Chapter 7
Thyroid Gland

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Normal Cytology

The thyroid gland is an endocrine organ located anterior to the trachea and consists of two lobes connected at the midline by the isthmus. Depending on demographics and nutritional factors, the thyroid gland weighs between 14 and 18.5 g [1–3]. Pyramidal lobe, a normal component of the thyroid gland, can be seen in 15–75% [4]. Ultimobranchial bodies give rise to C cells (calcitonin-secreting cells), mostly seen in the mid-upper portion of thyroid lobes rather than peripheral areas and isthmus [4].

Fine needle aspiration (FNA) examination of the thyroid gland usually shows thyroid follicular cells that are smaller in size, arranged in a macrofollicular pattern, monolayer sheets, or often in mixed macro- and microfollicular patterns (Figs. 7.1 and 7.2). Follicular cells are small, close to the size of red blood cells, with round to oval nuclei, finely granular chromatin material, and smooth nuclear membrane. In addition, follicular cells can show pigment accumulation, such as hemosiderin. Colloid is usually present in the background, and appearance is variable in different cytology preparations and can either be watery or dense or thick. A watery colloid consists of a thin colloid layer and should be distinguished from the background serum. Color appearance is also variable and pink-orange or green in Papanicolaou and violet-blue with or without cracking artifact in Diff-Quik stain preparations. Calcium oxalate crystals can also be seen [5].

Other elements that are present include macrophages, cyst lining cells, lymphocytes, and Hurthle cells. Hurthle cells are oncocytic or oxyphilic cells with abundant granular cytoplasm and nucleoli that can be conspicuous [6]. They appear green or orange on the Papanicolaou stain and purple on Diff-Quik preparation.

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S. M. Gilani, G. Cai (eds.), *Non-Neoplastic Cytology*,
https://doi.org/10.1007/978-3-031-44289-6_7

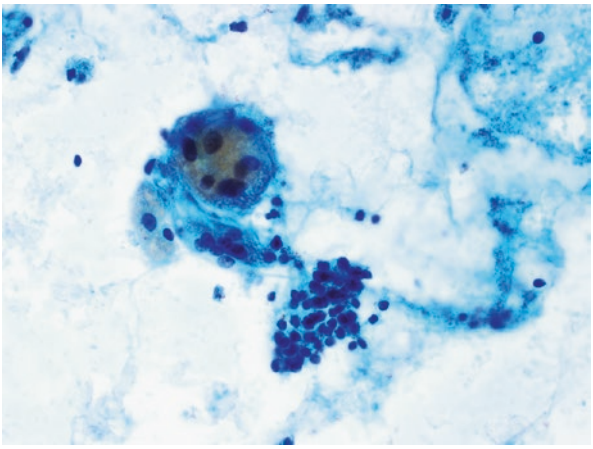


Fig. 7.1 Benign follicular cells with histiocytes (Papanicolaou stain × 400)

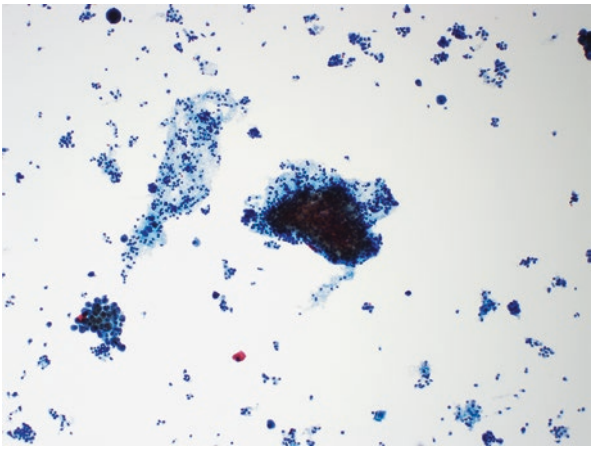


Fig. 7.2 Cellular specimen with mixed microfollicular and macrofollicular cells with histiocytes. No cytologic atypia is seen. Overall features showed mix population of cells and consistent with cellular goiter (ThinPrep × 100)

Adequacy Criteria

Thyroid FNA cytology evaluation should have at least six groups of follicular cells with at least ten cells in each group, preferably on one slide. There are a few exceptions to this adequacy criterion in certain scenarios, such as abundant colloid (Figs. 7.3 and 7.4), lymphocytic thyroiditis, or nuclear atypia in follicular cells [7]. Follicular cells should be well preserved without any obscuring artifact.

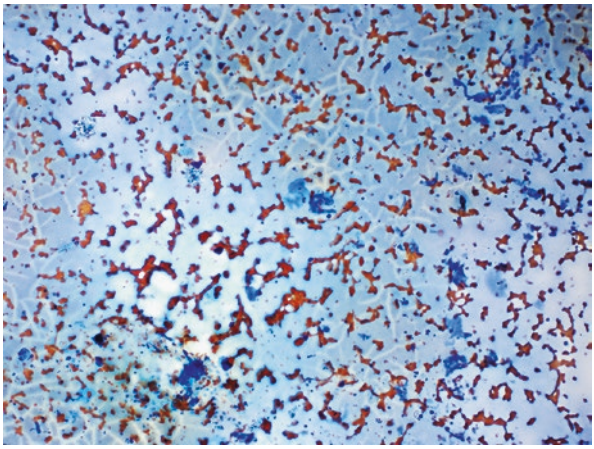


Fig. 7.3 Thin colloid with background histiocytes (Diff-Quik × 100)

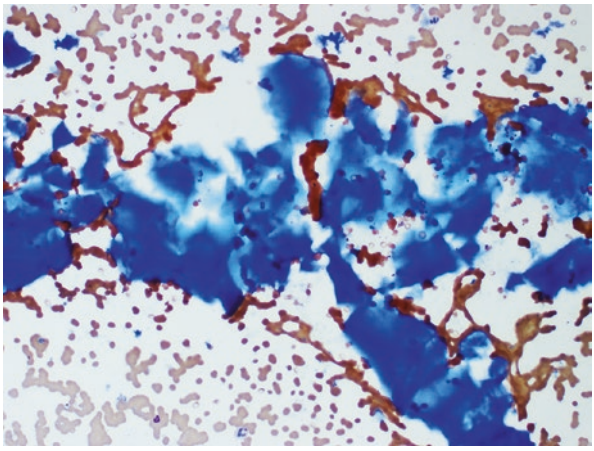


Fig. 7.4 Thick colloid and background red blood cells (Diff-Quik × 200)

Artifacts

Certain artifacts should be in consideration while evaluating thyroid FNA cytology specimens. (Table 7.1).

