Hashimoto's Thyroiditis or Papillary Carcinoma

36

Yun Zhu and Tiesheng Wang

Abstract

The nuclei of the oxyphilic or non-oxyphilic follicular epithelium in Hashimoto's thyroiditis often exhibit considerable nuclear atypia, showing a range of nuclear changes that mimic those encountered in papillary thyroid carcinoma. Syncytial tissue fragments with or without any architectural configurations; enlarged nuclei with finely granular, powdery, or watery chromatin and nuclear contour irregularity; nuclear pseudoinclusions; nuclear grooves; and multiple micro- and/or macronucleoli could be applicable as the minimal criteria for the cytological diagnosis of papillary carcinoma. It is essential to remain in conservative diagnosis until the minimal criteria of papillary thyroid carcinoma is fulfilled. One single cytological feature of papillary carcinoma proves to be meaningless to conclude malignancy in Hashimoto's thyroiditis since Hashimoto's thyroiditis shows several overlapping features with papillary carcinoma.

Follicular epithelium in Hashimoto's thyroiditis may display a range of nuclear changes that mimic those encountered in papillary thyroid carcinoma (PTC), constituting important diagnostic pitfalls. Suspecting PTC on fine needle aspiration (FNA) of the thyroid with only Hashimoto's thyroiditis is not unusual in our practice. In this chapter, we demonstrate three cases that were misinterpreted, aiming to identify the cytological features leading to misinterpretation in Hashimoto's thyroiditis, and explore how to avoid an overdiagnosis of malignancy (see Chaps. 3, 19 and 23).

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36.1 Case 1: Follicular Carcinoma, Minimally Invasive Type

36.1.1 Clinical History

A 23-year-old woman with a family history of PTC was admitted to our hospital for a physical examination. Ultrasound detected an 8 × 8 × 9 mm, regularly shaped, partially circumscribed, and heterogeneous isoechoic thyroid nodule with thin halo in isthmus. Ultrasound-guided FNA (US-FNA) was performed as the patient strongly requested for.

Cytological examination revealed an extremely cellular aspirate showing large numbers of tissue fragments with papillary-like architecture (Fig. 36.1) in a background of sparsely scattered lymphocytes (Figs. 36.1 and 36.2) and some multinucleated giant cells (Fig. 36.3). The cell nuclei were enlarged and slightly crowded with granular chromatin and inconspicuous nucleoli (Fig. 36.2), showing some equivocal features of conventional PTC. Overwhelmingly papillary-like fragments of follicular cells, a paucity of background lymphocytes, and a few cells exhibiting worrisome

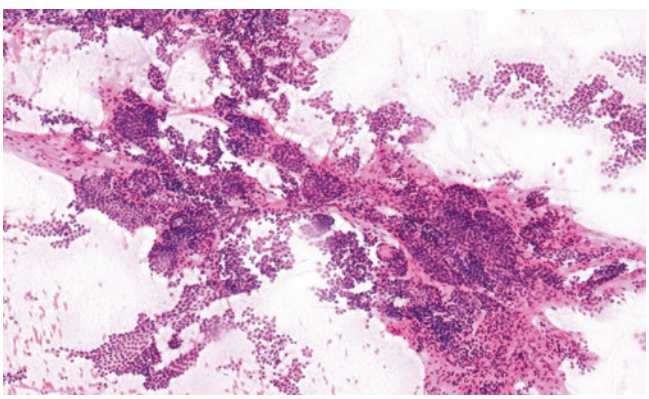

Fig. 36.1 Medium power view of the papillary-like architecture. The component cells are minimally enlarged and round with granular chromatin. Nuclear characteristics of papillary carcinoma are rarely observed besides the architecture

