Thyroid tumours with a follicular pattern of growth
Tumores del tiroides com patrón folicular

Long Course, SEAP Congress, Cadis, May 23, 2013

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Nuestro deseo es que todas las presentaciones de los cursos sean lo más concretas posibles con el fin de trasmitir mensajes claros, precisos y cortos.

Ricardo González Cámpora
Presidente de la SEAP-IAP
Most frequent diagnostic problems of thyroid pathology in a consultancy practice

1. Is there a focus (or some foci) of papillary carcinoma in “this” Hashimoto’s thyroiditis or “this” nodular goiter?

2. Is this lesion an adenoma, a follicular carcinoma or a follicular variant of papillary carcinoma? Could this be a UMP?

3. Is this a well differentiated carcinoma with a solid pattern of growth or a poorly differentiated carcinoma?

4. How would you classify this Hürthle cell lesion?
Follicular patterned, encapsulated neoplasms

- Adenoma
- Minimally invasive follicular ca
- Encapsulated Follicular variant of PTC

From 2000 on, also Tumours of uncertain malignant potential, “UMPs”
Thyroid nodule & Adenoma

Differential diagnosis:
Is it necessary? And, if yes, is it possible?

Up to 60% of nodules in multinodular goiters are monoclonal (WHO, 2nd ed)
Encapsulated follicular patterned tumours
Intratumoural lymph vessel density is related to presence of lymph node metastases and separates encapsulated from infiltrative papillary thyroid carcinoma.
Follicular patterned, encapsulated neoplasms

Adenoma

Minimally invasive follicular ca

Encapsulated follicular variant of PTC

From 2000 on, also Tumours of uncertain malignant potential, “UMPs”
Malignancy in follicular patterned thyroid tumours

Capsular and/or VASCULAR INVASION

Pattern of growth
- Solid, insular, trabecular
- Embryonal, fetal
- Normofollicular
- Macrofollicular

Nuclear features
- PTC NUCLEI
PITFALLS IN THE “VASCULAR INVASION” FRONT
What is the best way to diagnose parenchymatous/vascular invasion?

- Cytopathology: No
- Histopathology: Yes
- Detection of biomarkers in the plasma/blood: May be
- Conventional molecular pathology and high throughput approaches: No
WHAT ABOUT FOLLICULAR-CELL TUMOURS WITH EQUIVOCAL CAPSULAR INVASION?
Follicular tumour with a thin capsule
Benign vs Malignant

Follicular carcinoma

Follicular tumour of uncertain malignant potential

Follicular adenoma

Malignancy in follicular patterned thyroid tumours

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
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</tr>
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<tr>
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WHAT ABOUT FOLLICULAR TUMOURS WITH INTERMEDIATE NUCLEI?
IMMUNOHISTOCHEMICAL MARKERS OF PAPILLARY THYROID CARCINOMA

- Cytokeratin 19
- Lewis X and S Lewis X
- Galectin 3
- HBME 1
- Fibronectin
- ....................
Galectin-3 and HBME-1 expression in well-differentiated thyroid tumors with follicular architecture of uncertain malignant potential

8 cases with questionable invasion
13 cases with questionable nuclear changes

No diagnostic value in concrete cases

Papotti M et al, Mod Pathol 18:541, 2005

The same holds true for molecular pathology
B-RAF (V600E) MUTATIONS IN 176 PAPILLARY THYROID CARCINOMAS

Warthin-like PTC > 75%
Conventional PTC ~ 50%

Encapsulated follicular variant PTC < 5%

Soares et al, Oncogene 2003
Trovisco et al, J Pathol, 2004
Lima et al, JCEM 89:4267, 2004
ENCAPSULATED TUMOUR

WHAT TO DO WHEN THE NUCLEI ARE NOT TYPICAL?
LOOK FOR TYPICAL NUCLEI ELSEWHERE

AND, MOST IMPORTANTLY, LOOK FOR (VASCULAR) INVASION
• Well differentiated tumor of uncertain malignant potential

• Well differentiated carcinoma, NOS

WHO book on Endocrine Tumours, 3rd edition, 2004
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<thead>
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<tr>
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<tr>
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<tr>
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<tr>
<td>Medullary carcinoma</td>
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<td>Poorly differentiated carcinoma</td>
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WHO book on Endocrine Tumours, 3rd edition, 2004
Malignancy in Hürthle cell tumours

Diagnostic hints

Capsular/vascular invasion

Nuclear features
Follicular variant of PTC

Three main types:

- Encapsulated
- Poorly circumscribed
- Diffuse, aggressive, multinodular

Multicentricity

Vascular invasiveness

Lung and bone metastases
What about encapsulated, non-invasive follicular variant of PTC?

Is it clinically malignant?
Problems of encapsulated follicular or papillary carcinoma

PARTIAL vs TOTAL THYROIDECTOMY

• Encapsulated, non-angioinvasive follicular variant of PTC (with or without BRAF mutation?) and encapsulated, non-angioinvasive follicular carcinoma do not imply total thyroidectomy.
  (The same holds true for follicular and well differentiated tumours of uncertain malignant potential)

• It is mandatory to have very good sonography data & to study thoroughly the surgical specimens

Rosai, Sobrinho-Simões,… 2010

TAKE HOME LESSON: In every encapsulated lesion look for vascular invasion
Follicular carcinoma

Minimally invasive

Angioinvasive

Widely invasive

Rosai et al, 2004
WHO book on Endocrine Tumours, 2004
240 cases (1978-2003) with nodal and/or distant metastases [Excluding medullary, poorly diff and undiff ca]

NOT A SINGLE CASE OF:

Follicular tumour of uncertain malignant potential

Well differentiated tumour of uncertain malignant potential

Minimally invasive follicular carcinoma without vascular invasion

Encapsulated follicular variant of PTC without invasion

Magalhães et al, 2010
• Follicular adenoma
• Minimally invasive FTC (without angioinvasion)
• Encapsulated FVPTC (without angioinvasion)
• Follicular tumour, UMP
• Well differentiated tumour, UMP

Lobectomy or Lobectomy plus isthmectomy
• Minimally invasive FTC with angioinvasion
• Encapsulated FVPTC with angioinvasion
• PTC, FTC and PDTC

Total thyroidectomy plus radioactive iodine