Table 7.1 Artifacts and contaminants

	Differential diagnosis
Presence of cells form adjacent structures	
Ultrasound gel material (Fig. 7.5)	Colloid
Skeletal muscle (Fig. 7.6)	Colloid
Parathyroid tissue	Follicular cells
Thymic tissue [8]	Lymphocytes Lymphoma
Ciliated respiratory epithelial cells	Follicular cells
Presence of thyroid lesional cells	
Stripped follicular cells in smears (Fig. 7.7)	Lymphocytes
Macrophages (specially in ThinPrep)	Hurthle cells
Epithelioid histiocytes with elongated pale nuclei	Nuclear atypia/PTC

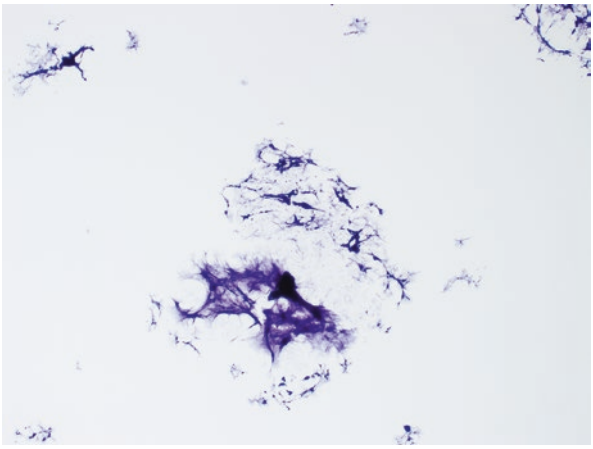


Fig. 7.5 Gel material used during the ultrasound procedure appears as amorphous material and should not be confused with colloid (ThinPrep × 400)

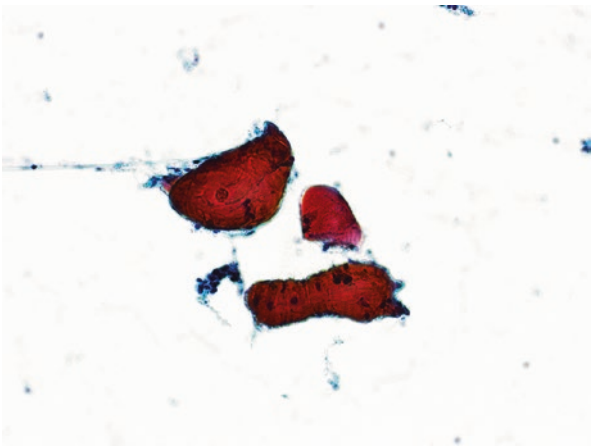


Fig. 7.6 Skeletal muscle fibers with striations can mimic colloid (Papanicolaou stain × 400)

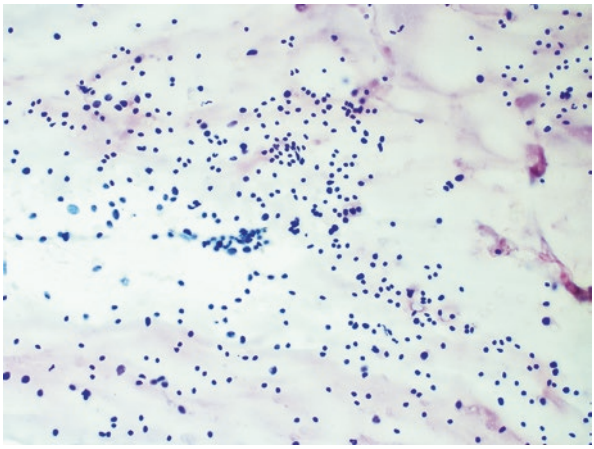


Fig. 7.7 Smearing artifact can produce a discohesive population of follicular cells which can resemble lymphocytes (Papanicolaou stain × 200)

Graves' Disease

Graves' disease is an important cause of hyperthyroidism and is an autoimmune condition caused by circulating autoantibodies [21]. On ultrasound, it may show hypervascularization with an "inferno pattern" can be seen in color-doppler studies [22, 23]. Thyroid scintigraphy can show diffusely elevated uptake within the gland [24]. Overall, there is a diffuse enlargement of the gland which can cause hyperplastic thyroid follicles and peripherally scalloped colloid. Tall columnar cells with eosinophilic cytoplasm and scattered lymphocytes can be seen. However, nuclei are usually round, but nuclear clearing and papillary hyperplasia can pose diagnostic challenges. After radioactive iodine treatment, nuclear atypia and oncocytic metaplasia can be seen. The differential diagnosis includes papillary thyroid carcinoma; identifying the clinical history of Graves' disease or RAI treatment is essential in such cases. Recognizing isolated nuclear features should be evaluated cautiously to avoid overinterpretation in the background of Graves' disease.

Hashimoto's (Chronic Lymphocytic) Thyroiditis

Hashimoto's thyroiditis (HT) is an important cause of hypothyroidism and is autoimmune thyroiditis caused by antithyroid antibodies (such as antithyroid peroxidase and anti-thyroglobulin) [25]. Radiologically, it appears as a diffusely enlarged gland with various patterns (echogenicity) and can show variable changes [26]. Morphologic evaluation of the specimen shows oncocytic cells, a mixed population of lymphocytes, and plasma cells with a variable number of colloid materials (Fig. 7.8). Isolated nuclear cytologic atypia can be seen in HT, which may result in overinterpretation (Fig. 7.9) [27]. Oncocytic cells (Hurthle cells) can also show atypia which is more recognized as an endocrine type of atypia or degenerative