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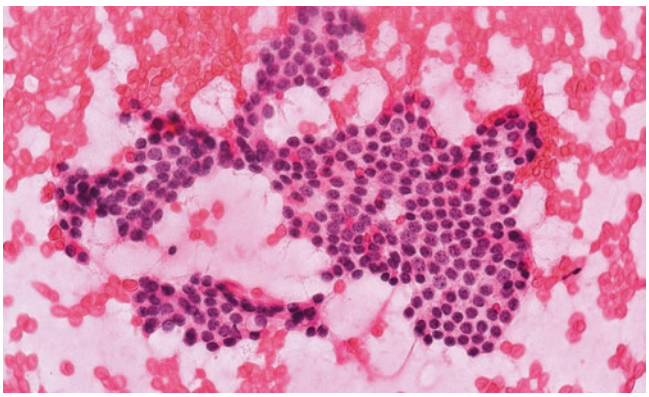

Fig. 36.2 High magnification showing anastomosing trabeculae of follicular cells with syncytial arrangement. The nuclei are enlarged, slightly crowded, and altered in polarity with granular chromatin and nucleoli. The background is clean and lacks colloid

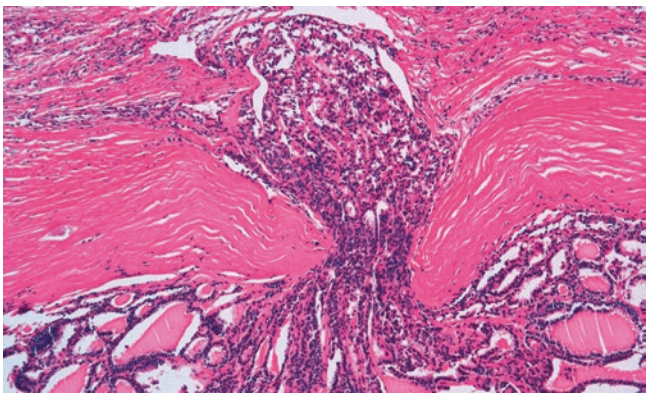

Fig. 36.4 The invasion is seen as involving the entire and going beyond the capsule. Follicular cells in this follicular carcinoma have slightly crowded and overlapped nuclei with compact or coarsely granular chromatin, but do not exhibit worrisome nuclear features of PTC

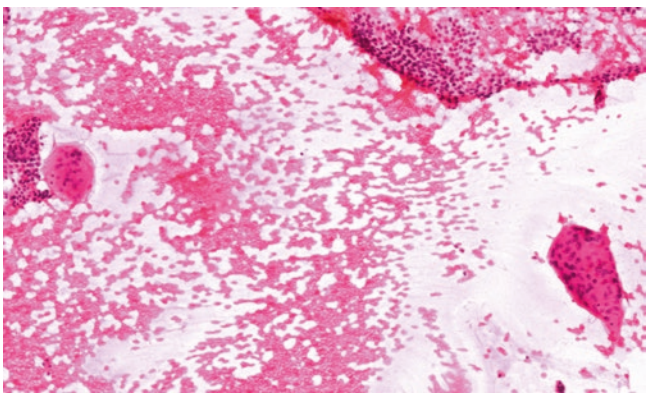

Fig. 36.3 Note two isolated multinucleated giant cells in the aspirate. This aspirate is interpreted as "indeterminate – not exclude papillary carcinoma"

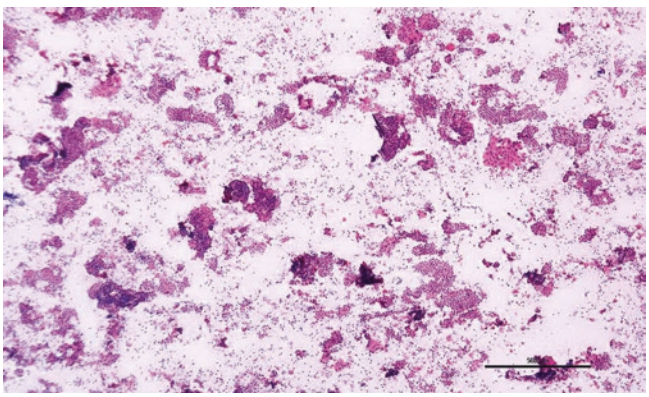

Fig. 36.5 Extremely cellular aspirate in a background of Hashimoto's thyroiditis on the low-power view. Note the follicular cells, Hürthle cells, and inflammatory cells in varying proportions on the medium-power view

nuclear features of PTC as well as the family history led to the diagnosis of "indeterminate—not exclude PTC."

