

第38回Radiology Ultrasound研究会(RaD-US)学術講演会
2013年6月22日(土)
東京都済生会中央病院

甲状腺の病理

元井 紀子

Noriko Motoi, MD, PhD

公益財団法人がん研究会がん研究所病理部

甲状腺の病理

- 甲状腺癌の分類
- 甲状腺癌の病理像
- 希少例、診断困難例の紹介
- 液状化細胞診と分子病理学的アプローチ

Histological Classification of Thyroid tumor

Origin	Classification		n (*)	(%)
Follicular epithelial				
(benign)	Follicular adenoma	濾胞腫瘍	14	1.8
(malignant)	Papillary ca	乳頭癌	564	71.9
	Follicular ca	濾胞癌	42	5.4
	Poorly differentiated ca	低分化癌	42 (P33, F3, U6)	5.4
	Undifferentiated (anaplastic) ca	未分化癌	26	3.3
(Tumor-like lesion)	Adenomatous goiter	腺腫様甲状腺腫	70	8.9
C cell	Medullary ca	髄様癌	13	1.7
Non-epithelial	Malignant lymphoma	悪性リンパ腫	18	2.3
Others	Sarcoma, metastatic tumor etc.	肉腫、転移性腫瘍など	46	5.9
	TOTAL		784	100

(* JFCR : 2005-2009)

Thyroid Cytology - The Bethesda System ベセスダシステム

Diagnostic Categories		Risk of Malignancy (%)	Usual Management
Nondiagnostic or Unsatisfactory (検体不達)	Cyst fluid only Virtually acellular specimen Other (obscuring blood, clotting artifact, etc)	1-4	Repeat FNA with ultrasound guidance
Benign (良性)	benign follicular nodule, lymphocytic (Hashimoto) thyroiditis granulomatous (subacute) thyroiditis	0-3	Clinical follow-up
Atypia of Undetermined Significance/ Follicular Lesion of Undetermined Significance (AUS/FLUS)		5-15	Repeat FNA
Follicular Neoplasm or Suspicious for a Follicular Neoplasm (濾胞性腫瘍)	Specify if Hurthle cell (oncocytic) type	15-30	Surgical lobectomy
Suspicious for Malignancy (悪性の疑い)		60-75	Near-total thyroidectomy or surgical lobectomy
Malignant (悪性)	Papillary thyroid carcinoma, Poorly differentiated carcinoma, Medullary thyroid carcinoma Undifferentiated (anaplastic) carcinoma, Squamous cell carcinoma, Carcinoma with mixed features (specify), Metastatic carcinoma, Non-Hodgkin lymphoma, other	97-99	Near-total thyroidectomy

甲状腺の病理

- 甲状腺癌の分類
- 甲状腺癌の病理像
- 希少例、診断困難例の紹介
- 液状化細胞診と分子病理学的アプローチ

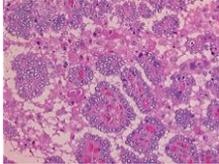
Pathology of Thyroid, N Motoi 2013

乳頭癌 PAPILLARY CARCINOMA

Thyroid – 乳頭癌 Papillary carcinoma



- 核所見が重要
1. スリガラス状核
Ground-glass nuclei (nuclear clearance)
 2. 核溝 Nuclear groove
 3. 核内細胞質封入像
Intranuclear cytoplasmic inclusion (pseudoinclusion)
 4. 重畳核 overlapping nuclei

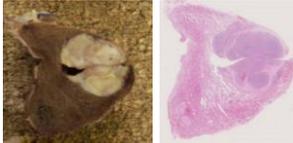


- 乳頭状構造
濾胞状構造
-- follicular variant
- 線維増生
石灰化 (砂粒小体 psammoma body)
硝子化
嚢胞形成 (Cyst formation)

Pathology of Thyroid, N Motoi 2013

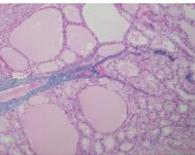
濾胞癌 FOLLICULAR CARCINOMA

Thyroid – Follicular carcinoma



- Type of invasion
- Minimally invasive
--- vs. Follicular adenoma
 - Widely invasive

Malignant tumor of Follicular epithelial origin
Lack the characteristic findings of papillary ca.