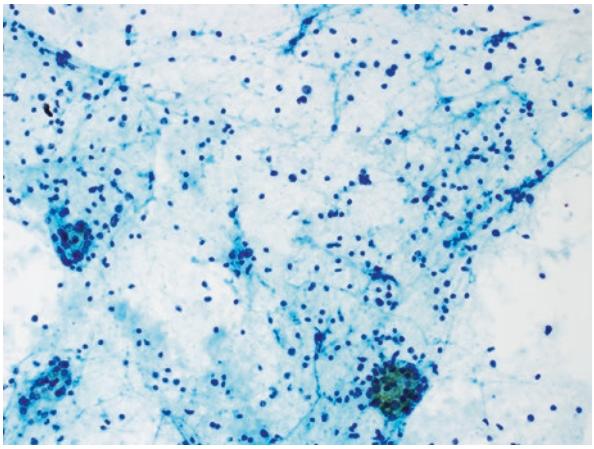


Fig. 7.8 Lymphocytic thyroiditis (Papanicolaou stain × 200)

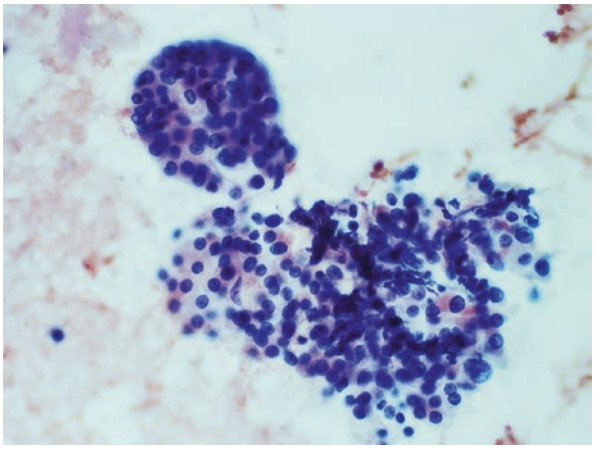


Fig. 7.9 Lymphocytic thyroiditis with reactive nuclear changes (Papanicolaou stain × 400)

atypia. The differential diagnosis includes lymphoma or papillary thyroid carcinoma. B-cell lymphoma is the most common primary thyroid non-Hodgkin lymphoma [28]. Lymphoma shows a monomorphic population of neoplastic lymphoid cells, while in HT, lymphocytes are polymorphous. Obtaining an additional pass for flow cytometry would be helpful in suspected cases of lymphoma. Papillary thyroid carcinoma should have typical nuclear features such as nuclear crowding, clearing, grooves, enlargement, and intranuclear pseudoinclusions.

De Quervain (Sub-Acute Granulomatous) Thyroiditis

De Quervain (sub-acute granulomatous) thyroiditis is a self-limiting inflammatory condition, mostly due to viral infection, usually presents with pain in the thyroid gland and hyperthyroidism. On imaging, color doppler studies usually show

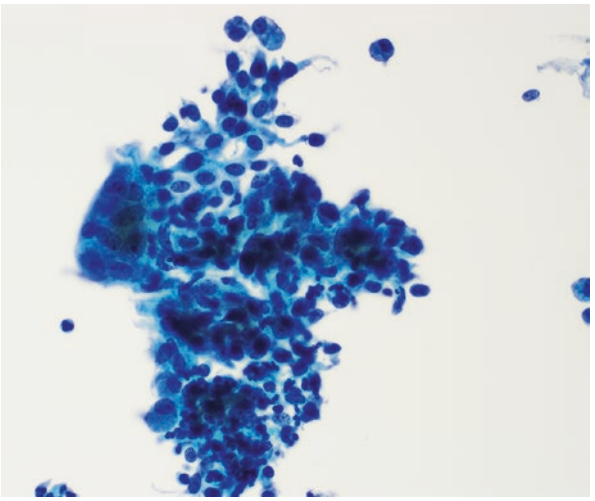


Fig. 7.10 Histiocytic aggregate with a multinucleated giant cell and background inflammatory cells (ThinPrep × 400)

decreased flow with low uptake on radionucleotide scans [29]. Morphologic evaluation shows epithelioid histiocytes, multinucleated giant cells, and inflammatory cells (neutrophils in the early stage, then lymphocyte and plasma cells) (Fig. 7.10). The differential diagnosis includes other forms of thyroiditis, such as granulomatous thyroiditis, palpation thyroiditis, and papillary thyroid carcinoma. Granulomatous thyroiditis usually shows epithelioid histiocytes, and granuloma formation and infectious etiology (fungal and mycobacteria) should be ruled out. Palpation thyroiditis can have multinucleated giant cells but usually lack inflammatory infiltrate. Papillary thyroid carcinoma can come in differential diagnosis, especially in cellular cytology specimens with many multinucleated giant cells and epithelioid histiocytes, which can show nuclear clearing and overlapping. However, the lack of atypical nuclear features of PTC and the presence of inflammatory infiltrate with multinucleated giant cells and epithelioid histiocytes help to differentiate these two entities.

Riedel Thyroiditis

It is an uncommon fibrosing process involving the thyroid gland and usually presents as a firm neck mass [30]. There is a suggestion in the literature that Riedel thyroiditis is within the spectrum of IgG4-related diseases. [31] Morphologically, it shows fibrosis and inflammatory infiltrates, mostly plasma cells. Due to fibrosis, the cytology specimen is usually paucicellular. The differential diagnosis includes a paucicellular variant of anaplastic thyroid carcinoma (ATC) [14]. However, atypia is more in ATC cases, and PAX-8 stain would be helpful for further characterization.

Amyloid Goiter

Amyloid goiter can present as thyroid gland enlargement due to primary or secondary amyloidosis [32]. However, the most frequent setting in which amyloid is seen in the thyroid gland is medullary thyroid carcinoma. Cytology specimens are usually not cellular and mainly consist of amorphous amyloid material, which can resemble colloid material (Figs. 7.11 and 7.12). However, the presence of associated vasculature can be seen in amyloid [33]. Amyloid has been reported in parathyroid, which can mimic medullary thyroid carcinoma [34]. Medullary carcinoma is usually positive for neuroendocrine markers and calcitonin stains. Amyloid material is highlighted by Congo red stain and shows apple-green birefringence under polarized light [35]. Amyloid usually appears as *bright yellow-green* fluorescence when Thioflavin-T stain is examined under an immunofluorescent microscope. See Table 7.2.