On gross examination of the isthmus, a 0.8 cm, solitary reddish-brown, well-circumscribed nodule with thick capsule was identified. Histopathological examination showed that the tumor cells split the thick and fibrotic capsule with complete transgression, which led to the diagnosis of follicular carcinoma minimally invasive type (Fig. 36.4). Most follicular cells in this follicular carcinoma exhibited slightly crowded and overlapped nuclei with compact or coarsely granular chromatin and did not show worrisome nuclear features of PTC. (see Chaps. 1, 21 and 22 for true positive PTC for comparison in which several large branching tissue fragments of follicular cells with central fibrovascular cores (Fig. 1.13a of Chap. 1) and typical nuclear features of PTC as pale powdery chromatin (Fig. 1.29 of Chap. 1), nucleoli, nuclear grooves (Fig. 1.31 of Chap. 1), and intranuclear cytoplasmic inclusions (Fig. 1.30 of Chap. 1) in a clean background are discussed.

36.2 Case 2: Hashimoto's Thyroiditis with Marked Hürthle Cell Metaplasia

36.2.1 Clinical History

This was a 49-year-old woman who underwent a health check. Neck ultrasound scan discovered a diffusely enlarged gland with developing fibrosis. A hypoechoic focus of 3 × 3 × 4 mm in size with irregularly blurred margins in the right lobe of thyroid gland was noticed. Papillary thyroid microcarcinoma (PTMC) was suspected sonographically. Therefore, US-FNA was performed.

Cytological examination revealed extremely cellular aspirates with follicular cells, Hürthle cells, and inflammatory cells in varying proportions (Figs. 36.5 and 36.6). Mildly enlarged and overlapped cells are arranged in syncytial fashion (Fig. 36.7) and exhibited poorly defined cell borders. The atypical nuclei showed finely granular chromatin,

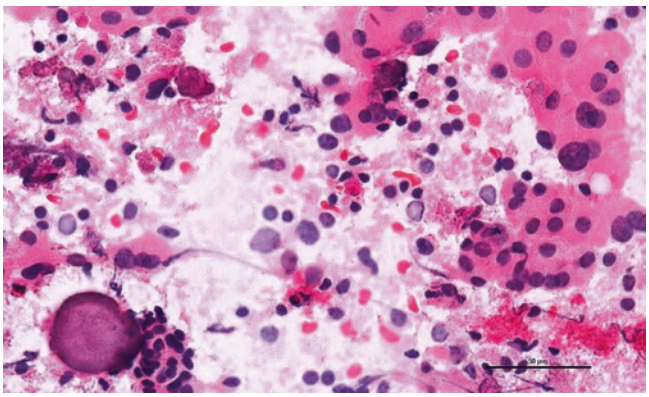

Fig. 36.6 High magnification shows tissue fragments of markedly pleomorphic Hürthle cells with bizarre nuclei. This arrangement is not consistent with that of Hürthle cell neoplasm. The low left field shows a probably psammoma body

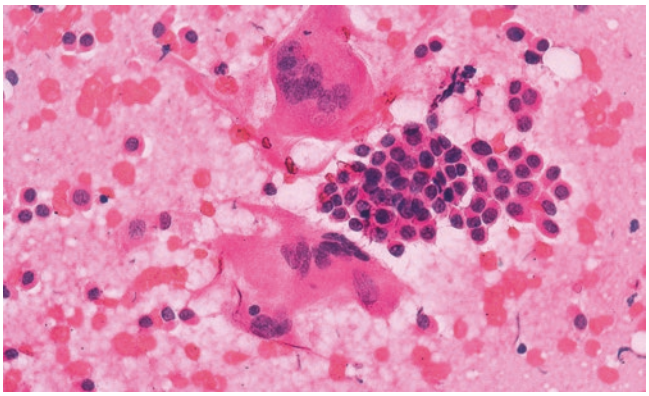

Fig. 36.7 One group of mildly enlarged and overlapped cells arranged in a syncytial fashion with poorly defined cell border and atypical nuclei. The nuclei exhibit finely granular chromatin, micronucleoli, and occasional nuclear grooves. Multinucleated giant cells are also noticed

