Challenging cases in endocrine / neuroendocrine pathology

CASE 2

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• A 73-year old female with right neck lymphadenopathy,
  • Dominate nodule in the right thyroid lobe (55mm).
  • Radiological examination - pulmonary metastases.
• FNA biopsy of the dominant thyroid nodule and the enlarged lymph node was performed.
...findings from thyroid tumor were nondiagnostic - only necrotic tissue...

...from lymph node were consistent with metastasis of carcinoma with oncocytic features (probably thyroid carcinoma)“.  

The patient was submitted to total thyroidectomy with right neck lymph nodes dissection.
Macroscopic examination

The thyroidectomy specimen weighted 63 g. (Right lobe 65X50X30 mm; Left lobe 45X30X20 mm)

**Right lobe:**

Multilobulated tan-brown nodule measuring 55 mm with areas of hemorrhage and necrosis.

In the rest of the gland there were several more nodules ranging from 5 to 15 mm at maximum diameter with colloidal appearance.

**Lymphadenectomy specimens:**

Thirty-three lymph nodes measuring 3–20 mm in diameter.
Microscopic examination
Microscopic examination
Microscopic examination
Microscopic examination: Lymphadenectomy specimens

In total 9 of 33 lymph nodes were positive for metastasis.

Level VI. Anterior (Central) Compartment: 3 negative lymph nodes.

Level V (sublevels VB): Positive 5 of 11 lymph nodes.

Level III. Middle Jugular Group: Positive 2 of 5 lymph nodes.

Level IIA, III, IV: Positive 1 of 6 lymph nodes.

Level IIB: 6 negative lymph nodes.

Level I (Sublevel IB): 3 negative lymph nodes (0/3)
Microscopic examination: Lymphadenectomy specimens

H&E, 40X

H&E, 200X
Microscopic examination: lymphadenectomy specimens

Lymph node metastasis present at level III and VB.
1. Widely invasive Hürthle cell carcinoma or follicular thyroid carcinoma.
2. Poorly differentiated thyroid carcinoma (PDTC).
3. Neuroendocrine tumors:
   • Medullary thyroid carcinoma (MTC),
   • Intrathyroid parathyroid carcinoma,
   • Metastatic neuroendocrine tumor.
4. Metastasis (Renal cell carcinoma?).

In collision with papillary thyroid carcinoma/microcarcinoma!
1. Additional tissue processing.
2. Additional clinical information.
3. Immunohistochemical analysis.
Additional processing of the thyroid tissue was performed. There was no evidence of papillary thyroid carcinoma (PTC), scars, foci of calcification or psammoma bodies. At the time of thyroid gland surgery, the clinical data on the presence of other malignancies were unknown.
Immunohistochemistry: Thyroid tumor

PAX8 200x
Positive: EMA, CK7, pan-cytokeratins, vimentin.
Negative: CD10, calcitonin, chromogranin A, synaptophysin, CEA.
Immunohistochemistry: Lymph node metastasis

Tg 100x

TTF1 100x

Ki67 100x

p53 100x
Immunohistochemistry: Lymph node metastasis
<table>
<thead>
<tr>
<th>Primary antibody</th>
<th>Primary Thyroid tumor</th>
<th>Primary Thyroid tumor metastasis</th>
<th>Papillary/cystic metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroglobulin</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>TTF1</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>PAX8</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>p53</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CD10</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ki-67</td>
<td>~30%</td>
<td>~20%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>pan-cytokeratin</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CK7</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

PAX 8 is commonly expressed in epithelial tumors of the thyroid and parathyroid glands, kidney, thymus, and female genital tract.

The patient was previously surgically and chemotherapy treated from ovarian carcinoma 8 years ago (2008).

Original pathohistological report:
- Ovarian Serous Cystadenocarcinoma;
- Stage pT1b, FIGO Stage unknown.

Chemotherapy - eight cycles of paclitaxel (taxol) and carboplatin.
Immunohistochemistry: Lymph node metastasis
Immunohistochemistry: Lymph node metastasis
Diagnostic pitfalls of thyroid pathology

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“PDTC encompasses two major types of tumours: the so-called insular or insular-like carcinomas and a heterogeneous group of tumours that fit into the umbrella descriptive designation of PDTC”
M. Sobrinho Simões, 2005

Pitfalls in thyroid tumour pathology

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This review provides an itemized listing of major diagnostic pitfalls in the field of thyroid tumour pathology, emphasizing the features that the authors have found most useful in their recognition and avoidance.