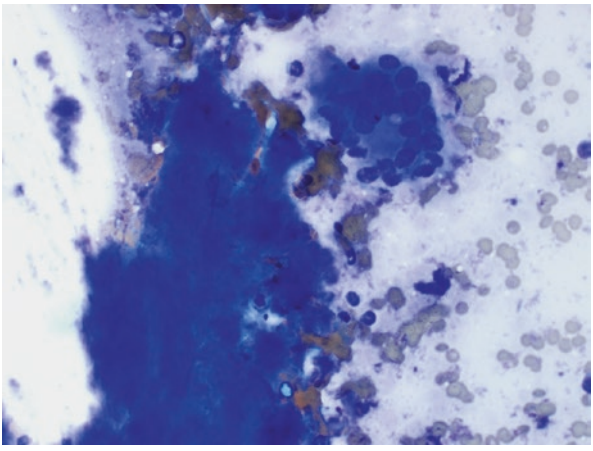


Fig. 7.11 Amyloid material with scattered spindle cells and multinucleated giant cells (Diff-Quik x 400)

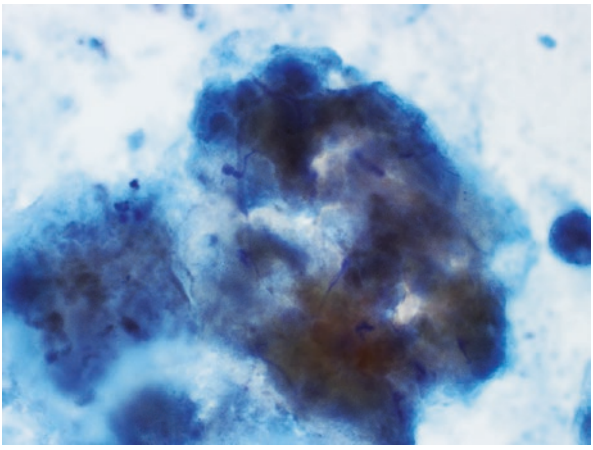


Fig. 7.12 Amyloid material with scattered spindle cells and multinucleated giant cells (Papanicolaou stain × 400)

Table 7.2 Benign and reactive conditions and differential diagnosis

Conditions	Cytomorphologic features	Differential diagnosis	Diagnostic clues
Graves' disease	Hyperplastic changes but decrease with treatment, papillary projections with scalloped colloid	Papillary thyroid carcinoma (PTC)	PTC—nuclear features of PTC are present
	RAI effects: Nuclear atypia, cytoplasmic vacuolization, lymphocytes, histocytes, Hurthle cell changes, and lack of microfollicular and papillary archetecture [9, 10]	PTC, and other higher-grade carcinomas (primary/anaplastic, metastatic carcinoma) [11]	RAI—prior history of RAI
Chronic lymphocytic (Hashimoto's) thyroiditis	Mature mixed lymphocytes, scattered plasma cells, Hurthle cells which may show focal nuclear atypia, tingible-body macrophages, colloid can be scant	Lymphoma PTC	Lymphoma—predominance of monotonous proliferation, concerning clinical / imaging features PTC—look for classic nuclear features
De Quervain (sub-acute granulomatous) thyroiditis	Tender enlarged thyroid gland, multinucleated giant cells (frequent) and inflammatory cells. Well-formed granulomas and histiocytes with elongated pale nuclei can be seen	Palpation thyroiditis Thyroiditis (infectious) PTC	Palpation thyroiditis—patchy, lack neutrophils Infectious thyroiditis—clinical history, AFB/GMS stains PTC—classic nuclear features
Riedel thyroiditis	Bland spindle cells, fibrous tissue fragments, Myofibroblast-like cells, inflammatory cells, lack atypia and mitosis [12]	Fibrosing Hashimoto's thyroiditis (FHT) [13] Paucicellular variants of anaplastic carcinoma (ATC) [14] Solitary fibrous tumor (SFT) [15]	FTH—Oncocytic/Hurthle cells, lymphocytes, and plasma cells [13] SFT—Immunohistochemical stains (STAT6) ATC—should have nuclear atypia, necrosis, and mitosis
Papillary hyperplasia	Papillary architecture usually lacking nuclear features of PTC. Focal atypia can be seen, and cautious evaluation is required to avoid over interpretation [16]	PTC	PTC—should have well-formed classic nuclear features

(continued)

Table 7.2 (continued)

Conditions	Cytomorphologic features	Differential diagnosis	Diagnostic clues
Sarcoidosis	Non-necrotizing granulomatous inflammation, epithelioid histiocytes with elongated pale nuclei	Other thyroiditis (infectious) PTC	Infectious thyroiditis—special stains PTC—well-formed nuclear features
Amyloid goiter	Amorphous eosinophilic material, fat cells [17], chronic inflammatory cells	MTC Systemic or localized amyloidosis Hyalinizing trabecular tumor	For MTC—calcitonin stain or serum calcitonin levels For amyloid (primary vs. secondary)—Congo red stain positive [18] and under polarized light apple green birefringence Thioflavin T stain bright yellow-green fluorescence under immunofluorescence microscope [19, 20]

RAI Radioactive iodine, *PTC* Papillary thyroid carcinoma, *MTC* Medullary thyroid carcinoma

Thyroid Cystic Lesions

1. *Thyroid nodule with degenerative cystic changes:* Cystic thyroid nodules contain macrophages, watery colloid, mixed pattern follicular cells, and may be Hurthle cells. Cyst-lining cells can also be seen in flat sheets with slightly elongated nuclei but with distinct borders (Fig. 7.13) [36]. They can show Hurthloid, or spindled morphology, occasional nuclear grooves, degenerative change, rare mitosis, and reactive atypia can be seen and should be evaluated cautiously to avoid overinterpretation. Papillary thyroid carcinoma with cystic changes comes in the differential diagnosis, which should show classic nuclear features of PTC such as nuclear crowding, overlapping, nuclear grooves, pseudoinclusions, and papillary architecture.
2. *Thyroglossal duct cyst:* Thyroglossal duct cysts are usually in the midline neck and near the hyoid bone. FNA usually yield low cellularity specimen, mainly consisting of inflammatory cells, macrophages, and scant epithelial component/lining cells such as ciliated respiratory type epithelium or squamous epithelial cells. The Cyst wall may contain thyroid follicular cells. Carcinoma can arise in TGDC, which is mostly PTC [37]. The differential diagnosis of TGDC includes other cystic lesions such as dermoid cyst, which usually consists of adnexal structures, and brachial cleft cyst, primarily located in the lateral neck.