micronucleoli, and occasional nuclear grooves (Fig. 36.8). A probably psammoma body (Fig. 36.6), multinucleated giant cells (Fig. 36.7), and extremely crowded cells with three-dimensional arrangement (Fig. 36.8) were also noticed; thus a diagnosis of suspicious for PTC was rendered. Histological sections revealed Hashimoto's thyroiditis with marked Hürthle cell metaplasia and nuclear atypia (Figs. 36.9 and 36.10), but neoplastic cells were not found.

36.3 Case 3: Hashimoto's Thyroiditis with an Atypical Hyperplastic Nodule

36.3.1 Clinical History

This was a 45-year-old woman who was suffering from Hashimoto's thyroiditis for over 10 years. Ultrasound images showed multiple hypoechogenic areas varying in

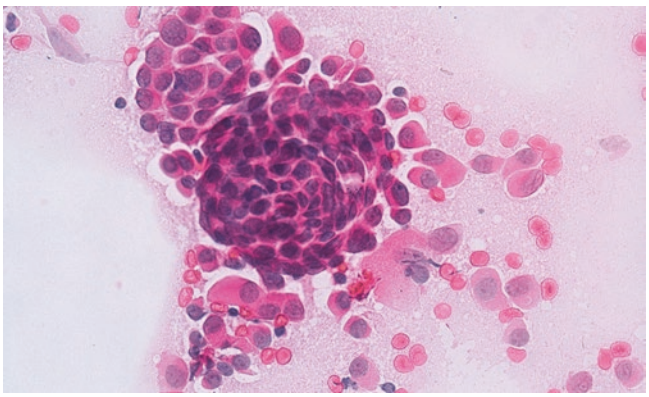

Fig. 36.8 A syncytial fragment with extremely crowded nuclei, smooth external contour, and three-dimensional appearance. Scattered follicular cells in the peripheral area exhibit finely granular chromatin and occasional nuclear grooves. This aspirate is interpreted as suspicious of papillary carcinoma

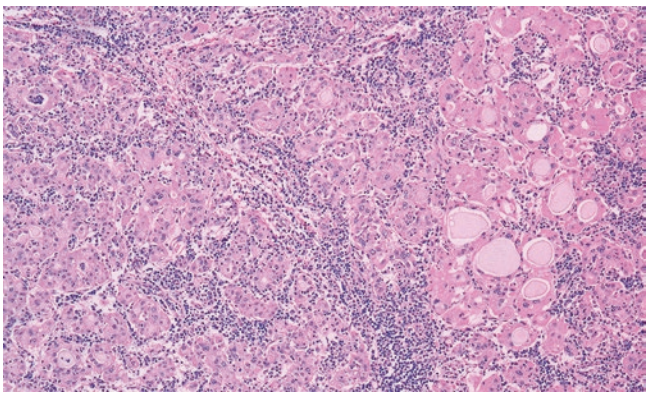

Fig. 36.9 Subsequent thyroidectomy revealed Hashimoto's thyroiditis, but not a neoplastic nodule

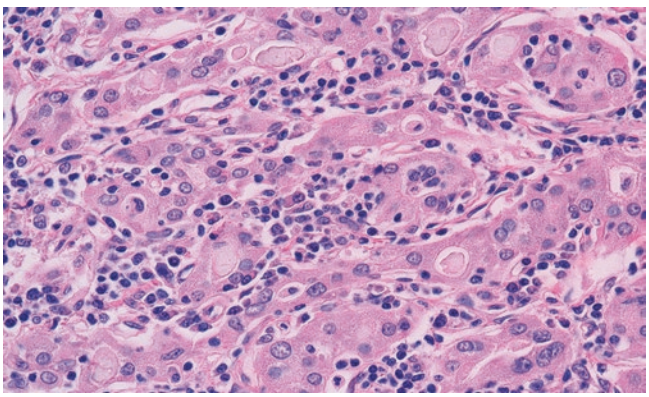

Fig. 36.10 High magnification showing mildly crowded Hürthle cell metaplasia with mild nuclear atypia. Note interfollicular lymphoid cell infiltration

