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GENITOURINÁRNE MALIGNITY

Országhová Z, Mego M, Chovanec M.
Long-Term Cognitive Dysfunction in Cancer Survivors
Front. Mol. Biosci. 8:770413. doi: 10.3389/fmolb.2021.770413

Cancer-related cognitive impairment (CRCI) is a frequent side effect experienced by an increasing number of cancer survivors with a significant impact on their quality of life. Different definitions and means of evaluation have been used in available literature; hence the exact incidence of CRCI remains unknown. CRCI can be described as cognitive symptoms reported by cancer patients in self-reported questionnaires or as cognitive changes evaluated by formal neuropsychological tests. Nevertheless, association between cognitive symptoms and objectively assessed cognitive changes is relatively weak or absent. Studies have focused especially on breast cancer patients, but CRCI has been reported in multiple types of cancer, including colorectal, lung, ovarian, prostate, testicular cancer and hematological malignancies. While CRCI has been associated with various treatment modalities, including radiotherapy, chemotherapy, hormone therapy and novel systemic therapies, it has been also detected prior to cancer treatment. Therefore, the effects of cancer itself with or without the psychological distress may be involved in the pathogenesis of CRCI as a result of altered coping mechanisms after cancer diagnosis. The development of CRCI is probably multifactorial and the exact mechanisms are currently not completely understood. Possible risk factors include administered treatment, genetic predisposition, age and psychological factors such as anxiety, depression or fatigue. Multiple mechanisms are suggested to be responsible for CRCI, including direct neurotoxic injury of systemic treatment and radiation while other indirect contributing mechanisms are hypothesized. Chronic neuroinflammation mediated by active innate immune system, DNA-damage or endothelial dysfunction is hypothesized to be a central mechanism of CRCI pathogenesis. There is increasing evidence of potential plasma (e.g., damage associated molecular patterns, inflammatory components, circulating microRNAs, exosomes, short-chain fatty acids, and others), cerebrospinal fluid and radiological biomarkers of cognitive dysfunction in cancer patients. Discovery of biomarkers of cognitive impairment is crucial for early identification of cancer patients at increased risk for the development of CRCI or development of treatment strategies to lower the burden of CRCI on long-term quality of life. This review summarizes current literature on CRCI with a focus on long-term effects of different cancer treatments, possible risk factors, mechanisms and promising biomarkers.

SARKÓMY

Lee CJ, Schöffski P, Modave E, van Wezel T, Boeckx B, **Sufliarsky J**, Gelderblom H, Blay JY, Debiec-Rychter M, Sciot R, Bovée JVMG, Lambrechts D, Wozniak A.
Comprehensive Molecular Analysis of Inflammatory Myofibroblastic Tumors Reveals Diverse Genomic Landscape and Potential Predictive Markers for Response to Crizotinib
Clin Cancer Res. 2021 Dec 15;27(24):6737-6748.

Purpose: The European Organization for Research and Treatment of Cancer (EORTC) clinical phase II trial 90101 „CREATE" showed high antitumor activity of crizotinib, an inhibitor of anaplastic lymphoma kinase (ALK)/ROS1, in patients with advanced inflammatory myofibroblastic tumor (IMFT). However, recent findings suggested that other molecular targets in addition to ALK/ROS1 might also contribute to the sensitivity of this kinase inhibitor. We therefore performed an in-depth molecular characterization of archival IMFT tissue, collected from patients enrolled in this trial, with the aim to identify other molecular alterations that could play a role in the response to crizotinib.

Experimental design: Twenty-four archival IMFT samples were used for histopathological assessment and DNA/RNA evaluation to identify gene fusions, copy-number alterations (CNA), and mutations in the tumor tissue. Results were correlated with clinical parameters to assess a potential association between molecular findings and clinical outcomes.

Results: We found 12 ALK fusions with 11 different partners in ALK-positive IMFT cases by Archer analysis whereas we did not identify any ROS1-rearranged tumor. One ALK-negative patient responding to crizotinib was found to have an ETV6-NTRK fusion in the tumor specimen. The CNA profile and mutational landscape of IMFT revealed extensive molecular heterogeneity. Loss of chromosome 19 (25% of cases) and PIK3CA mutations (9% of cases) were associated with shorter progression-free survival in patients receiving crizotinib.

Conclusions: We identified multiple genetic alterations in archival IMFT material and provide further insight into the molecular profile of this ultra-rare, heterogeneous malignancy, which may potentially translate into novel treatment approaches for this orphan disease.

INÉ MALIGNITY

Bystricky B, Kohutek F, Miklatkova Z, Sedlacek T, Gal V, Lohajova Behulova R.
Spontaneous Regression of Merkel Cell Carcinoma: Case Report
Int Med Case Rep J. 2021 Oct 2;14:711-717.

Merkel cell carcinoma (MCC) is a rare skin neuroendocrine tumor presumably arising from Merkel cells in the basal layer of epidermis. It is an aggressive tumor predominantly found on the head and neck area of elderly people, with a mortality rate around 41% for all stages. Complete spontaneous regression of MCC is seldom observed, mostly in elderly women. We describe complete spontaneous regression of large, histologically confirmed MCC in an elderly woman after biopsy, which occurred incidentally, while waiting for radical surgery with skin flap. Next-generation sequencing with SOPHiA Solid Tumor Plus Solution did not reveal any relevant gene mutations or rearrangements. An update of literature for these very rare cases is provided.