Thymomen onder de loop

Thema middag thymomen
29-11-2019

M. Abdul Hamid
Klinisch patholoog, MUMC+
Inhoud

* Anatomie
* Fysiologie
* Wat is een thymus tumor
* Rol van de patholoog
Fysiologie

“Mysterieus orgaan”
“Seat of the soul”
“Mysterieus orgaan”
“Seat of the soul”

Galen of pegamum (130-200AD)
Fysiologie

Thymogenese
- maturatie
- differentiatie
- selectie
AIRE gen
Wat is een thymus tumor
Thoracic wall: Metastases, Synovial sarcomas, Bone tumors

Posterior mediastinum:
Neurogenic tumors, Paragangliomas, Enteric cysts

Parietal pleura: Plaques, Mesotheoliomas, Metastases

Middle mediastinum:
Lymphomas, Metastases, Esophageal diverticula and tumors, Paragangliomas, Bronchogenic Cysts

Visceral pleura: SFT, Mesotheoliomas

Pericardium: Cysts

Anterior/superior mediastinum:
Tumors of the thymus, Thymic cysts, Lymphomas, Para-thyroidal tumors, Strumae, Metastases, Germ cell tumors, Mesotheoliomas
Rol van de patholoog
Welke technieken heeft een patholoog tot zijn beschikking?

- Macroscopie
- Microscopie
  - Histochemie
  - Cytochemie
  - Immunohistochemie
  - Moleculaire technieken
Thymus tumor classificatie

- 1961 Bernatz et al (lymfocytair, epitheliaal, mixed, spindle)
- 1978 Levine en Rosai (benigne vs maligne)
- 1987 Lewis (thymoom, thymus carciinoom, mixed thymoom met carciinoom, thymoom met maligne potentieel)
- 1985 Marino and Muller Hermelink (corticaal vs medullair thymoom)
- Rosai 1999 (classificeren op basis van origine, PA consensus)
- 2004 WHO classificatie
- 2015 WHO classificatie
Principles of classification of thymomas and thymic carcinomas

WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart

Thymomas resemble normal thymus and produce immature T-cells
Principles of classification of thymomas and thymic carcinomas

WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart

Thymic carcinomas resemble other carcinomas

- squamous
- clear cell
- basaloid
- mucoepidermoid
- Lymphoepithelioma-like
- neuroendocrine
Reasons for separating thymomas from thymic carcinomas

<table>
<thead>
<tr>
<th></th>
<th>Thymomas</th>
<th>Thymic carcinomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>1.5 per million</td>
<td>1.5 per 10 millions</td>
</tr>
<tr>
<td>Myasthenia gravis/other autoimmune diseases</td>
<td>often</td>
<td>almost never</td>
</tr>
<tr>
<td>Lymph node metastases</td>
<td>very uncommon</td>
<td>common</td>
</tr>
<tr>
<td>Prognosis</td>
<td>better</td>
<td>worse</td>
</tr>
</tbody>
</table>
Is the classification of thymomas an academic "caprice"?

Cancer 2002;95:420
Interobserver variation in the classification of thymic tumours—a multicentre study using the WHO classification system.


Department of Pathology, Leeds Teaching Hospital NHS Trust, Leeds, UK.

Abstract
AIMS: To test the reproducibility of the current World Health Organization (WHO) classification of thymic epithelial neoplasms at the level of interobserver variation within a group of pathologists with experience and expertise in thymic pathology.

METHODS AND RESULTS: Ninety-five thymic tumours were circulated to a group of 17 pathologists.

Classification of thymic epithelial neoplasms is still a challenge to thoracic pathologists: a reproducibility study using digital microscopy.

Wang H, Shen CA, Beerly MD, Bel P, Altmann D, Anderson DM, Greenberg MS, Nakada SJ, Monard A

From the Departments of Pathology (Drs Wang and Monard), Epidemiology and Biostatistics (Dr Sima), and Surgery (Dr Issar, Memorial Sloan-Kettering Cancer Center, New York; the Department of Pathology, Mount Sinai School of Medicine, New York; the Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, Maryland; and the Departments of Pathology and Laboratory Medicine, University of North Carolina at Chapel Hill, Chapel Hill (Dr Swanson), and the Maastricht University Medical Centre, Maastricht, The Netherlands.

Abstract
CONTEXT: Thymic epithelial tumours are rare, constituting interpretative challenges for pathologists. Digital imaging can be useful as an educational tool for these rare tumours.