size in both lobes. Among them, a 13 × 11 × 10 mm focal hypoechogenic lesion was detected in the right lobe with ill-defined margins and microcalcification (Fig. 36.11), raising a possibility of PTC. Consequently, FNA was per-

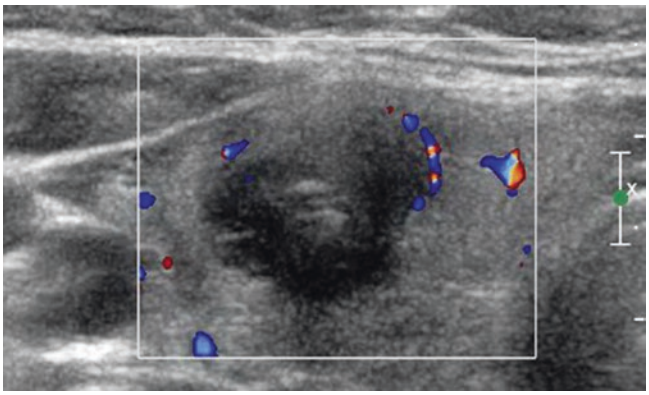

Fig. 36.11 Ultrasound image shows a focal hypoechogenic lesion with an ill-defined margin and microcalcification

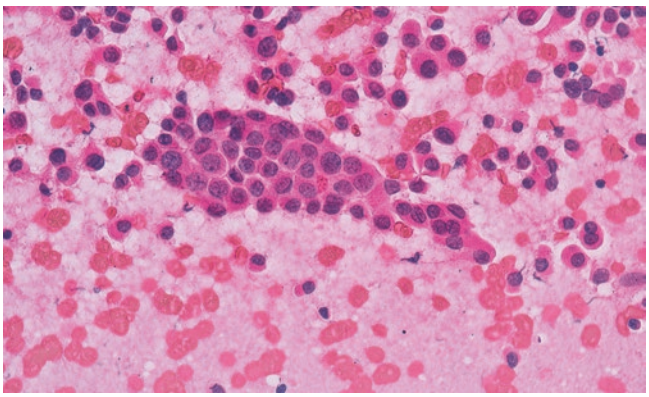

Fig. 36.14 The chromatin is finely granular. The nucleoli and grooves are present

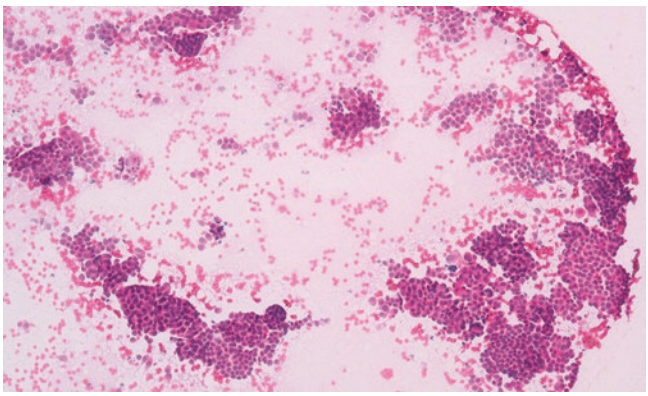

Fig. 36.12 Showing syncytial or monolayered tissue fragments of follicular cells in neither follicular nor papillary pattern

