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Clonal evolution and heterogeneity in metastatic head and neck cancer-An analysis of the Austrian Study Group of Medical Tumour Therapy

Abstract

BACKGROUND:

Tumour heterogeneity and clonal evolution within a cancer patient are deemed responsible for relapse in malignancies and present challenges to the principles of targeted therapy, for which treatment modality is often decided based on the molecular pathology of the primary tumour. Nevertheless, the clonal architecture in distant relapse of head and neck cancer is fairly unknown.

PATIENTS AND METHODS:

For this project, we analysed a cohort of 386 patients within the Austrian Registry of head and neck cancer. We identified 26 patients with material from the primary tumour, the distant metastasis after curative first-line treatment and a germline sample for analysis of clonal evolution. After pathological analyses, these samples were analysed using a targeted massively parallel sequencing (MPS) panel of 257 genes known to be recurrently mutated in head and neck cancer plus a genome-wide SNP-set.

RESULTS:

Despite histological diagnosis of distant metastasis, no corresponding mutation in the supposed metastases was found in two of 23 (8.6%) evaluable patients suggesting a primary tumour of the lung instead of a distant metastasis of head and neck cancer. We observed a branched pattern of evolution in 31.6% of the analysed patients. This pattern was associated with a shorter time to distant metastasis, compared with a pattern of punctuated evolution. Structural genomic changes over time were also present in 7 of 12 (60%) evaluable patients with metachronous metastases.

CONCLUSION:

Targeted MPS demonstrated substantial heterogeneity at the time of diagnosis and a complex pattern of evolution during disease progression in head and neck cancer. Copy number analyses revealed additional changes that were not detected by mutational analyses. Mutational and structural changes contribute to tumour heterogeneity at diagnosis and progression.