OBJECTIVES: To evaluate the diagnostic reproducibility of thymic tumours among thoracic pathologists.
Key features of Type A:
- Bland-appearing ovoid to spindled cells
- Absence of mitotic figures
- Sparse lymphocytes in most areas
- Epithelial cells may express CD20

Key features of Type B1:
- Bland-appearing round epithelial cells lost in a sea of cortical thymocytes
  - Mitotic figures usually frequent in thymocytes
  - Epithelial cells may have small nucleoli
- Scattered pale spots that recapitulate normal thymic medulla
Key features of Type B2:
- Epithelial cells more frequent, but many cortical thymocytes are still present
- Tumor cells may have nucleoli and form clusters
- Lack areas of medullary differentiation

Key features of Type AB:
- Bland-appearing epithelial cells range from round to spindled in discrete areas
- Lymphocyte-rich areas usually resemble B1, not B2 thymomas
- Epithelial cells may express CD20, like Type A thymomas

Key features of Type B3:
- Epithelial cells form sheets
- Lymphocytes are sparse
- Epithelial cells are atypical, with 'raisinoid', crinkled, or (less frequently) vesicular nuclei and often distinct cell borders
Thymic carcinomas resemble other carcinomas

- squamous
- clear cell
- basaloid
- mucoepidermoid
- Lymphoepithelioma-like
- neuroendocrine
Autoimmunity in different thymomas

A medullary
B1 cortical
B2 well diff. CA

Autoimmunity
## Paraneoplastic autoimmunopathies

<table>
<thead>
<tr>
<th>Condition</th>
<th>Condition</th>
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<tbody>
<tr>
<td>Addison’s disease</td>
<td>Panhypopituitarism</td>
</tr>
<tr>
<td>Agranulocytosis</td>
<td>Pernicious anemia</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>Polymyositis</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>Pure red cell aplasia</td>
</tr>
<tr>
<td>Autoimmune colitis (GvHD-like)</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
<td>Rippling muscle disease</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>Scleroderma</td>
</tr>
<tr>
<td>Intestinal pseudo-obstruction</td>
<td>Sensory motor neuropathy</td>
</tr>
<tr>
<td>Limbic encephalitis</td>
<td>Stiff-person syndrome</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Thyroiditis</td>
</tr>
<tr>
<td>Neuromyotonia</td>
<td></td>
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*NOTE: In the majority of these diseases, the immunopathogenesis has not been resolved.*
Diagnostiek

Sampling error
Thymus tumor classificatie

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Stadiering
- 1981 Massaoka (anatomische classificatie)
- 1994 Massaoka Koga
- 2015 TNM
Stage I (T1): thymus, mediastinal fat, mediastinal pleura, N0, M0

Stage II (T2): pericardium, N0, M0
Stage IIIA (T3): N0, M0

Stage IIIB (T4): N0, M0
**Stage IVA (any T):** N1 or M1a

**Stage IVB (any T):** N2 or M1b
Pathologische uitkomsten MUMC

Meer dan 400 robot thymusoperaties in MUMC sinds 2004: 130 thymomen/TC

- Wat voor typen thymomen zien we?
- Wat voor stadiëringen hebben de thymomen?
- Hoe volledig is de operatie uitgevoerd (is de gehele tumor verwijderd, of is er nog iets achtergebleven?). Data wordt nog verzameld.

Cijfers MUMC:

<table>
<thead>
<tr>
<th>Type</th>
<th></th>
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<tbody>
<tr>
<td>Type A</td>
<td>15 (12%)</td>
</tr>
<tr>
<td>Type AB</td>
<td>23 (18%)</td>
</tr>
<tr>
<td>Type B1</td>
<td>11 (8%)</td>
</tr>
<tr>
<td>Type B2</td>
<td>45 (35%)</td>
</tr>
<tr>
<td>Type B3</td>
<td>30 (23%)</td>
</tr>
<tr>
<td>Type C</td>
<td>5 (4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>29 (22%)</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>43 (33%)</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>33 (25%)</td>
</tr>
<tr>
<td>Stage III</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>3 (2%)</td>
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</tbody>
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Uitvoerder: Drs. Marcuse (promovenda)
Take home message

• Thymomen (uitdaging in diagnosestellung)
  • Expertise centrum
  • Panel
  • Richtlijnen

• Auto-immuniteit bij thymomen nog onbegrepen
  • Meer wetenschappelijk onderzoek

• Toekomst perspectieven
  • ???
The future will bring more answers!