Invasive pituitary neuroendocrine tumor molecular markers

There are few studies on the mechanism of pituitary neuroendocrine tumor (PA) destroying bone.

Zhu et al. aimed to investigate the role of MEG8/miR-454-3p/TNFα in bone-invasive pituitary neuroendocrine tumors (BIPAs). In this study, they reported that lncRNA MEG8 and TNF-α are upregulated in BIPA tissues while miR-454-3p is downregulated, which is associated with poor progression-free survival (PFS). Functional assays revealed the role of up-regulated MEG8 and down-regulated miR-454-3p in promoting bone destruction. Mechanistically, MEG8 promotes TNF-α expression by sponging miR-454-3p, which ultimately leads to the occurrence of bone destruction. The mechanism is confirmed in vivo and in vitro. Therefore, this data illustrated a new regulatory mechanism of MEG8/miR-454-3p/TNF-α in BIPAs. It may provide a useful strategy for diagnosis and treatment for BIPA patients [1].

A review summarized the known molecular basis of the invasiveness of pituitary neuroendocrine tumors. The study pointed out that Hypoxia-inducible factor-1α, pituitary tumor transforming gene, vascular endothelial growth factor, fibroblast growth factor-2, and matrix metalloproteinases (MMPs, mainly MMP-2, and MMP-9) are core molecules responsible for the invasiveness of pituitary neuroendocrine tumors. The reason is that these molecules have the ability to directly or indirectly induce cell proliferation, epithelial-to-mesenchymal transition, angiogenesis, degradation, and remodeling of the extracellular matrix. HIF-1α induced by hypoxia or apoplexy inside the adenoma might be the initiating factor of invasive transformation, followed by angiogenesis for overexpressed VEGF, EMT for overexpressed PTTG, degradation of ECM for overexpressed MMPs, creating a suitable microenvironment within the tumor. Together, they form a complex interactive network. More investigations are required to further elucidate the mechanisms underlying the invasiveness of pituitary neuroendocrine tumors [2].

Prior attempts have been made to define morphologic features and molecular markers more commonly associated with invasive adenoma or pituitary carcinoma to help predict tumor behavior and discriminate between the two prior to identification of metastatic disease. These include quantification of the degree of cytologic atypia and mitotic activity, examination of proliferation markers such as Ki-67 using the MIB-1 antibody and cell-cycle molecules such as p27 and galectin-3, and gene expression of p53, MGMT, and MMP-9 [3] [4] [5] [6] [7].

The aim of a study in 2017 was to identify the differences in expression of molecular markers between primary and relapsed pituitary neuroendocrine tumors (as an aggressiveness indicator), as well as between secreting and non-secreting pituitary neuroendocrine tumors. Tumor fragments were collected from 51 patients with invasive pituitary neuroendocrine tumors. Of these, 10 cases were operated on a second time due to tumor recurrence. The tumor fragments were retrieved from the archives of the Department of Pathology, Emergency County Hospital, Cluj-Napoca, Romania. Immunohistochemical staining was performed for nine markers on 51 invasive pituitary

neuroendocrine tumors: Ki-67, beta-catenin, E-cadherin, Bcl-2, galectin-3, p53, p27, CD117, and CD44. They compared the expression differences between two groups: the first one including primary and relapsed invasive pituitary neuroendocrine tumors, and another one including prolactin (PRL)-secreting and non-secreting invasive pituitary neuroendocrine tumors. Ki-67, p53, and Bcl-2 expressions were found significant in the PRL-secreting group. CD44 immunostaining was significant only in relapsed invasive pituitary neuroendocrine tumors. For the β-catenin, E-cadherin, galectin-3, p27, and CD117 expression levels were not registered statistically significant differences between these groups. This study is the first one to report a statistically significant difference between the expression of CD44 in primary and relapsed invasive pituitary neuroendocrine tumors and it could be used as a negative impact prognostic marker [8].

TNF-α and its related lncRNAs and MicroRNAs represent potential therapeutic targets for bone-invasive pituitary neuroendocrine tumors in the future [9].

1)
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