

AB024. PS01.06. Exploring the genomic heterogeneity of the combined B2-B3 thymoma and nodal metastasis

Margaret Ottaviano¹, Vincenzo Damiano¹, Marina Capuano¹, Marianna Tortora¹, Pasqualina Perrone¹, Maria Russo², Umberto Malapelle², Giancarlo Troncone², Giovannella Palmieri¹

¹Department of Clinical Medicine and Surgery, ²Department of Public Health, University of Naples Federico II, Naples, Italy

Background: The association between thymic epithelial tumors (TETs) and other malignancies, mostly reported as hematologic neoplasm, is widely known, however the involved pathogenic mechanism remains unclear. Large scale efforts to shed light on genetic mutations in cancer such as the cancer genome atlas (TCGA) have analysed samples obtained from resection of the primary tumor, however, genomic data in the field of advanced-stage TETs about primary and metastatic tumor are still lacking, except for sporadic reports of TP53 and KIT mutations in thymic carcinoma. Moreover, recent published data, have underlined the low mutational burden and the rarity of common cancer-related mutated genes in thymoma samples. The identified mutational load of an unusual case of B2-B3 thymoma is here explored.

Methods: A 57-year-old Caucasian female with a history of multiple malignancies [cervical squamous carcinoma, renal clear cell carcinoma, chronic myeloid leukemia (CML)] underwent radical thymomectomy with a diagnosis of B2-B3 thymoma. Two years later a latero-cervical lymph node was resected and histologically confirmed as thymoma metastasis. DNA was extracted from clinical tissue samples; microdissection procedure carried out on stained slides selectively distinguishes two primary tumor and one lymph node metastasis sections respectively. DNA for each sample was used for Libraries construction and purification on the Ion

Chef (Thermo Fisher) by the Ion AmpliSeq™ Cancer Hotspot Panel v2 (Life Technologies). This panel gives 207 amplicons covering 2,800 mutational hotspot regions in 50 genes. Templates were sequenced on PGM (Life Technologies). All detected variants were reviewed with the Integrative Genomics Viewer (IGV V.2.1, Broad Institute, Cambridge, Massachusetts, USA) and only variants with greater than or equal to 5× allele coverage and a quality score greater than or equal to 20, within an amplicon that covered at least 100× alleles, were called, and the frequency of each mutant allele was recorded.

Results: In each samples of primary tumor, 9 genes (18%) were mutated, with a total of 15 genes (30%) considering both samples. Only 2 genes were mutated in the nodal metastasis sample and the PIK3CA mutated gene has been not found in the primary tumor. The same KIT mutation has been identified in all the samples with a high frequency, other common cancer-related mutated genes such as: IDH1, FBXW7, SMO, NOTCH-1, PTEN, ATM, RB1, SMAD4, EGFR, BRAF, RAS, TP53, SRC, FBW7, were identified.

Conclusions: According to our knowledge, this is the first case recorded of B2-B3 thymoma with the identification of several mutated genes, already recognized to be involved in tumorigenesis mechanism of other solid tumors. In the light of the medical history of our patient we assume a KIT role as driven gene in the tumorigenesis of both thymoma and CML. Up to date the patient is thymoma free and under treatment with Dasatinib for CML control. Deep genomic information is further needed to investigate the development of target therapy.

Keywords: B2-B3 thymoma; multiple malignancy; kit mutation; next generation sequencing

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