- Criteria of malignancy
1. Capsular invasion
 2. Vascular invasion
 3. Extra-thyroidal metastasis (LN, bone, lung)

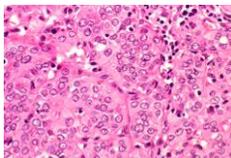
Not related to cellular atypia. (– Atypical adenoma)

Necrosis, high mitotic rate,

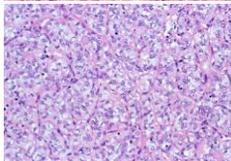
Pathology of Thyroid, N Motoi 2013

低分化癌 POORLY DIFFERENTIATED CARCINOMA

Thyroid – 低分化癌 Poorly differentiated carcinoma



- Poorly differentiated ca.
- Growth pattern
 - solid
 - trabecular
 - sheet-like
 - Insular
- No/Little colloid formation
- No/Little nuclear atypia
 - D/D: Undifferentiated ca



Pathology of Thyroid, N Motoi 2013

未分化癌 UNDIFFERENTIATED/ ANAPLASTIC CARCINOMA

Undifferentiated carcinoma

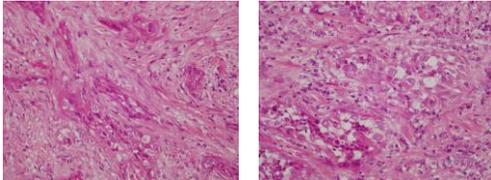


Marked architectural and cytologic atypia

Necrosis, Hemorrhage,
Pleomorphism – spindle cell, giant cell

Osteoclastic giant cells
Reactive bone and/or cartilage formation

(synonymous: carcinosarcoma)



Pathology of Thyroid, N Motoi 2013

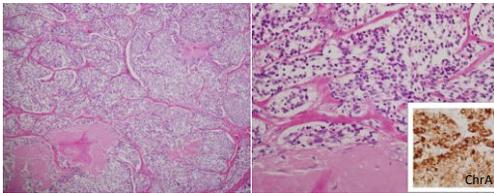
髓様癌 MEDULLARY CARCINOMA

Thyroid - Medullary carcinoma



C cell origin – calcitonin
Neuroendocrine tumor, Amyloid deposition
IHC: Chromogranin A, CEA

Hereditary background (20-30%)
ret functional mutation
MEN 2A, 2B, FMC



Pathology of Thyroid, N Motoi 2013

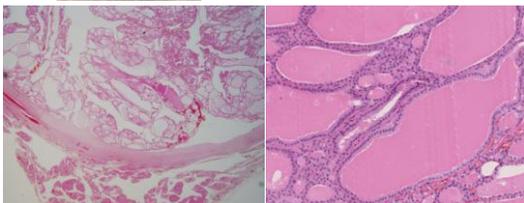
良性病変 BENIGN LESION

Thyroid Follicular adenoma

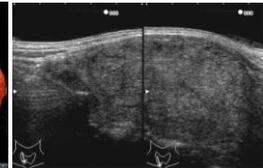


Thyroid follicular tumor
Lack criteria of malignancy

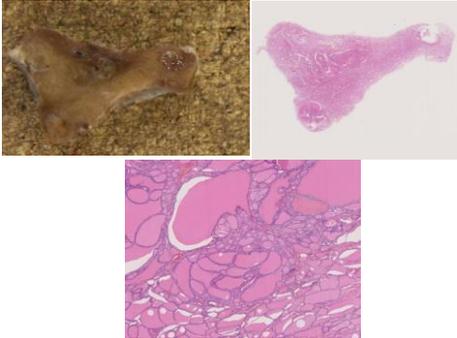
Encapsulated tumor
No vascular invasion
No metastasis



Thyroid – Adenomatous goiter



Adenomatous nodule/ goiter



甲状腺の病理

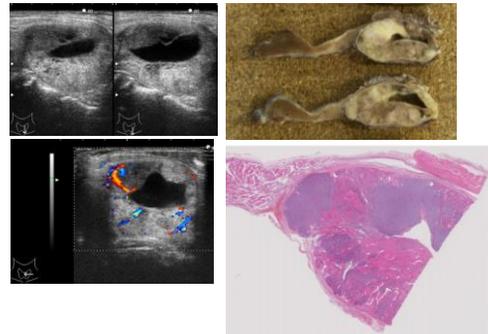
- 甲状腺癌の分類
- 甲状腺癌の病理像
- 希少例、診断困難例の紹介
- 液状化細胞診と分子病理学的アプローチ

H07-19848

Atypical adenoma
or
encapsulated undifferentiated carcinoma
???

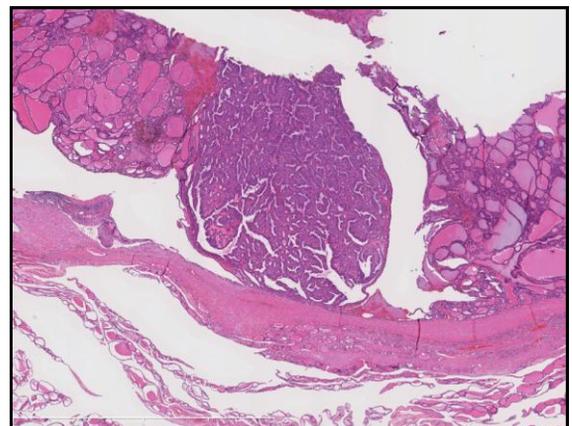
Atypical follicular adenoma 異型濾胞腺腫

H07-19848



Difficult case

PAPILLARY CA. OR AD GOITER?



