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IN THYROLO

The 19th International Congress of Cytology (Pacifico Yokohama)



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Case 1 Foreign-body granuloma



A nodular lesion (arrow) appeared 2 years after total thyroidectomy for papillary carcinoma. Thyroglobulin level in needle washout fluid was low. In the cytological smear, foreign-bodies (suture thread), multinucleated giant cells, histiocytes, neutrophils, and fibroblasts are seen.

Case 2 Esophageal diverticulum



A lesion is usually present at the posterior of left thyroid lobe. As it looks like thyroid nodule ultrasonographically, FNA may be performed. Squamous cells, bacteria, and food debris are seen in the cytological smear.

Case 3 Median cervical cyst



Unilocular cyst located at the upper portion of the isthmus.





Cytology: LBC smears usually exhibits more epithelial cells than conventional smears in fluid materials. Therefore, we recommend the former for cystic lesions. Numerous foamy cells and a small number of squamous cells are seen on the smear.

Histology: The cyst wall is composed of granulation tissue and an aggregation of histiocytes. Thyroid tissue is not present. The inner surface is focally covered with squamous cells and ciliated cells (arrow).

Case 4 Lateral cervical cyst







Whitish-yellow viscous liquid was aspirated. Squamous cell, anucleate squamous cells, and necrotic debris are seen.

Case 5 Hypopharyngeal piriform sinus fistula









Acute suppurative thyroiditis is frequently caused by this lesion. In addition to numerous neutrophils, ciliated cell and squamous cells may be seen.

Case 6 Subacute thyroiditis





III-defined low-echoic lesion is present in the left lobe. Grossly, irregular-shaped whitish nodule are seen.



Cytology: Multinucleated giant cells, lymphocytes, histiocytes, and epithelioid cell are seen. **Histology**: Subacute thyroiditis is characterized by granulomas composed of epithelioid cells and multinucleated giant cells, associated with lymphocytic infiltration and fibrosis. The granulomas focus on an individual thyroid follicle.

Case 7 Hashimoto's disease (nodular type)





Ill-defined, low-echoic lesion (white arrow) is seen in the right lobe. Grossly, it is whitish and solid nodule (red arrow).



Cytology: Oxyphilic cells show sheet-like, trabecular, and microfollicular clusters. N/C ratio is not increased, and intranuclear cytoplasmic inclusions are not observed. Lymphocytes are noticed on the background and within oxyphilic cell clusters. In LBC smear, oxyphilic cells are relatively increased because of a loss of lymphocytes. Some multinucleated giant cells are seen.

Histology: The nodule is consistent with Hashimoto's thyroiditis, except for encapsulation. The follicles composed of oxyphilic cells are mostly small-sized and contain multinucleated giant cells.

Case 8 IgG4-related thyroiditis



Cytology: The findings are consistent with Hashimoto's thyroiditis. Oxyphilic cells show sheet-like, small cluster, and trabecular clusters. Follicular pattern is not observed. Nuclear grooves are occasionally observed. Intranuclear cytoplasmic inclusion is not seen. Lymphocytes and plasma cells are seen on the background and within oxyphilic cell clusters.

Histology: Hashimoto's thyroiditis with prominent plasma cell infiltration and fibrosis indicate IgG4-related thyroiditis.

Case 9 Graves' disease (post-radiation therapy)



The thyroid is occupied with band-like hyaline fibrous connective tissue. Small-sized follicles composed of large atypical follicular cells with hyperchromatic nuclei and prominent nucleoli are seen. The presence of the bizarre follicular cells probably results from preceding radiation therapy.

Case 10 Black thyroid



Follicular cells contain black to brown pigments. The pigments are also observed in the lumen of the thyroid follicles, individually or phagocyted by macrophages.

Case 11 Needle trace



A variety of histological reactions are caused by FNA. The findings change differ with the duration between aspiration and operations. Granulation tissue with cholesterol crystals is seen in this case. The size is almost same to a gauge of the needle (22G). It looks like involuted nodular goiter.

Case 12 Thyroid Cyst





Ultrasound reveals a unilocular cyst. The wall is thick and associated with calcification. Grossly, cyst wall is brownish, indicating hemorrhage.



Cytology (LBC): There are histiocytes, proteinaceous materials, degenerated RBC, and a few anucleated squamous cells. According to the Bethesda system, this case is categorized into "Nondiagnostic" or "Unsatisfactory".

Histology: The cyst wall is composed of granulation tissue surrounded by fibrotic tissue. Fibrin materials and hemosiderin-laden macrophages are seen in the lumen.

