Cytological features of solid variants of papillary thyroid carcinoma: a fine needle aspiration cytology study of 18 cases

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Objective: Solid variants of papillary thyroid carcinoma (SV-PTC) are rare, and there have been few reports describing the cytological findings of such variants.

Methods: The cytological features of cellular specimens aspirated from 18 histologically confirmed SV-PTC cases were evaluated, retrospectively.

Results: Solid and small papillary clusters were observed in 14 (77.8%) and 13 (72.2%) cases, respectively. The incidences of large papillary clusters (11.1%) and sheet-like arrangements (11.1%) were low. Nuclear features were consistent with conventional PTC. The background was clean, and there were no colloid materials, foamy histiocytes, multinucleated giant cells, psammoma bodies, or necrotic materials.

Conclusions: Solid clusters and small papillary clusters in conjunction with a clean background are diagnostic clues that indicate SV-PTC cytologically. It is thought that small papillary clusters reflect the micropapillary growth pattern seen within the lumen of middle-sized follicular structures. The presence of nuclear findings typical of conventional PTC and the absence of mitotic figures and necrotic materials are important for distinguishing SV-PTC from poorly differentiated carcinoma.

Keywords: thyroid, papillary carcinoma, solid variant, aspiration cytology, small papillary cluster, micropapillary growth

Introduction

Solid variants of papillary thyroid carcinoma (SV-PTC) are rare,¹,² and account for ~3% of papillary thyroid carcinoma (PTC) cases.²⁻⁴ SV-PTC tend to occur in children²,⁴ and were reported in > 30% of patients with PTC after the Chernobyl nuclear accident.³,⁵ Histologically, SV-PTC are characterised by a predominantly solid growth pattern, the presence of cytological features typical of PTC, and the absence of necrosis.¹,⁴⁻⁶ The prognosis of SV-PTC is comparable with that of PTC and differs from that of poorly differentiated thyroid carcinoma (PDTC) that also exhibits a solid growth pattern.²,⁴,⁵

The clinical and histological features of SV-PTC have been well documented, but reports describing the cytological features are limited.¹,³,⁷⁻⁹ However, Giorgadze et al.³ examined pre-operative fine needle aspiration (FNA) samples from 13 cases of pure SV-PTC and concluded that SV-PTC were heterogeneous tumours. Because SV-PTC have been well established as a subtype of PTC, we hypothesized that aspiration cytology samples would reveal the
characteristic features of SV-PTC. The aim of the present study was to establish the cytological characteristics of SV-PTC. Therefore, we examined cytological specimens aspirated from 18 histologically confirmed SV-PTC cases, retrospectively.

Materials and methods

We reviewed a pathology report database of 5717 patients with PTC that underwent surgery at Kuma Hospital from January 2011 to December 2015. Nineteen (0.33%) patients had SV-PTC. A histological diagnosis of SV-PTC required the following: (i) a solid or insular or trabecular growth pattern in >50% of the primary tumour nodule, (ii) the presence of cytological features typical of PTC, and (iii) the absence of necrosis. Ultrasound-guided aspiration cytology was performed using a 22-gauge needle without local anaesthesia. Smears were produced using the conventional method and were stained with Papanicolaou stain. When bloody samples were aspirated, we removed the blood components by tilting the preparations immediately after the smearing. We analysed the smears of 18 SV-PTC cases, retrospectively. One case was excluded because it was classed as ‘Unsatisfactory’ according to ‘the Bethesda System for Reporting Thyroid Cytopathology’.10 The following cytological features were examined: (i) cellularity, (ii) background components (lymphocytes, foamy histiocytes, multinucleated giant cells, ropy colloid, psammoma bodies, and necrotic materials), (iii) cellular arrangements (predominant isolated pattern, solid clusters, small and large papillary clusters, trabecular arrangement, sheet-like arrangement, and follicular arrangement), and (iv) cellular morphology (ground-glass chromatin, intranuclear cytoplasmic inclusions, grooved nuclei, nuclear indentation, irregular-shaped nuclei, metaplastic cytoplasm, and mitotic figures). A solid cluster was defined as a three-dimensional aggregation of carcinoma cells without stromal or colloid components. Small and large papillary clusters were defined as a papillary tissue fragment associated with fibrous connective tissue stroma, composed of <100 carcinoma cells and more than 200 carcinoma cells, respectively. We also reviewed clinical data that were obtained from the medical records of Kuma Hospital. Ultrasound interpretation was performed according to ultrasound classification for thyroid nodules at Kuma Hospital.11

Results

Clinical findings

The patients included 15 women and 3 men, with a mean age of 42 years (range, 12–68 years). There were no cases with a history of ionising radiation exposure. Ultrasonographically, the greatest dimension of the tumours ranged from 0.5 to 3.7 cm (mean, 2.0 cm), and tumours were classed as undetermined, suspicious for malignancy, and malignant in 5, 3, and 10 cases, respectively.