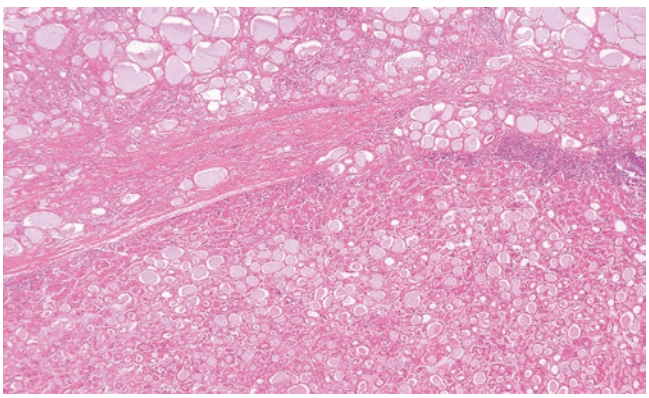

Fig. 36.15 Low-power view shows a partly encapsulated tumor with a follicular growth pattern coexisted with Hashimoto's thyroiditis

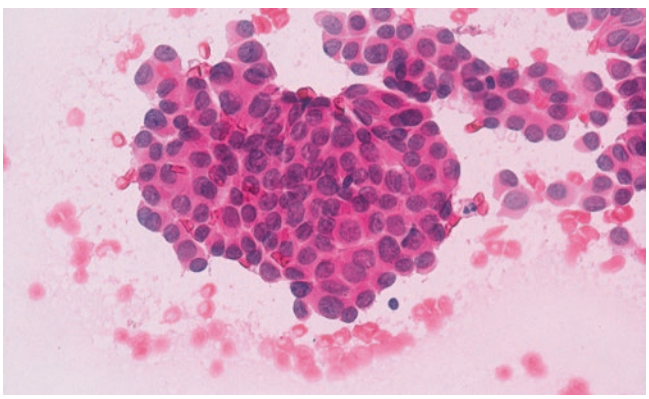

Fig. 36.13 Markedly crowded and overlapped nuclei with an irregular nuclear contour

formed. Cytological examination showed a few of syncytial or monolayered tissue fragments of follicular epithelium with markedly crowded and overlapped nuclei with nuclear contour irregularity (Figs. 36.12 and 36.13). The chromatin was finely granular to powdery. Nucleoli and nuclear grooves were present (Fig. 36.14). A diagnosis of PTC was rendered. Histological sections revealed a well-circumscribed follicular pattern tumor in a background of Hashimoto's thyroiditis (Fig. 36.15). Some areas of this tumor presented mildly enlarged nuclei with nuclear contour irregularity and pale chromatin, reminiscent of PTC (Fig. 36.16), which might include differential diagnosis of follicular variant papillary thyroid carcinoma (FVPTC). However, there are debates on diagnostic criteria of this variant, and observer variation between benign follicular adenoma and malignant FVPTC was reported to be significant [1]. Chinese pathologists apply stricter criteria to noninvasive follicular pattern tumors with questionable PTC-type nuclei. Finally, a diagnosis of Hashimoto's thyroiditis with an atypical hyperplastic nodule was rendered, which was probably equivalent to FVPTC in the Western practice or NIFTP (noninvasive follicular thyroid neoplasm with papillary-like nuclear features) proposed recently by Nikiforov et al. [2] (see Chaps. 21, 24 and 25).

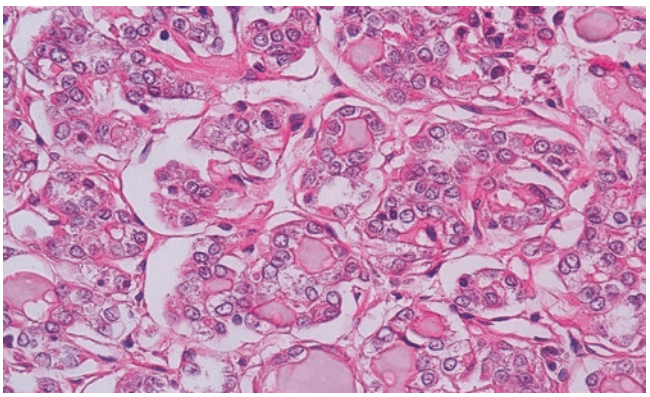

Fig. 36.16 Mildly enlarged nuclei with finely dispersed chromatin, empty appearance, and prominent nuclear membrane