Case 13 Adenomatous goiter (follicular pattern)





The cut surface of the nodules are variable. Aspiration cytology was performed from the encapsulated and solid nodule (arrow).



Cytology: Follicular cells are embedded within abundant colloid materials. The follicular cells show sheet-like and follicular clusters. The nuclei are variable in size and hyperchromatic. N/C ratio is not high. Naked and isolated follicular cells look like lymphocytes. **Histology**: The nodules are composed of various-sized follicles.

Case 14 Adenomatous goiter (papillary pattern)





Ultrasonography reveals a well-defined, slightly hypoechoic, homogeneous nodule.



Cytology: Follicular cells show papillary and follicular clusters. The nuclei are round to ovoid in shape. There are no nuclear findings characteristic of papillary carcinoma. **Histology:** Papillary growth are seen, but nuclear findings indicating papillary carcinoma are not observed.

Case 15 Dyshormonogenetic goiter





The thyroid is markedly increased in size due to multiple goiter.



The nodules are composed of monotonous microfollicles mimicking follicular adenoma or carcinoma. However, MIB-1 labeling index of the nodules is less than 1% and vascular invasion and/or distant metastasis are not detected. One nodule exhibits follicular cells with signet ring cells appearance. The thyroid follicles located in non-nodular area are composed of enlarged follicular cells and the lumen is not filled with colloid (empty). These findings are characteristic of thyroglobulin gene mutation. Immunohistochemically, the thyroglobulin is accumulated in the cytoplasm of the follicular cells.

Case 16 Follicular adenoma (mucinous stroma)





Encapsulated nodule with cystic formation is seen in the right lobe. Solid portion of the nodule is translucent.



Cytology: The background is not colloid but mucinous. Capillary plexus is noted. Small follicular cells exhibit cell clusters, pseudo-cribriform pattern, or isolated pattern. Intracytoplasmic hyaline droplet is seen, but the meaning is obscure.

Histology: Follicular adenoma is lobulated and has abundant stromal mucin.

Case 17 Follicular adenoma, oxyphilic cell variant





Encapsulated nodule contains small cystic area. Cut surface of the nodule is brownish.



Cytology: Oxyphilic cells appear as sheet-like, trabecular, or small follicular clusters. The capillaries are embedded within the cell clusters. The cytoplasm is abundant and granular. The nuclei show various sizes, hyperchromasia, granular chromatin pattern, enlarged nucleoli, and binuclei. **Histology**: Encapsulated nodule is composed of oxyphilic cells showing microfollicular and trabecular patterns. Papillary growth is focally seen, but no nuclear feature consistent with papillary carcinoma is observed.

Case 18 Atypical adenoma





A well-defined yellowish nodule is located in the right lobe.



Cytology: Small round cells with high N/C ratio appear as microfollicular pattern. The sizes of the follicles are imagined from those of hyaline colloid. The findings are consistent with follicular neoplasm. Large cells with hyperchromatic nuclei are scattered.

Histology: Large and bizarre atypical cells are observed, but infiltrative growth, large prominent nucleoli, mitotic figures, necrosis, and neutrophilic infiltration suspecting malignancy are not present. MIB-1 labeling index was less than 1%.

Case 19 Widely invasive follicular carcinoma



in capillaries.



The tumor is lobulated and solid. Macroscopically, capsular invasion is apparent (arrow).



Cytology: Monotonous follicular cells appear as microfollicular pattern. They tend to aggregate around capillaries (Upper left). The microfollicles are three-dimensional. **Histology**: Carcinoma cells show trabecular and microfollicular growth patterns. The stroma is rich

Case 20 Widely invasive follicular carcinoma, oxyphilic cell variant





The tumor is encapsulated, but apparent capsular invasion are visible at two portions (7 and 11 o'clock.) The cut surface is brownish.



Cytology: The smear is mainly composed of oxyphilic cells that have abundant, thick, granular, and densely lightgreen-stained cytoplasm with distinct cell border. Binuclei are scattered. **Histology**: Oxyphilic cells show microfollicular and trabecular growth patterns. Stromal edema is focally seen.

Case 21 Follicular carcinoma (needle tract implantation)





The patient has a history with the resection of thyroid nodule 3 years ago. Two nodules (arrow) appeared in the subcutaneous tissue of the neck.



Cytology: The smear is cellular. Carcinoma cells show microfollicular, trabecular, and threedimensional clusters. The nuclei are enlarged and hyperchromatic.

