Abstract for half-time review I Halla Vidarsdottir, PhD candidate

Molecular and immunohistochemical profiling of pulmonary metastases and prognostic biomarkers in metastatic colorectal cancer

Background: The lung is a common site for metastases. Differentiation between primary lung cancers and pulmonary metastases of different types is important when selecting oncological and surgical treatment, and immunohistochemical (IHC) staining aids in histopathological diagnostics. Pulmonary metastasectomy is part of curative treatment in metastatic colorectal cancer (mCRC), but there is a great need for additional prognostic and predictive biomarkers.

Aims:
1) Diagnostic IHC markers that can differentiate between lung cancers and pulmonary metastases of different types
2) Tumour genetics in CRC with pulmonary and liver metastases
3) Prognostic biomarkers for CRC with surgically treated pulmonary metastases.

Material and methods:
Tissue microarrays (TMA) from unselected cases of resected primary lung cancer (n=665) and pulmonary metastases (n=440) were stained for 10 different IHC markers: CK7, CK20, CDX2, CK5, p40, p63, TTF-1 (three different clones), napsin A, GATA3 and PAX8. TMAs with tumours from all patients who underwent pulmonary metastasectomy for mCRC at Skåne University Hospital in Lund from 2000-2014 have been constructed and compilation of clinical data is ongoing. Tumours from mCRC cases with multiple metastases will be analysed with targeted NGS, and TMAs will be stained for candidate immunohistochemical biomarkers.

Preliminary results:
TTF-1 positivity varied between clones, 89-93% for lung adenocarcinomas (AC), 0-8% for lung squamous cell carcinomas (SCC) and 2-8% for pulmonary metastases from CRC. Of primary lung ACs 84% expressed napsin A, 10% p63, 7% CDX2, 2% CK20 and GATA3. Only 68% of the lung ACs were positive for CK7, TTF-1 and napsin A and negative for other
markers. Primary lung SCCs expressed CK5, p40 and p63 in 94-97% of cases, while 44% expressed CK7, 20% GATA3 and 7% CDX2. Pulmonary metastases from CRC expressed CK20 in 83% and CDX2 in 99%. Pulmonary metastases from RCC expressed PAX8 in 74%, CK7 in 7% and napsin A in 7% of the cases. Of pulmonary metastases from breast cancer 93% expressed GATA3, 78% CK7 and 15% CK5.

**Significance:** Information on expression patterns of IHC markers facilitates histopathological diagnostics. Genetic abnormalities in lung metastases and heterogeneity between primary tumour, lung and liver metastases is of biological interest potential clinical importance, and there is a great need to identify novel prognostic and predictive biomarkers.

**Publications:**