3. *Parathyroid cyst:* Parathyroid cysts are rare, mainly around the inferior parathyroid gland [38] and the left thyroid lobe. They can present in any age group, but most cases are noted between the third and sixth decade [39]. Cyst aspirate is usually clear but less cellular and consists of cyst contents and scant cuboidal epithelial cells. Cyst fluid analysis can be sent for parathyroid hormone levels analysis [40, 41]. The differential diagnosis includes thyroid follicular cells or thyroid cysts. If cell block is available, performing PTH or thyroid origin markers such as Thyroglobulin and TTF-1 would be helpful to differentiate these two entities. See Table 7.3.

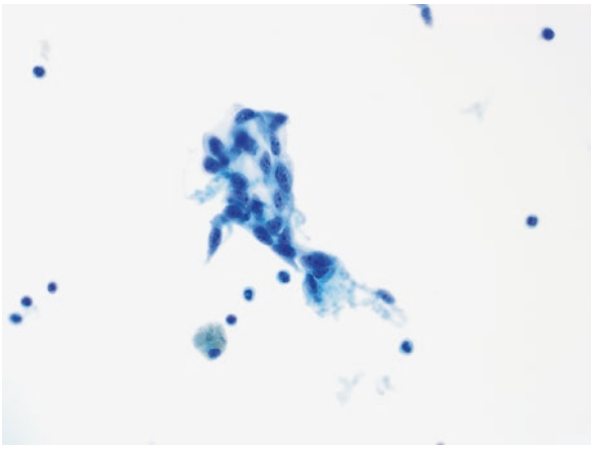


Fig. 7.13 Cyst lining cells with reactive changes and background histiocyte (ThinPrep × 400)

Table 7.3 Cystic lesions

Cystic lesions	Cytomorphologic features	Differential diagnosis
Thyroid nodule with degenerative cystic changes	Cysts contents including macrophages, follicular cells, Hurthle cells, cyst lining cells with reactive changes, watery colloid	Cystic PTC—classic nuclear features of PTC should be seen
Thyroglossal duct cyst	Cyst contents including macrophages, inflammatory cells, scant epithelial cells,	Epidermoid and dermoid cyst—mostly keratinizing squamous lining Brachial cleft cyst—lateral neck cyst
Parathyroid cyst	Clear aspirate, Hypocellular, cyst contents, scant epithelial cells	Thyroid cyst—aspirate is not clear, mostly brownish. PTH levels in aspirate are helpful

Pigments, Crystals, and Calcifications

Pigments

Pigmented material (Fig. 7.14) can be seen in thyroid parenchymal cells, including hemosiderin, lipofuscin, due to tetracycline (minocycline, Black Thyroid) and melanin.

Hemosiderin

Hemosiderin pigment is a coarse granular golden yellow to brown pigment derived from erythrocyte breakdown. Hemosiderin deposition can be seen in macrophages and follicular cells primarily due to secondary causes such as cystic degenerative changes or prior FNA or biopsy procedures. An Iron stain (Prussian blue) highlights hemosiderin as blue cytoplasmic material.

Minocycline

Oxidative changes, deposition of derivative, or degradation products of minocycline can result in dark brown granular pigmentation of follicular cells [42, 43]. It is usually seen in a long-standing history of taking tetracycline (minocycline). Pigment may stain positive for Fontana-Masson and bleach with potassium permanganate but negative for iron stain [42, 44].

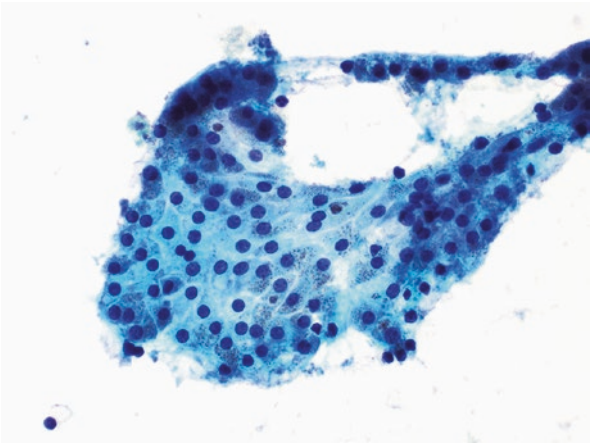


Fig. 7.14 Sheet of follicular cells with granular pigment (brownish) (ThinPrep × 400)

Lipofuscin

Cytoplasmic deposition of yellow to brown pigment is seen with aging and usually stain positive for lipofuscin stain and PAS-positive but negative for iron stain [44].

Melanin

Melanin is a fine granular brown-black cytoplasmic pigment. It is infrequently seen in the thyroid gland. However, rare cases of melanin-producing medullary thyroid carcinoma have been reported [45, 46]. Melanin stain with Fontana-Masson stain but negative for PAS.

Crystals

Calcium oxalate crystals are seen in the thyroid gland, specifically with colloid. They are birefringent under polarized light and can be found in all types of thyroid lesions and normal thyroid tissue [47]. They are more prevalent in goiter and adenomas [47]. the differential diagnosis includes calcifications. These crystals are rare in parathyroid tissue, and findings crystals by using polarized light microscopy would be helpful to differentiate thyroid tissue from parathyroid tissue in diagnostically challenging situations [48].

Calcifications

Dystrophic calcification: It is due to the deposition of calcified material in necrotic tissue or due to degenerative changes. They are usually coarse, dense, and irregular and do not show lamellation.

Psammoma bodies: They are basophilic and show concentric lamellation. They are often associated with papillary thyroid carcinoma. They can also be seen in benign conditions [49]. However, finding an isolated psammoma body without any atypical cells in thyroid aspirate may necessitate a comment on the presence of psammoma calcification with further correlation with clinical and imaging findings [50].

Infections

They are uncommon but can be seen due to bacterial, fungi, and mycobacterial infections.