Histology: The encapsulated nodule is located in the subcutaneous adipose tissue and shows capsular invasion. One nodule is lobulated. There are no findings consistent with the nuclei of papillary carcinoma. Well-differentiated thyroid carcinomas revealing needle tract implantation usually show high MIB-1 labeling index.

Case 22 Hyalinizing trabecular tumor





The margin of the tumor is not perfectly smooth. Color Doppler shows hypervascular flow, called "tumor inferno". Cut surface is solid and yellowish white.



Cytology: The hyaline materials are located at the center of cell clusters and radially elongated. The border between hyaline materials and the tumor cells is obscure. Cell border of the tumor cells is indistinct. Intranuclear cytoplasmic inclusions (ICIs) and yellow bodies (YBs) (red arrow) are seen. **Histology**: The tumor cells mainly show trabecular pattern with intra- and inter- trabecular hyaline materials. ICIs and YBs (yellow arrow) are seen. Psammoma bodies are not located in the stroma but the lumen.

Case 23 Papillary carcinoma, conventional





The tumor is well-demarcated, but the border is irregular. Tiny calcification is seen. The size of the tumor is less than 1cm (microcarcinoma).



Cytology: Papillary tissue fragments associated with stroma component are seen. Duct-like appearance means papillary cluster without stromal component (LBC). Convoluted nuclei are characteristic of papillary carcinoma in SurePath smear.

Histology: Tumor cells mainly show papillary growth. Ground glass chromatin, nuclear grooves, intranuclear cytoplasmic inclusions, nuclear overlapping are seen.

Case 24 Papillary carcinoma, follicular variant





A solid nodule with calcification is seen at the upper portion of the left lobe. Cut surface is homogeneous and somewhat shiny, like follicular neoplasm.



Cytology: Tumor cells show follicular clusters. Intranuclear cytoplasmic inclusions, nuclear grooves, lobulated nuclei, irregular-shaped nuclei are seen.

Histology: Tumor cells mainly show follicular pattern, and have nuclear features consistent with papillary carcinoma, except for ground glass nuclei.

Case 25 Papillary carcinoma, macrofollicular variant





A encapsulated tumor like follicular neoplasm is seen.



Cytology: There are abundant colloid in the background. Tumor cells appear as two-dimensional sheet. Nuclear grooves, irregular-shaped nuclei, and crowded nuclei are seen.

Histology: Encapsulated follicular lesion composed mainly of large follicles showing ground glass nuclei, nuclear overlapping, irregular-shaped nuclei, and nuclear groove.

Case 26 Papillary carcinoma, tall cell variant





The tumor is solid, whitish, and invasive.



Cytology: The tumor cells are tall or polyhedral, and show densely stained abundant cytoplasm, low N/C ratio, and elongated cytoplasm (tail formation).

Histology: The carcinoma cells show trabecular or papillary growth. Most of the tumor are composed of tall columnar cells whose heights are more than three times as tall as their width.

Case 27 Papillary carcinoma, cribriform variant





Well-demarcated, whitish tumor occupies right lobe. Grossly, it looks like follicular neoplasm.



The case is teenage female.

Cytology: The smear is cellular. Large solid clusters with window (consistent with empty lumen) are seen. Nuclear chromatin is not ground glass but granular. The tumor cells are tall columnar. The nuclei are short spindle.

Histology: Cribriform pattern without colloid, papillary growth of tall cells, solid growth composed of spindle cells, and morules with peculiar nuclear clearing are seen.

Immunostaining: β-catenin is positive for the nuclei and cytoplasm. ER and PgR are positive except for morules.

Case 28 Papillary carcinoma, Warthin tumor-like





A nodule with indistinct border is seen in the thyroid showing Hashimoto's thyroiditis.



Cytology: There are a large number of lymphocytes and plasma cells in the background. Tumor cells show abundant, densely stained cytoplasm. The nuclei are irregular shaped, like those of histiocytes.

Histology: Eosinophilic tall columnar tumor cells show papillary growth. The stroma contains lymphocytes and plasma cells. Lymph follicles are scattered.

Case 29 Papillary carcinoma, solid variant





A nodule with calcification is present in the left lobe.



Cytology: Tumor cells exhibit intranuclear cytoplasmic inclusions and nuclear grooves. The clue indicating solid variant is a patternless pattern (neither sheet, follicle, nor papillary pattern). **Histology**: Tumor cells mainly proliferate as alveolar structure. The tumor cells are morphologically similar to conventional papillary carcinoma. Poorly differentiated carcinoma is more atypical.

