eight cases.[1,3-9] Here we present the cytologic, histologic, and immunohistochemical findings and the review of literature including its differential diagnosis.

Case Report

A 22-year-old woman complained of a bulging neck mass at the primary clinic. She was diagnosed with “papillary carcinoma” on fine-needle aspiration at a local pathology laboratory. She was transferred to our hospital for surgical treatment. The slides of aspiration cytology were not available for review. The ultrasonography demonstrated a well-defined hypoechoic mass, measuring 3.9 × 3.4 cm in the left lobe of the thyroid. The cervical lymph nodes were unremarkable. She underwent operation.

During the process of frozen section diagnosis, the touch preparation cytology was performed. The frozen section
slide showed mostly papillary epithelial configuration intermixed with focal spindle cell component. The touch preparation slides showed tight clusters of spindle or ovoid tumor cells with papillary configuration. The frozen section diagnosis was papillary carcinoma. On the histologic examination, the tumor was a highly cellular biphasic tumor characterized by fasciculated spindle cells with streaming pattern and tubulopapillary epithelial structures. The fasciculated spindle cells had scanty cytoplasm and elongated nuclei with indistinct cell borders. The epithelial cells of the tubulopapillary structures showed abundant cytoplasm and round to ovoid nuclei. The tumor cells were positive for cytokeratin, vimentin, c-kit, epithelial membrane antigen (EMA), and thyroid transcription factor-1 (TTF-1). However, the tumor cells were negative for thyroglobulin, calcitonin, CD99, S-100 protein, CD34, smooth muscle actin, HBME-1, and galectin-3. The final diagnosis was SETTLE. After the final diagnosis was made, touch preparation slides were reviewed. The smears showed tight clusters with high cellularity in a bloody background. Most cellular clusters showed papillary configuration. However, some clusters showed spindle cells with scanty cytoplasm and indistinct cell borders. The spindle cells showed elongated and cigar-shaped nuclei with fine chromatin and inconspicuous nucleoli [Figure 1]. No intranuclear cytoplasmic inclusions or nuclear grooves were seen. After the operation, the patient is doing well without any evidence of recurrence or metastasis for 12 months.

Discussion

We experienced a touch preparation cytology of SETTLE during the frozen section diagnosis and described the characteristic cytologic features. We searched reports including the cytologic findings of SETTLE in PubMed and found only eight cases in the English literature.[1,3-9] All of them were case reports with fine-needle aspiration cytology. No touch preparation cytology of SETTLE was found as such as our case. Most reports have described the cytologic findings of SETTLE as highly cellular smears composed of spindle cells and/or epithelial cells. The previously reported cases, along with their characteristic cytologic findings, are summarized in Table 1.

Recently, Recondo et al.[2] reported a case of SETTLE with a comprehensive review of the literature. They summarized the clinical characteristics of all published SETTLE cases. SETTLE predominantly affected children and young adults. Their mean age was 19 years with a range of 2-59 years. Clinically, SETTLE presented as a painless neck mass. Twenty-six percent of the patients developed metastatic disease. SETTLE showed the latency to develop metastasis with a mean time of 10 years.

Table 1: The cytologic findings of SETTLE described in the literature

| Cases  | Age (years) | Sex | Size (cm) | Cytologic findings                                                                 | Cytologic diagnosis | Ref. |
|--------|-------------|-----|-----------|-----------------------------------------------------------------------------------|---------------------|------|
| Case 1 | 14          | F   | 2.4       | Highly cellular smears consisting of mainly spindle cells                          | SETTLE              | [1]  |
| Case 2 | 15          | M   | 3         | Numerous cohesive clumps of spindled and elongated cells                          | Synovial sarcoma    | [3]  |
| Case 3 | 12          | F   | 2.9       | Cellular smears with dissociated cells, naked oval nuclei and aggregates           | MC or SETTLE        | [4]  |
| Case 4 | 16          | F   | 1.9       | Moderately cellular smears consisting of single and loosely grouped spindle cells  | MC                  | [5]  |
| Case 5 | 8           | M   | 5         | Highly cellular smears with neoplastic ovoid to spindle cells                     | MC                  | [6]  |
| Case 6 | 15          | M   | 3         | Richly cellular smears consisting of predominantly spindle cells and glandular     | Synovial sarcoma    | [7]  |
|        |             |     |           | epithelial cells                                                                  |                     |      |
| Case 7 | 29          | M   | 3         | Cohesive clusters of monomorphic spindle cells with ill-defined cytoplasm          | SETTLE              | [8]  |
| Case 8 | 11          | M   | 5.3       | Spindle elements with elongated nuclei, fine chromatin, and small nucleoli         | MC                  | [9]  |
| Our case | 22         | F   | 3.9       | Highly cellular and biphasic pattern composed of dense groups of spindle cells and intermixed epithelial clusters | PC                  |      |

M: Male, F: Female, SETTLE: Spindle epithelial tumor with thymus-like differentiation, MC: Medullary carcinoma, PC: Papillary carcinoma

Figure 1: (a and b) The smears were highly cellular and showed a biphasic pattern composed of dense groups of spindle cells and intermixed epithelial clusters. The spindle cells revealed scanty cytoplasm and uniform, elongated, or cigar-shaped nuclei. (c) The epithelial cells showed abundant cytoplasm and variable sized oval nuclei with indistinct nucleoli. (d) The tumor showed a biphasic histologic pattern composed of a spindle cell component and a tubulopapillary epithelial cell component. (a: ×100, b: ×200, c: ×400, d: H and E, ×100)
Grossly, SETTLE usually presents as an encapsulated or partially circumscribed mass with grayish to tan cut surface. Microscopically, SETTLE shows a highly cellular biphasic pattern and is composed of cellular sheets, short fascicles, interlacing bundles or attenuated storiform arrangement of spindle cells, and glandular epithelial component. The nuclei of spindle cells are oval to elongated and characterized by distinct nuclear membrane, inconspicuous nucleoli, and evenly distributed chromatin. The glandular tumor cells show narrow tubular, tubulopapillary, trabecular, or pseudopapillary structures. Immunohistochemically, the tumor cells show immunoreactivity for pan-cytokeratin, smooth muscle actin, c-kit and vimentin, and no immunoreactivity for thyroglobulin, calcitonin, S-100 protein, chromogranin, synaptophysin, CD34, CD99, and TTF-1.

We described a case of SETTLE of the thyroid gland with touch preparation cytologic findings. Although the incidence is very rare, SETTLE should be included in the differential diagnosis when a spindle cell neoplasm is encountered in touch preparation cytology in young patients with a thyroid mass. The touch preparation cytology during the frozen section diagnosis may be helpful to confirm the diagnosis of thyroid cancer.

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Conflicts of interest
There are no conflicts of interest.

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