Acute Suppurative Thyroiditis

It usually presents with fever, pain, and neck swelling due to bacterial infection, primarily by gram-positive bacteria (Staphylococcus aureus and Streptococcus species) [51]. Cytomorphologic exam may show inflammatory cells with a predominance of acute inflammation and necroinflammatory debris.

Granulomatous Thyroiditis

It can be infectious or non-infectious. Fungal (Aspergillus, Histoplasma, Candida spp., and others) [52, 53] and mycobacterial infections can cause inflammation, granuloma formation, and multinucleated giant cells reaction. Special stains and cultures are helpful for the identification and further characterization of the microorganism. Differential diagnosis includes non-infectious etiologies, including De Quervain (sub-acute) thyroiditis and sarcoidosis.

Thyroid Follicular Cells in Neck Region

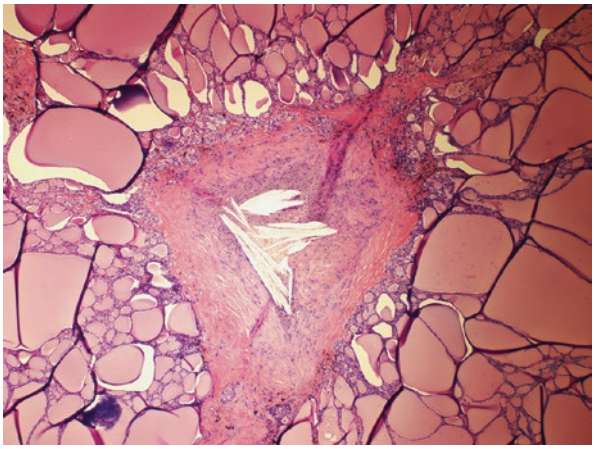
Thyroid follicular cells can be seen in the central and lateral neck with associated differential diagnoses (Table 7.4).

Table 7.4 Thyroid follicular cells in the neck region

Thyroid parenchymal cells in neck region	Cytomorphologic features	Differential diagnosis	Diagnostic clues
1. Central neck [54–59]			
Thyroglossal duct cyst (TGDC)	Follicular cells, cysts contents, inflammatory cells	Papillary thyroid carcinoma (PTC)	PTC—can arise in TGDC and look for nuclear features
In lymph node	Follicular cells, lymphocytes	Metastatic PTC	PTC—if classic nuclear features of PTC are present. Presence of psammoma bodies (should be separated from dystrophic calcification)
Ectopic thyroid	Bland follicular cells and colloid	Lingual thyroid Substernal goiter PTC	Lingual thyroid—usually around base of tongue

Table 7.4 (continued)

Thyroid parenchymal cells in neck region	Cytomorphologic features	Differential diagnosis	Diagnostic clues
2. Lateral Neck [52–59]			
Parasitic nodule	Bland thyroid follicular cells, usually no lymphocytes except in Hashimoto's thyroiditis	Metastatic PTC	Evaluate for nuclear features, correlation with clinical and imaging features, any prior history of thyroid carcinoma
In lymph node	Thyroid parenchymal cells	Metastatic PTC Parasitic nodule with Hashimoto's thyroiditis	Nuclear features of PTC Additional work-up (clinical/imaging correlation) to rule out malignancy Any prior history of thyroid carcinoma



Figs. 7.15 Prior FNA-related changes with histocytes, fibrosis, cholesterol cleft formation, and surrounding follicular cells with nuclear atypia (H&E × 40)

FNA Induced Changes in Thyroid Gland and Differential Diagnosis

Fine needle aspiration (FNA) cytology helps in diagnosing thyroid lesions. However, the FNA procedure of the thyroid results in certain cytologic and histologic alterations, which are well described in the literature (Figs. 7.15). Early changes (less than 3 weeks) include the presence of hemorrhage, hemosiderin-laden macrophages, and granulation tissue. Morphologic changes that appear later include hemosiderin-laden macrophages, reactive cellular changes, fibrosis, and presence of

myofibroblast cells, nuclear changes such as nuclear enlargement and clearing, metaplastic changes (squamous or oncocytic), infraction, cholesterol granuloma formation, vascular proliferation, and plumped endothelial cells [60–63]. In diagnostically challenging cases, cytomorphologic comparison with the prior FNA cytology may be helpful, if available.

Pitfalls

The presence of cytologic atypia and the above-described change in repeat thyroid FNA may pose diagnostic challenges. Nuclear atypia can stimulate features of papillary thyroid carcinoma. However, nuclear atypia due to post-FNA change is usually focal and lacks other features of PTC, such as intranuclear pseudoinclusions. The presence of spindle cells or myofibroblast-like cells, either due to reactive stromal changes or granulation tissue formation, can bring in a diagnosis of sarcoma or anaplastic thyroid carcinoma. Simultaneously, infarction due to prior procedure can stimulate necrosis which can be seen in thyroid malignancies.

Conclusion

To conclude, recognizing these cytologic changes and then the correlation with the clinical history (such as clinical/ imaging features and history of prior FNA procedure) is essential. Findings should be evaluated cautiously to avoid overinterpretation.

Acknowledgments None.

Conflict of Interest None.

References

1. Hegedüs L, Perrild H, Poulsen LR, Andersen JR, Holm B, Schnohr P, Jensen G, Hansen JM. The determination of thyroid volume by ultrasound and its relationship to body weight, age, and sex in normal subjects. J Clin Endocrinol Metab. 1983;56(2):260–3.
2. Pankow BG, Michalak J, McGee MK. Adult human thyroid weight. Health Phys. 1985;49(6):1097–103.
3. Mansberger AR Jr, Wei JP. Surgical embryology and anatomy of the thyroid and parathyroid glands. Surg Clin North Am. 1993;73(4):727–46.
4. Sinos G, Sakorafas GH. Pyramidal lobe of the thyroid: anatomical considerations of importance in thyroid cancer surgery. Oncol Res Treat. 2015;38(6):309–10.