Keywords: thyroid carcinoma, thyroid tumours

Abbreviations: Castle, carcinoma showing thymus-like elements; FNA, fine-needle aspiration; PTC, papillary thyroid carcinoma
Poorly differentiated thyroid carcinoma with oncocytic and clear cell features.

Collision LN metastasis of PDTC with ovarian serous cancer.

**Present case:**

- High mitotic activity (>8 mitoses per 10 HPF).
- High Ki67 labelin index.
- Necrosis.
- Diffuse p53 positivity.
- Solid and nested architecture.
- Cellular polymorphism.
- Widely invasive growth with
- Angioinvasion.

**Diagnosis of PDTC**

- Malignant thyroid tumor of follicular cells
  - Follicular carcinoma
    - Papillary carcinoma (etc)
      - NO
        - STI pattern
      - YES
        - Typical PTC nuclei throughout
    - Solid variant of papillary carcinoma
      - YES
        - Presence of at least one of the following: convoluted nuclei or necrosis or mitoses
      - NO
    - Follicular carcinoma (solid growth pattern)
      - NO
        - PD CARCINOMA
          - pure
            - with coexistent papillary carcinoma
              - other type of carcinoma
            - with round nuclei
            - with convoluted nuclei
      - YES

<table>
<thead>
<tr>
<th>Authors</th>
<th>Journal</th>
<th>Year</th>
<th>Collision metastasis</th>
<th>Reported cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lax SF et al.</td>
<td>Virchows Archiv.</td>
<td>1994</td>
<td>PTC and MTC</td>
<td>1</td>
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<tr>
<td>Papi G et al.</td>
<td>Endocr Pathol.</td>
<td>2003</td>
<td>PTC and MTC</td>
<td>1</td>
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<tr>
<td>Meshikhes AW et al.</td>
<td>Saudi Med J.</td>
<td>2004</td>
<td>PTC and MTC</td>
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<tr>
<td>Seki T et al.</td>
<td>Endocr Pathol.</td>
<td>2004</td>
<td>PTC and MTC</td>
<td>2</td>
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<tr>
<td>Nicolas MM et al.</td>
<td>Arch Pathol Lab Med.</td>
<td>2005</td>
<td>PTC and MTC</td>
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<tr>
<td>Alavi S et al.</td>
<td>J Med Case Reports.</td>
<td>2011</td>
<td>PTC and MTC</td>
<td>1</td>
</tr>
<tr>
<td>Ann D et al.</td>
<td>J Korean Thyroid Assoc.</td>
<td>2013</td>
<td>PTC and MTC</td>
<td>1</td>
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<tr>
<td>Rausch Th et al.</td>
<td>Pathology–Research and Practice.</td>
<td>2010</td>
<td>PTC and SCC</td>
<td>1</td>
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<tr>
<td>Alhanafy AM et al.</td>
<td>J Clin Diagn Res.</td>
<td>2016</td>
<td>PTC and SCC</td>
<td>1</td>
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<tr>
<td>Wang ZC et al.</td>
<td>Head Neck Pathol.</td>
<td>2015</td>
<td>PTC and UNC</td>
<td>1</td>
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<tr>
<td>Zeng H et al.</td>
<td>Surg Today.</td>
<td>2012</td>
<td>PTC and BC</td>
<td>1</td>
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<tr>
<td>Gao Q et al.</td>
<td>Breast Care.</td>
<td>2014</td>
<td>PTC and BC</td>
<td>1</td>
</tr>
</tbody>
</table>

BC - breast carcinoma, SCC-squamous cell carcinoma, UNC- undifferentiated nonkeratinizing carcinoma
**Ovarian cancer with distant metastatic LN**

