Pitfalls in thyroid tumor pathology

Prof. Valdi Pešutić-Pisac MD, PhD
Too many or....

THE ROOKIE
Tumour herniation through a torn capsule simulating capsular invasion

- fibrous capsule with a sharp discontinuity, suggestive of mechanical rupture
- As a general rule, one should question the presence of true capsular invasion if the suspicious area is present only at the very edge of the submitted tissue.
Reactive vascular proliferation simulating vascular invasion

- may simulate vascular invasion by tumour
- endothelial papillary hyperplasia (Masson’s lesion) possibly as the result of fine-needle aspiration (FNA)

- These changes can coexist with true vascular invasion by tumour and it is probable that some of them are actually a secondary event resulting from intravascular tumour growth.
Pseudoinfiltration of skeletal muscle by benign thyroid tissue

- At the periphery of the thyroid gland, there is a close anatomical relationship between the outermost thyroid follicles and the skeletal muscle fibres of the region.

- **hyperplastic conditions**, Graves’ disease, these proliferating follicles may grow in between the muscle fibres in a seemingly infiltrative fashion.
Parasitic nodules simulating metastatic thyroid carcinoma

- presence of thyroid tissue in the lateral neck, anatomically separate from the main thyroid gland
- perfectly benign nature and representative of so-called parasitic, accessory or sequestered nodules
- complicating factor is that parasitic nodule may be affected by Hashimoto’s thyroiditis.
Nuclear clearing in benign conditions resembling the nuclear changes of papillary thyroid carcinoma

- in diffuse hyperplasia (Graves’ disease)
- pronounced degree of nuclear clearing is frequently found in the follicular cells of Hashimoto’s thyroiditis
- In both of these situations the nuclear changes are diffuse throughout the gland
Nuclear bubbles simulating nuclear pseudoinclusions

(‘pseudopseudoinclusions’)

- The mechanism of formation of these bubbles is unclear.
- Likelihood they represent an artefact of tissue processing due to an excessively high temperature of the water bath in which the tissue sections have been floated.
Benign papillary structures simulating the papillae of PTC

- tend to point towards the centre of a cystically dilated follicle
Solid variant of PTC overdiagnosed as poorly differentiated (insular) carcinoma

- PTC, particularly when occurring in children
- Insular: tumour necrosis, variable mitotic activity and nuclear hyperchromasia.
Solid cell nests simulating papillary microcarcinoma

- Solid cell nests are remnants of the fifth (ultimobranchial) body that can be found incidentally within the thyroid gland.
- Many of the cells within the nests have longitudinal grooves of a type similar to that seen in PTC.
- Negativity for thyroglobulin and TTF-1 and strong nuclear reactivity for p63.
Cystic degeneration in PTC metastatic to a cervical lymph node simulating branchial cleft cyst
Multinodular pattern of invasion in oncocytic follicular carcinoma simulating nodular hyperplasia

- Solid, trabecular, fibrous bands
Oncocytic medullary carcinoma simulating oncocytic follicular cell tumour

- Production of melanin
- Request a battery of immunostains
- Calcitonin, chromogranin, CEA, thyroglobulin
CASTLE simulating poorly differentiated or undifferentiated thyroid carcinoma

- Thyroglobulin and TTF-1 are negative, whereas CD5 is often positive
- Disease tends to occur in younger patients
Paucicellular anaplastic thyroid carcinoma simulating Riedel’s thyroiditis

- The diagnosis can be supported at the immunohistochemical level by demonstrating reactivity for keratin (although usually not for thyroglobulin and TTF-1)
Intrathyroid parathyroid neoplasm simulating a primary thyroid tumour

- Tumours and hyperplasias
- Homogeneous population of relatively small cuboidal cells with pale to clear cytoplasm
- Rich vascular network
Metastatic lesions in the thyroid

- Is it a primary thyroid tumour?
- If yes, is it a follicular-cell or a parafollicular-cell tumour?
- Tumour is negative for both markers one has to consider, after having excluded the diagnoses of undifferentiated carcinoma, primary soft tissue tumour and calcitonin-negative medullary carcinoma, the possibility of a metastatic lesion
- clear cell carcinoma of the kidney - DD: clear cell follicular adenoma or clear cell follicular carcinoma
- lobular carcinoma of the breast - DD: medullary carcinoma, mainly due to the folliculotropic nature of the metastatic cells
- mucinous carcinoma of the digestive or respiratory tract - DD: primary mucinous carcinoma of the thyroid
- squamous cell carcinoma of the superior aero-digestive tract - DD: squamous cell carcinoma of the thyroid
- neuroendocrine carcinomas - DD: medullary carcinoma
Do never have.....

- Excessive reliance on immunohistochemical results for the diagnosis of PTC
**Surprise.......**
The most important points concern the

- acknowledgement of the difficulties in diagnosing minimally invasive follicular carcinomas

- and follicular-patterned lesions of the thyroid displaying nuclei which are difficult to characterize as typical of papillary thyroid carcinoma (PTC)
As a consequence of the aforementioned difficulties it has been decided to accept the utilization, as rarely as possible, of the following designations:

- “follicular tumour of uncertain malignant potential”
- “well differentiated tumour of uncertain malignant potential”
- “well-differentiated carcinoma, not otherwise specified”
Follicular-patterned lesions

- *the following questions are:*
- it is a *benign* lesion or a *malignant*?

- In case we think it is malignant, is it a minimally invasive follicular carcinoma or a follicular variant of PTC?
two separate problems in the diagnosis of encapsulated tumours with follicular architecture:

- deciding whether minor nuclear changes justify a diagnosis of follicular variant of PTC
- deciding whether minor degrees of capsular penetration justify a diagnosis of malignancy
It is crucial to emphasise that in regular surgical pathology practice this term should not be used as a substitute for adequate capsular sampling.
The problem of the identification (and pathological meaning) of small foci of PTC-nuclei in benign lesions is not restricted to follicular adenomas.

such finding is particularly frequent in Hashimoto’s thyroiditis and nodular (adenomatous) goitres and often poses diagnostic problems.
we would not advise to jump to a diagnosis of Hashimoto’s associated PTC in the absence of a microscopically well-defined neoplasm.

In other words, only make a diagnosis of PTC on a background of Hashimoto’s thyroiditis when you are able to identify a fairly typical papillary microcarcinoma.
The problems raised by nodular goitres displaying PTC-like nuclei

- very abundant and are present throughout the different nodules one has to rule out the diagnosis of a rare form of follicular variant of PTC designated as diffuse or multinodular follicular variant of PTC.
- If the large, clear and irregular nuclei are rare and do not form any clusters do not go beyond the diagnosis of nodular (adenomatous) goitre.
- If such nuclei are concentrated in one of the nodules and tend to form one or several microcarcinomas, then we make a diagnosis of follicular variant of PTC.
the diagnosis of the follicular variant of PTC has become one of the hottest topics

- this variant of PTC is being currently overdiagnosed due to the too liberal utilization of the PTC nuclear criteria
- There are three morphologic subtypes of the follicular variant of PTC:
  - poorly circumscribed, encapsulated and multinodular (diffuse) form.
  - The encapsulated form is the most difficult to diagnose because in many instances it overlaps either with adenoma/nodular goitre or with minimally invasive follicular carcinoma
Take home lesson: even if one is seeing a lesion resembling a “fetal” follicular adenoma one should look carefully for the nuclear features.
....is it over too much?
Thyroid pathology – team work