5. Reid JD, Choi CH, Oldroyd NO. Calcium oxalate crystals in the thyroid. Their identification, prevalence, origin, and possible significance. Am J Clin Pathol. 1987;87(4):443–54.
6. Auger M. Hürthle cells in fine-needle aspirates of the thyroid: a review of their diagnostic criteria and significance. Cancer Cytopathol. 2014;122(4):241–9.
7. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. Thyroid. 2017;27(11):1341–6.
8. Frates MC, Benson CB, Dorfman DM, Cibas ES, Huang SA. Ectopic Intrathyroidal Thymic tissue mimicking thyroid nodules in children. J Ultrasound Med. 2018;37(3):783–91.
9. Granter SR, Cibas ES. Cytologic findings in thyroid nodules after 131I treatment of hyperthyroidism. Am J Clin Pathol. 1997;107(1):20–5.
10. El Hussein S, Omarzai Y. Histologic findings and cytological alterations in thyroid nodules after radioactive iodine treatment for Graves' disease: a diagnostic dilemma. Int J Surg Pathol. 2017;25(4):314–8.
11. Centeno BA, Szyfelbein WM, Daniels GH, Vickery AL Jr. Fine needle aspiration biopsy of the thyroid gland in patients with prior Graves' disease treated with radioactive iodine. Morphologic findings and potential pitfalls. Acta Cytol. 1996;40(6):1189–97.
12. Harigopal M, Sahoo S, Recant WM, DeMay RM. Fine-needle aspiration of Riedel's disease: report of a case and review of the literature. Diagn Cytopathol. 2004;30(3):193–7.
13. Baloch ZW, Feldman MD, LiVolsi VA. Combined Riedel's disease and Fibrosing Hashimoto's thyroiditis: a report of three cases with two showing coexisting papillary carcinoma. Endocr Pathol. 2000;11(2):157–63.
14. Wan SK, Chan JK, Tang SK. Paucicellular variant of anaplastic thyroid carcinoma. A mimic of Reidel's thyroiditis. Am J Clin Pathol. 1996;105(4):388–93.
15. Rodriguez I, Ayala E, Caballero C, De Miguel C, Matias-Guiu X, Cubilla AL, Rosai J. Solitary fibrous tumor of the thyroid gland: report of seven cases. Am J Surg Pathol. 2001;25(11):1424–8.
16. Pusztaszeri MP, Krane JF, Cibas ES, Daniels G, Faquin WC. FNAB of benign thyroid nodules with papillary hyperplasia: a cytological and histological evaluation. Cancer Cytopathol. 2014;122(9):666–77.
17. Nijhawan VS, Marwaha RK, Sahoo M, Ravishankar L. Fine needle aspiration cytology of amyloid goiter. A report of four cases. Acta Cytol. 1997;41(3):830–4.
18. Ozdemir BH, Uyar P, Ozdemir FN. Diagnosing amyloid goitre with thyroid aspiration biopsy. Cytopathology. 2006;17(5):262–6.
19. Puchtler H, Waldrop FS, Meloan SN. A review of light, polarization and fluorescence microscopic methods for amyloid. Appl Pathol. 1985;3(1–2):5–17.
20. Saeed SM, Fine G. Thioflavin-T for amyloid detection. Am J Clin Pathol. 1967;47(5):588–93.
21. Wémeau JL, Klein M, Sadoul JL, Briet C, Vélayoudom-Céphise FL. Graves' disease: introduction, epidemiology, endogenous and environmental pathogenic factors. Ann Endocrinol (Paris). 2018;79(6):599–607.
22. Ralls PW, Mayekawa DS, Lee KP, Colletti PM, Radin DR, Boswell WD, Halls JM. Color-flow Doppler sonography in graves disease: "thyroid inferno". AJR Am J Roentgenol. 1988;150(4):781–4.
23. Vita R, Di Bari F, Perelli S, Capodicasa G, Benvenga S. Thyroid vascularization is an important ultrasonographic parameter in untreated Graves' disease patients. J Clin Transl Endocrinol. 2019;19(15):65–9.
24. Avs AK, Mohan A, Kumar PG, Puri P. Scintigraphic profile of thyrotoxicosis patients and correlation with biochemical and Sonological findings. J Clin Diagn Res. 2017;11(5):OC01–3.
25. Hu S, Rayman MP. Multiple nutritional factors and the risk of Hashimoto's thyroiditis. Thyroid. 2017;27(5):597–610.
26. Sostre S, Reyes MM. Sonographic diagnosis and grading of Hashimoto's thyroiditis. J Endocrinol Investig. 1991;14(2):115–21.
27. Khaled CS, Khalifeh IM, Shabb NS. Interpretive errors in Fine-needle aspiration of thyroid: a 13-year institutional experience in Lebanon. Acta Cytol. 2022;66(1):23–35.