36.4 Discussion

Hashimoto's thyroiditis is a main pitfall of overdiagnosis of PTC in thyroid cytology as reported in many literatures [3–9] (see Chap. 3). There are various cytologic features simulating PTC in Hashimoto's thyroiditis (see Chaps. 3, 19, 23, 24 and 25). In adequate specimens, it would not make us confused too much for diagnosis of Hashimoto's thyroiditis. However, the nuclei of the oxyphilic or non-oxyphilic follicular epithelium in Hashimoto's thyroiditis often exhibit considerable nuclear atypia, and there may have aggregates of a few of follicles containing cells that are indistinguishable from those seen in PTC as shown in Figs. 36.6, 36.8, and 36.10 [8–10]. It is one of the most significant pitfalls especially when the aspirate is strikingly cellular such as in Case 1 [6, 7]. Useful cytological features to differentiate Hashimoto's thyroiditis from PTC are also listed in Table 19.1 of Chap. 19. Kini et al. suggested that the minimal criteria for the diagnosis of PTC should include a syncytial-type tissue fragment of follicular epithelium, regardless of its architectural pattern, showing a typical nuclear morphology, i.e., pale-appearing enlarged nuclei with fine, dusty, or powdery chromatin, and a chromatin bar or ridge, single or multiple micro- and/or macronucleoli, and intranuclear cytoplasmic inclusions (Table 36.1) [6]. It has been proved to be extremely effective in our experience.

Harvey et al. reviewed thyroid FNA cases whose diagnoses were suspicious or positive for a thyroid neoplasm but the subsequent thyroidectomy specimen revealed Hashimoto's thyroiditis only and have concluded that lymphocyte-infiltrating epithelial cell group is a significant feature that would help differentiate between thyroid neoplasm and Hashimoto's thyroiditis [7]. The tissue fragments of follicular cells intimately permeated by lymphoid cells occur much more frequently in thyroiditis alone than in PTC coexisted with Hashimoto's thyroiditis in cytologic specimens. However, the cytologic evaluation greatly depends on the area sampled by the biopsy needle. When the nodule is discrete and encapsulated or non-capsulated but enlarged with few lymphoplasmacytic infiltrate, coexisting thyroiditis can be overlooked since the lymphocytes are extremely sparse or not sampled. Conversely, Hashimoto's thyroiditis with nonneoplastic follicular or Hürthle cell nodules usually has a lymphocytic infiltrate. Therefore, aspiration biopsy will exhibit follicular cells, Hürthle cells, and inflammatory cells in varying proportions as shown in Case 2 (Figs. 36.6 and 36.10), indicating a nonneoplastic process.

In case that the cellularity is marginal, sparsely scattered follicular cells exhibiting several features may seem to accord with the minimal criteria for the diagnosis of PTC, which may render a definite diagnosis really difficult [6]. Fortunately, a repeated FNA or a core needle tissue biopsy often solves the problem, and such circumstance occurs rarely in our experience.

Table 36.1 Minimal criteria for the cytological diagnosis of PTC

1.	Syncytial tissue fragments with or without any architectural configurations
2.	Enlarged nuclei with finely granular, powdery, or watery chromatin and nuclear contour irregularity
3.	Nuclear pseudoinclusions
4.	Nuclear grooves
5.	Multiple micro- and/or macronucleoli

36.5 Conclusion

It is essential to remain in conservative diagnosis until the minimal criteria of PTC is fulfilled. One single cytological feature of PTC proves to be meaningless to conclude malignancy in Hashimoto's thyroiditis since Hashimoto's thyroiditis shows several overlapping features with PTC. Extreme caution should also be taken when there are focal features suggestive of PTC, and the authors recommend to apply AUS category of the Bethesda, Thy 3a of the British system, TIR3A of the Italian system, or Indeterminate B (others) of the Japanese system instead of definite malignancy or suspicious for malignancy to these samples (see Chaps. 5–9 and 23).

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