Original cytology reports

According to the original cytology reports, there were 2, 3, and 13 cases of ‘atypia of undetermined significance (AUS)’, ‘suspicious for malignancy’, and ‘malignant’, respectively. In all ‘AUS’ and ‘suspicious for malignancy’ cases, PTC was suspected. The estimated diagnoses in the 13 ‘malignant’ cases were PTC in 7, follicular variant of PTC in 1, SV-PTC in 2 and PDTC in 3.

Cytological findings

The cytological findings of the aspirates obtained from the 18 SV-PTC cases are summarised in Table 1. All aspirated materials provided sufficient cellular material, and 12 (66.7%) cases exhibited high cellularity. The background was clean. There were no colloidal materials such as watery colloid, hyaline colloid, or ropy colloid. Three (16.7%) cases had a small number of lymphocytes. There was no evidence of foamy histiocytes, multinucleated giant cells, Psammoma bodies, or necrotic materials. The carcinoma cells tended to be less cohesive than conventional PTC, and isolated cells were the predominant pattern in 3 (16.7%) cases (Figure 1a). Three-dimensional solid clusters were detected in 14 (77.8%) cases (Figure 1b). There were no structures or colloids within the clusters, and endothelial wrapping was not present around the clusters. Thirteen (72.2%) cases had small papillary clusters (Figure 1c). Spindle-shaped nuclei corresponding to those of endothelial cells or fibroblasts were present in the clusters. Capillary lumens were occasionally observed in the stromal material. Nuclear palisading with an ordered arrangement was not apparent at cluster peripheries. Two of the 13 cases with small papillary clusters (11.1%) also exhibited large papillary clusters that are seen in conventional PTC with

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Table 1. Cytological findings in 18 solid variants of papillary thyroid carcinoma

| Characteristic                        | N (%) |
|---------------------------------------|-------|
| High cellularity                      | 12 (66.7) |
| Background components                 |       |
| Lymphocytes                           | 3 (16.7) |
| Foamy histiocytes                     | 0 (0)  |
| Multinucleated giant cells            | 0 (0)  |
| Ropy colloid                          | 0 (0)  |
| Psammoma bodies                       | 0 (0)  |
| Necrotic materials                    | 0 (0)  |
| Predominant isolated pattern          | 3 (16.7) |
| Solid clusters                        | 14 (77.8) |
| With endothelial wrapping             | 0 (0)  |
| Small papillary clusters              | 13 (72.2) |
| Large papillary clusters              | 2 (11.1) |
| Trabecular arrangement                | 4 (22.2) |
| Sheet-like arrangement                | 2 (11.1) |
| Follicular arrangement                | 5 (27.8) |
| Ground-glass chromatin                | 14 (77.8) |
| Intranuclear cytoplasmic inclusions   | 14 (77.8) |
| Grooved nuclei                        | 18 (100) |
| Nuclear indentation                   | 11 (61.1) |
| Irregular-shaped nuclei               | 17 (94.4) |
| Metaplastic cytoplasm                 | 0 (0)  |
| Mitotic figures                       | 0 (0)  |

Carcinoma cells were round with faintly stained cytoplasm, and an indistinct border. So-called metaplastic cells with densely stained cytoplasm were not observed. The nuclei were typical of PTC. Ground-glass chromatin (Figure 1d), intranuclear cytoplasmic inclusions (Figure 1d), grooved nuclei (Figure 1d), nuclear indentations (Figure 1e) and irregular-shaped nuclei were seen in 14 (77.8%), 14 (77.8%), 18 (100%), 11 (61.1%) and 17 (94.4%) cases, respectively. There were no mitotic figures.

Pathological findings

All cases exhibited invasive growth. Two cases were partially encapsulated, similar to widely invasive follicular carcinoma. Carcinoma cells showed solid and insular growth patterns (Figure 2a). In 14 out of 18 cases (77.8%), these patterns were predominant. The remaining 4 cases showed a mostly trabecular pattern. Micropapillary growth patterns mimicking kidney glomeruli were seen within the lumen of middle-sized follicular structures (Figure 2b). Papillary and follicular patterns that are present in a papillary growth pattern. Follicular, sheet-like and trabecular arrangements were seen in 5 (27.8%), 2 (11.1%) and 4 (22.2%) cases, respectively, but they were not the predominant pattern.

Figure 1. Cytological findings of solid variants of papillary thyroid carcinoma. (a) isolated pattern (Papanicoloau stain ×400 magnification). (b) solid cluster (Papanicoloau stain ×400 magnification). (c) small papillary cluster (Papanicoloau stain ×400 magnification). (d) ground-glass chromatin, intranuclear cytoplasmic inclusions and grooved nuclei (Papanicoloau stain ×1000 magnification). (e) nuclear indentation (Papanicoloau stain ×1000 magnification).
conventional PTC were observed focally in 3 and 8 cases, respectively. The carcinoma cells were morphologically typical of PTC. Atypical cells, mitotic figures, or necrosis were not observed. Psammoma bodies were present in 7 (38.9%) cases. Eight (44.4%) cases showed invasion to extrathyroidal connective tissue. Nine (50.0%) cases revealed central and/or lateral nodal metastasis. There were no cases with distant metastasis at the time of surgery.