28. Pedersen RK, Pedersen NT. Primary non-Hodgkin's lymphoma of the thyroid gland: a population-based study. Histopathology. 1996;28(1):25–32.
29. Frates MC, Marqusee E, Benson CB, Alexander EK. Subacute granulomatous (de Quervain) thyroiditis: grayscale and color Doppler sonographic characteristics. J Ultrasound Med. 2013;32(3):505–11.
30. Hennessey JV. Clinical review: Riedel's thyroiditis: a clinical review. J Clin Endocrinol Metab. 2011;96(10):3031–41.
31. Dahlgren M, Khosroshahi A, Nielsen GP, Deshpande V, Stone JH. Riedel's thyroiditis and multifocal fibrosclerosis are part of the IgG4-related systemic disease spectrum. Arthritis Care Res. 2010;62(9):1312–8.
32. Villa F, Dionigi G, Tanda ML, Rovera F, Boni L. Amyloid goiter. Int J Surg. 2008;6(Suppl 1):S16–8.
33. Yaeger KA, Hysell C, Pitman MB. Amyloid goiter. Diagn Cytopathol. 2010;38(10):742–3.
34. Ordoñez NG, Ibañez ML, Samaan NA, Hickey RC. Immunoperoxidase study of uncommon parathyroid tumors. Report of two cases of nonfunctioning parathyroid carcinoma and one intrathyroid parathyroid tumor-producing amyloid. Am J Surg Pathol. 1983;7(6):535–42.
35. Hill K, Diaz J, Hagemann IS, Chernock RD. Multiple myeloma presenting as massive amyloid deposition in a parathyroid gland associated with amyloid goiter: a medullary thyroid carcinoma mimic on intra-operative frozen section. Head Neck Pathol. 2018;12(2):269–73.
36. Faquin WC, Cibas ES, Renshaw AA. "atypical" cells in fine-needle aspiration biopsy specimens of benign thyroid cysts. Cancer. 2005;105(2):71–9.
37. Yang YJ, Haghir S, Wanamaker JR, Powers CN. Diagnosis of papillary carcinoma in a thyroglossal duct cyst by fine-needle aspiration biopsy. Arch Pathol Lab Med. 2000 Jan;124(1):139–42.
38. Cao H, Lai CK, Head CS, Sercarz JA. Cystic parathyroid presenting as an apparent thyroid goiter. Eur Arch Otorhinolaryngol. 2008;265(10):1285–8.
39. Papavramidis TS, Chorti A, Pliakos I, Panidis S, Michalopoulos A. Parathyroid cysts: a review of 359 patients reported in the international literature. Medicine (Baltimore). 2018;97(28):e11399.
40. Silva R, Cavadas D, Vicente C, Coutinho J. Parathyroid cyst: differential diagnosis. BMJ Case Rep. 2020;13(10):e232017.
41. Alvi A, Myssiorek D, Wasserman P. Parathyroid cyst: current diagnostic and management principles. Head Neck. 1996;18(4):370–3.
42. Keyhani-Rofagha S, Kooner DS, Landas SK, Keyhani M. Black thyroid: a pitfall for aspiration cytology. Diagn Cytopathol. 1991;7(6):640–3.
43. Tacon L, Tan CT, Alvarado R, Gill AJ, Sywak M, Fulcher G. Drug-induced thyroiditis and papillary carcinoma in a minocycline-pigmented black thyroid gland. Thyroid. 2008;18(7):795–7.
44. Senba M. Staining properties of melanin and lipofuscin pigments. Am J Clin Pathol. 1986;86(4):556–7.
45. Ikeda T, Satoh M, Azuma K, Sawada N, Mori M. Medullary thyroid carcinoma with a paraganglioma-like pattern and melanin production: a case report with ultrastructural and immunohistochemical studies. Arch Pathol Lab Med. 1998;122(6):555–8.
46. Kimura N, Ishioka K, Miura Y, Sasano N, Takaya K, Mouri T, Kimura T, Nakazato Y, Yamada R. Melanin-producing medullary thyroid carcinoma with glandular differentiation. Acta Cytol. 1989;33(1):61–6.
47. Katoh R, Kawaoi A, Muramatsu A, Hemmi A, Suzuki K. Birefringent (calcium oxalate) crystals in thyroid diseases. A clinicopathological study with possible implications for differential diagnosis. Am J Surg Pathol. 1993;17(7):698–705.
48. Wong KS, Lewis JS Jr, Gottipati S, Chernock RD. Utility of birefringent crystal identification by polarized light microscopy in distinguishing thyroid from parathyroid tissue on intraoperative frozen sections. Am J Surg Pathol. 2014;38(9):1212–9.
49. Ellison E, Lapuerta P, Martin SE. Psammoma bodies in fine-needle aspirates of the thyroid: predictive value for papillary carcinoma. Cancer. 1998;84(3):169–75.

50. Hunt JL, Barnes EL. Non-tumor-associated psammoma bodies in the thyroid. Am J Clin Pathol. 2003;119(1):90–4.
51. Paes JE, Burman KD, Cohen J, Franklyn J, McHenry CR, Shoham S, Kloos RT. Acute bacterial suppurative thyroiditis: a clinical review and expert opinion. Thyroid. 2010;20(3):247–55.
52. Goldani LZ, Zavascki AP, Maia AL. Fungal thyroiditis: an overview. Mycopathologia. 2006;161(3):129–39.
53. Berger SA, Zonszein J, Villamena P, Mittman N. Infectious diseases of the thyroid gland. Rev Infect Dis. 1983;5(1):108–22.
54. Barbieri A, Prasad ML, Gilani SM. Thyroid tissue outside the thyroid gland: differential diagnosis and associated diagnostic challenges. Ann Diagn Pathol. 2020;48:151584.
55. Thompson LD, Herrera HB, Lau SK. A Clinicopathologic series of 685 Thyroglossal duct remnant cysts. Head Neck Pathol. 2016;10(4):465–74.
56. Rosai J, Kuhn E, Carcangiu ML. Pitfalls in thyroid tumour pathology. Histopathology. 2006;49(2):107–20.
57. dos Santos VM, de Lima MA, Marinho EO, Marinho MA, dos Santos LA, Raphael CM. Parasitic thyroid nodule in a patient with Hashimoto's chronic thyroiditis. Rev Hosp Clin Fac Med Sao Paulo. 2000;55(2):65–8.
58. Triantafyllou A, Williams MD, Angelos P, Shah JP, Westra WH, Hunt JL, Devaney KO, Rinaldo A, Slootweg PJ, Gnepp DR, Silver C, Ferlito A. Incidental findings of thyroid tissue in cervical lymph nodes: old controversy not yet resolved? Eur Arch Otorhinolaryngol. 2016;273(10):2867–75.
59. Baloch ZW, LiVolsi VA. Post fine-needle aspiration histologic alterations of thyroid revisited. Am J Clin Pathol. 1999;112(3):311–6.
60. Recavarren RA, Houser PM, Yang J. Potential pitfalls of needle tract effects on repeat thyroid fine-needle aspiration. Cancer Cytopathol. 2013;121(3):155–61.
61. Eze OP, Cai G, Baloch ZW, Khan A, Virk R, Hammers LW, Udelsman R, Roman SA, Sosa JA, Carling T, Chhieng D, Theoharis CG, Prasad ML. Vanishing thyroid tumors: a diagnostic dilemma after ultrasonography-guided fine-needle aspiration. Thyroid. 2013;23(2):194–200.
62. Kini SR. Post-fine-needle biopsy infarction of thyroid neoplasms: a review of 28 cases. Diagn Cytopathol. 1996;15(3):211–20.
63. Batsakis JG, El-Naggar AK, Luna MA. Thyroid gland ectopias. Ann Otol Rhinol Laryngol. 1996;105(12):996–1000.