**Table II. Ovarian cancer with distant metastatic lymph nodes reported in the literature.**

<table>
<thead>
<tr>
<th>First author (year)</th>
<th>Age, years</th>
<th>Site</th>
<th>Side</th>
<th>Time</th>
<th>Site of primary lesion</th>
<th>Pathology</th>
<th>(Refs.)</th>
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<tbody>
<tr>
<td>Cebesoy et al (2008)</td>
<td>-</td>
<td>Supra-clavicular</td>
<td>Left</td>
<td>The time of diagnosis</td>
<td>Right</td>
<td>Serous</td>
<td>(13)</td>
</tr>
<tr>
<td>Rahman et al (2012)</td>
<td>49</td>
<td>Supra-clavicular</td>
<td>Left</td>
<td>The time of diagnosis</td>
<td>Left</td>
<td>Poorly differentiated serous-papillary</td>
<td>(5)</td>
</tr>
<tr>
<td>Fanti et al (2006)</td>
<td>51</td>
<td>Supra-clavicular</td>
<td>Left</td>
<td>After initial surgery</td>
<td>Left</td>
<td>Poorly differentiated serous-papillary</td>
<td>(14)</td>
</tr>
<tr>
<td>Ceccarelli et al (2011)</td>
<td>48</td>
<td>Axillary</td>
<td>Right</td>
<td>The time of diagnosis</td>
<td>Right</td>
<td>Poorly differentiated serous-papillary</td>
<td>(6)</td>
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<tr>
<td>Hockstein et al (1997)</td>
<td>78</td>
<td>Axillary</td>
<td>Right</td>
<td>The time of diagnosis</td>
<td>Bilateral</td>
<td>Adenocarcinoma</td>
<td>(15)</td>
</tr>
<tr>
<td>Saxena et al (2014)</td>
<td>45</td>
<td>Axillary</td>
<td>Right</td>
<td>The time of diagnosis</td>
<td>Right</td>
<td>Serous</td>
<td>(16)</td>
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<tr>
<td>Sibio et al (2014)</td>
<td>49</td>
<td>Axillary</td>
<td>-</td>
<td>The time of diagnosis</td>
<td>-</td>
<td>Serous papillary</td>
<td>(17)</td>
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<tr>
<td>Singer et al (2001)</td>
<td>46</td>
<td>Axillary</td>
<td>Right</td>
<td>15 years after OC</td>
<td>Bilateral</td>
<td>Serous papillary</td>
<td>(18)</td>
</tr>
<tr>
<td>Aydin et al (2009)</td>
<td>68</td>
<td>Axillary</td>
<td>-</td>
<td>Several years after OC</td>
<td>-</td>
<td>Serous papillary</td>
<td>(19)</td>
</tr>
<tr>
<td>Ozmen et al (2007)</td>
<td>47</td>
<td>Axillary</td>
<td>-</td>
<td>Two years after surgery</td>
<td>-</td>
<td>Intermediate differentiated serous</td>
<td>(20)</td>
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<tr>
<td>Skagias et al (2008)</td>
<td>74</td>
<td>Axillary</td>
<td>Right</td>
<td>4 years after OC</td>
<td>2 years after OC</td>
<td>Serous papillary</td>
<td>(21)</td>
</tr>
<tr>
<td>Orris et al (1999)</td>
<td>63</td>
<td>Axillary</td>
<td>Bilateral</td>
<td>Several years after OC</td>
<td>-</td>
<td>Adenocarcinoma</td>
<td>(22)</td>
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<td>Ang et al (2007)</td>
<td>59</td>
<td>Inguinal</td>
<td>Right</td>
<td>The time of diagnosis</td>
<td>Left</td>
<td>Moderately differentiated papillary serous</td>
<td>(23)</td>
</tr>
<tr>
<td>Yang et al (2014)</td>
<td>54</td>
<td>Inguinal</td>
<td>Right</td>
<td>The time of diagnosis</td>
<td>Right</td>
<td>Low-grade differentiated serous papillary</td>
<td>(8)</td>
</tr>
</tbody>
</table>

Increased risk of secondary thyroid malignancy in the ovarian cancer survivor.


Thyroid tumors are more common in female and both tumors are under the influence of estrogen and progesterone.

Influence of thyroid hormones on ovarian cancer genes and their mitogenic and anti-apoptotic effects.


Collision lymph node metastasis is a rare phenomenon that should be considered as a possibility in the presence of different morphological features in a metastatic tumor.

Like other primary thyroid carcinomas, PDTC could also have multiple faces. Also, the presence of incidental neck LN metastasis with psammoma bodies and papillary morphology does not have to be from a thyroid gland.
Thank you!