甲状腺の病理

- 甲状腺癌の分類
- 甲状腺癌の病理像
- 希少例、診断困難例の紹介
- 液状化細胞診と分子病理学的アプローチ

European Cytology Conference (ECC) 2012
Dubrovnik, Croatia (10/03/2012)

CLINICAL APPLICATION OF LIQUID BASED CYTOLOGY (LBC) FOR DIAGNOSIS AND GENETIC TEST OF THYROID LESIONS

Motoi Noriko.1, Arai Y.2, Suzuki N.2, Nomura K.1, Furuta N.2, Kanda H.1, Sato Y.1, Yamada K.3, Toda K.4, Sugitani I.4

1 Division of Pathology, The Cancer Institute, JFCR, Tokyo, Japan
2 Cytology, The Cancer Institute Hospital, Tokyo, Japan
3 Radiology, The Cancer Institute Hospital, Tokyo, Japan
4 Head and Neck, The Cancer Institute Hospital, Tokyo, Japan

日本臨床細胞学会総会(春) 2013 06 02
品川、東京

甲状腺穿刺吸引細胞診への液状化細胞診技術の応用

元井紀子^{1,2}、荒井祐司²、鈴木奈緒子²、神田浩明^{1,2}、佐藤由紀子^{1,2}、石川雄一^{1,2}、山田恵子³、戸田和寿⁴、杉谷巖⁴

1. 公益財団法人がん研究会 がん研究所 病理部
2. 同 がん研有明病院 細胞診断部
3. 同 がん研有明病院 超音波検査部
4. 同 がん研有明病院 頭頸科

LBCの利点

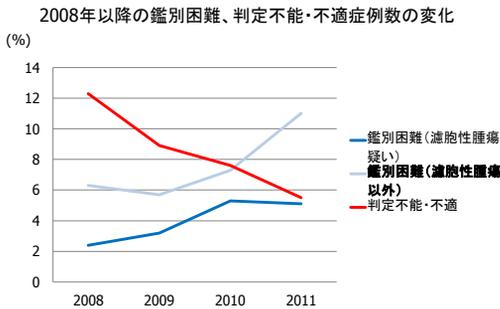
診断精度、効率の向上

- (1) 採取細胞を無駄にすることなく有効利用が可能である
- (2) 細胞の重なりが少なく、塗抹範囲の標準化された適正標本が得られる
- (3) 検鏡効率を向上させることができる
- (4) LBCは数週間単位で細胞保存が可能であり、標本を再度作成することができるので、患者への再検査の負担を軽減できる

発展性

- (5) 免疫染色や遺伝子検査などによる補助診断法に供することが可能で診断精度の向上が期待できる
- (6) 機械による標本作製およびスクリーニングの自動化への発展性がある。

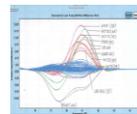
形態学的評価結果 Bethesda system (FNA症例: 1467例)



第55回日本甲状腺学会で発表

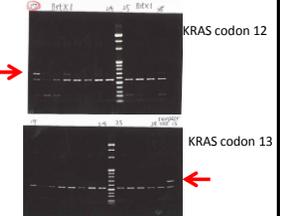
KRAS

High resolution melting (HRM)



GeneScanning (LightCycler 480[®]) Roche
Primers (KRAS exon 2)
FWD: 5'-gtggagattgatgataaacct-3'
REV: 5'-gaaatggcagagaaccttca-3'

PCR - RFLP (BstX1 for codon12, XcmI1 for codon 13)



Ref:
KRAS, Dieterle CP, et al. Clinical Cancer Research. 2004;10:641-650.
BRAF, Patel A, et al. Endocr Pathol. 2011;22:195-199.

References

- Rossi, E. D., Raffaelli, M., et al., *Diagnostic efficacy of conventional as compared to liquid-based cytology in thyroid lesions: evaluation of 10,360 fine needle aspiration cytology cases*. *Acta Cytol*, 2009. 53(6): p. 659-666.
- Rossi, E. D., Morassi, F., et al., *Thyroid fine needle aspiration cytology processed by ThinPrep: an additional slide decreased the number of inadequate results*. *Cytopathology*, 2010.
 - Single Institution = 553 cases
- Sidiropoulos, N., Dumont, L. J., et al., *Quality improvement by standardization of procurement and processing of thyroid fine-needle aspirates in the absence of on-site cytological evaluation*. *Thyroid*, 2009. 19(10): p. 1049-1052.
- Ohori, N. P., Nikiforova, M. N., et al., *Contribution of molecular testing to thyroid fine-needle aspiration cytology of "follicular lesion of undetermined significance/atypia of undetermined significance"*. *Cancer Cytopathol*, 2010. 118(1): p. 17-23.
 - 513 cases
 - Analysis for BRAF and RAS gene mutations and RET/PTC and PAX8/PPAR gamma gene rearrangements