Case 30 Papillary carcinoma, oxyphilic cell variant





A whitish nodule is seen at the upper portion of the left lobe (arrow).



Cytology: Papillary and sheet-like clusters are seen. The tumor cells show low N/C ratio, and the cytoplasm is abundant, densely-stained, and slightly granular. The cell border is distinct. The nuclei are irregular shaped, and have intranuclear cytoplasmic inclusions.

Histology: The nuclei are consistent with papillary carcinoma, and the cytoplasm is eosinophilic.

Case 31 Papillary carcinoma, diffuse sclerosing variant



The left lobe reveals numerous punctate echogenic foci without posterior acoustic shadowing (psammoma bodies). Grossly, the lesion occupies throughout the left lobe and isthmus.



Cytology: Numerous psammoma, lymphocytes bodies, mirror ball-like clusters, septate intracytoplasmic vacuoles, and densely stained cytoplasm are characteristic of this variant. **Histology**: Carcinoma cells are mainly present in the dilated lymph vessels. Carcinoma is associated with squamous metaplasia and numerous psammoma bodies. Thyroid shows chronic thyroiditis.

Case 32 Papillary carcinoma, cystic



Hobnail cells



Cytology: Aspirated material is fluid, and exhibits low cellularity and proteinaceous background. LBC smear is more cellular. Tumor cells appear as ball-like or mirror ball-like clusters, associated with hobnail cells. The cytoplasm tends to be abundant and weakly stained. Septate intracytoplasmic vacuoles are seen. Chromatin pattern is not ground glass. Tumor cells showing sheet-like pattern show high N/C ratio, dense cytoplasm, irregular shaped nuclei, and prominent nucleoli. Histology: Papillary carcinoma forms large cystic lesion that is not degenerative change.

Case 33 Papillary carcinoma, polycystic



Polycystic lesions are present at the anterior of the left lobe. The findings ultrasonographically look like benign nodules. Grossly, the lesions are sponge-like.

Histology: Multiple cystic papillary carcinoma lesions aggregate. Normal thyroid follicles lie between the lesions. Papillary carcinoma shows micropapillary growth and piling up.

Case 34 Papillary carcinoma, fasciitis-like stroma



Histology: The stroma is composed of abundant collagenous connective tissue with plump fibroblasts showing fascicular pattern. Small-sized blood vessels with thick wall are scattered.

Case 35 Papillary carcinoma with squamous cell metaplasia





A infiltrative nodular lesion is seen in the right lobe. The nodule is focally yellowish.



Cytology: In addition to conventional papillary carcinoma cells, cell clusters showing eddy formation are seen.

Histology: Squamous eddies are present in the fibrotic stroma. They are not squamous cell carcinoma, but metaplastic lesion.

Case 36 Papillary carcinoma (hobnail cell)





Subcutaneous nodule appeared 32 years after papillary thyroid carcinoma was resected (needle tract implantation).



Cytology: Hobnail cells and septate intracytoplasmic vacuoles are seen. **Histology**: Papillary growth with hobnail pattern and septate intracytoplasmic vacuoles are seen. Papillary carcinoma with prominent hobnail pattern is a moderately differentiated variant with aggressive clinical behavior.

Case 37 Poorly differentiated carcinoma





Whitish solid nodular lesion is present in the right lobe.



Cytology: Aspirated material is cellular. Tumor cells appear as large, solid cell clusters. There are no papillary or follicular clusters.

Histology: The tumor is composed of large atypical cells showing solid growth. The nuclei are hyperchromatic and the cytoplasm is abundant. The cell border is distinct.

Case 38 Anaplastic carcinoma





The tumor occupies throughout the right lobe, and shows necrosis and cystic degeneration.



Cytology: In the background, tumor diathesis such as necrotic materials, neutrophils, and cell debris, is prominent. The carcinoma cells are apparently atypical.

Histology: The findings of cytological and histological section are not same, because the tumor was resected after chemotherapy. The stroma exhibits lymphocytes, plasma cells, and foamy cells. The carcinoma cells tend to be more atypical. Papillary carcinoma as pre-existing lesion is co-existent.

Case 39 Anaplastic carcinoma with osteoclast-like multinucleated giant cell





The trachea is compressed by a tumor mass and shifts to the left.



Cytology: Carcinoma cells and osteoclast–like multinucleated giant cells are intermingled. Elongated cytoplasm of the carcinoma cells is highlighted in LBC smear. **Histology** (needle biopsy): Osteoclast-like multinucleated giant cells are conspicuous. **Immunostaining**: Carcinoma cells are positive for PAX8.