**Discussion**

SV-PTC, also known as a trabecular variant of PTC,6,8 is characterised microscopically by solid sheets of carcinoma cells with the typical nuclear features of PTC.1,4,9 Although the proportion of solid areas occupying the tumour differs,1,3,5,6 most reports have described that SV-PTC is composed of solid nests predominantly.1,6 In the present study, a histological diagnosis of SV-PTC was made according to the following features: a solid or insular or trabecular growth pattern in > 50% of the primary tumour nodule, the presence of cytological features typical of PTC and the absence of necrosis, as proposed by Nikiforov et al.6 Small areas of microfollicular and/or poorly formed papillae were intimately intermingled with solid areas.

Compared with conventional PTC, the prevalence of SV-PTC is higher in young patients,4,6 especially those exposed to ionising radiation.2,5 However, in the present study, the ages of patients with SV-PTC were similar to those reported for patients with conventional PTC. Also, there were no cases with a history of ionising radiation exposure. Therefore, we believe that such clinical information is not required for a cytological diagnosis of SV-PTC.

Nguyen and Lee8 reported the cytological features of three SV-PTC cases. Two of them showed irregular anastomosing thick cords composed of carcinoma cells, which reflected the histological growth pattern. Troncone et al.1 reported a case of SV-PTC that was recognised pre-operatively by FNAC as a solid variant. The smears were composed of solid tumour cell aggregates arranged in syncytial-type tissue fragments. Giorgadze et al.3 examined the cytological features of 13 SV-PTC cases and classified them into 3 patterns. The cohesive, syncytial tissue-fragment pattern was recognised as SV-PTC associated with encapsulation and indolent behaviour. The microfollicular or trabecular pattern was indistinguishable from that of the follicular variant of PTC and had intermediate behaviour. The single-cell pattern correlated with infiltrative tumour growth and was not unique to SV-PTC. According to the above studies, the architectural arrangement of carcinoma cells, such as irregular anastomosing thick cords, solid tumour cell aggregates and syncytial tissue fragments are important diagnostic parameters for SV-PTC. In the present study, solid clusters that were defined as carcinoma cells aggregations without stromal or colloid components were detected in the majority of SV-PTC cases. As solid clusters reflect a solid growth pattern histologically characteristic of SV-PTC, we believe these clusters are a diagnostic clue indicating SV-PTC.

Papillary clusters seen in conventional PTC with papillary growth are usually large, branching, and associated with thick fibrovascular stroma.12 Sheet-like arrangements are observed as a component of

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**Figure 2.** Pathological findings of solid variants of papillary thyroid carcinoma. (a) solid growth pattern (Hematoxylin and eosin stain ×200 magnification), and (b) micropapillary growth pattern mimicking the kidney glomeruli (Hematoxylin and eosin stain ×200 magnification).
papillary clusters or in the background. Considering histology, when the typical papillary pattern predominates, SV-PTC can be excluded. We focused on the presence of small papillary clusters composed of < 100 carcinoma cells that were associated with fibrous connective tissue stroma. These small papillary clusters might reflect poorly formed papillae that mimic the kidney glomeruli, as seen within the lumen of middle-sized follicular structures. We believe that these small papillary clusters could be a diagnostic indicator of SV-PTC when large papillary clusters or sheet-like arrangements are absent.

Histologically, SV-PTC must be differentiated from PDTC. SV-PTC and PDTC both have solid and trabecular growth patterns. Therefore, the cellular arrangement might not be useful for a differential diagnosis. SV-PTC exhibits the nuclear features characteristic of PTC, and PDTC has nuclei that are more atypical. Therefore, to distinguish between SV-PTC and PDTC, one should focus on the nuclear findings. Additionally, PDTC frequently exhibits mitotic figures, necrosis and endothelial wrapping of cell clusters. In the present study, all of the cases of SV-PTC had nuclear features typical of PTC, and no mitotic figures or necrotic materials were identified. Also, endothelial wrapping of cell clusters was not observed. Therefore, PDTC could be ruled out.

In conclusion, solid clusters and small papillary clusters in conjunction with a clean background are diagnostic clues that indicate SV-PTC cytologically. It is thought that small papillary clusters reflect the micropapillary growth seen within the lumen of the middle-sized follicular structure. The presence of nuclear findings typical of conventional PTC and the absence of mitotic figures and necrotic materials are important to differentiate SV-PTC from PDTC.

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The authors have no connection to any companies or products mentioned in this article.

Ethics statement

The authors confirm that the study complies with the guidelines of the ethics committee of Kuma hospital and that all subjects provided informed consent.

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