Case 40 Medullary carcinoma (aggressive)





Medullary carcinoma tends to occur at the upper one third of the lobe.



Cytology: Carcinoma cells are discohesive and do not show sheet-like, follicular, or papillary clusters. Chromatin pattern is salt & pepper. Nuclear grooves and intranuclear cytoplasmic inclusions (arrow) are seen. No amyloid materials are seen.

Histology: Carcinoma cells proliferate as alveolar and solid patterns. This case shows marked atypia, mitotic figures, vascular invasion, high MIB-1 labeling index; which are unusual findings in medullary carcinoma, and indicate aggressive behavior. Immunostaining: Calcitonin is positive.

Case 41 Medullary carcinoma (spindle cell)





Well-demarcated tumor is seen in the lower portion of the lobe, where is not prevailing site.



Cytology: Discohesive spindle cells aggregate without any specific arrangement. The cell shape is longer in LBC smear. The cytoplasm is weakly stained, and the cell border is indistinct. Chromatin pattern is salt & pepper.

Histology: Carcinoma cells proliferate as solid pattern. Entrapped thyroid follicles should not be confused to mixed medullary and follicular carcinoma component.

Immunostaining: Calcitonin is positive.

Case 42 Medullary carcinoma (pseudo-tubules)





A yellowish white, solid nodule is seen in the right lobe.



Cytology: Oval to short-spindled carcinoma cells are discohesive. The cytoplasm is weakly stained. Chromatin pattern is salt & pepper. Elongated cytoplasm is highlighted in LBC smear. **Histology**: Gland-like structure is visible. The structure is artifact caused by separation between carcinoma cells, pooling of proteinaceous fluid, or intra-alveolar hemorrhage.

Case 43 MALT lymphoma





Multinodular lesions are seen in the background of Hashimoto's thyroiditis. Aspiration cytology was performed for the nodule of the left lobe (arrow).





Cytology: Medium-sized lymphoid cells are predominant. Chromatin pattern is similar among different-sized lymphoid cells. Irregular-shaped (elongated, spindled, and convoluted) nuclei are seen. In LBC smear, the nuclei are markedly degenerated (swelling, smashed chromatin pattern, and discontinuous nuclear margin).

Histology: Packing and lymphoepithelial lesion are seen.

Case 44 Diffuse large B-cell lymphoma





Ultrasound examination reveals enlarged and hypoechoic thyroid. Resected thyroid tissue fragment is whitish.



Cytology: Large-sized lymphoid cells are predominant. Non-neoplastic small sized lymphocytes and histiocytes are also seen. The follicular cells are not typical oxyphilic cells.

Histology: Packing appearance is highlighted by cytokeratin AE1/AE3 immunostaining.

Case 45 ITET/CASTLE



Cytology: Aspirated materials are highly cellular. Carcinoma cells show solid three-dimensional clusters. Lymphocytes and plasma cells are observed not only in the background, but also within carcinoma cell clusters.

Histology: Carcinoma cells are round to oval and proliferate forming lobulated or anastomosing large solid nests. The stroma is abundant and associated with an infiltration of lymphocytes and plasma cells.

Immunostaining: CD5 is not always positive. CD5(-), PAX8(-), TTF-1(-), p63(+), cytokeratinAE1/AE3(+)

Case 46 Parathyroid cyst







Aspirated material is characteristic watery clear fluid. Cytological examination is not useful because of no parathyroid cells in the fluid. A measurement of PTH level in the fluid is the most important tool.

Case 47 Parathyroid cyst and Parathyroid adenoma



Parathyroid cyst and adenoma are coincidentally present. This case is not parathyroid adenoma with cystic degeneration. On color Doppler, parathyroid adenoma is suspected as a nodule with blood flow (arrow). Parathyroid adenoma is grossly yellowish brown (arrow).

Case 48 Parathyroid adenoma





A lobulated nodule is present at the posterior side of the left lobe (arrow).



Cytology: Aspiration cytology was performed because parathyroid tumor is not clinically suspected. The smear is cellular. Tumor cells appear as overlapping trabecular pattern without colloid. Chromatin pattern is coarse granular.

Histology: The nodule is composed of chief cells showing alveolar, trabecular, and solid growth. The stroma is rich in capillaries. Satellite nodules, fibrosis, and hemosiderin-laden macrophages are probably secondary to the preoperative aspiration procedure.

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