Invasive pituitary neuroendocrine tumor treatment

The majority of these adenomas can be treated successfully with transsphenoidal resection. However, more than one-third of adenomas are invasive, making complete surgical resection without unacceptable neurological deficits difficult. These more complicated adenomas require multimodal treatment and long-term follow-up for continued favorable outcomes. Initial surgical resection is indicated for decompression of the optic apparatus or cytoreduction before adjuvant therapy, even when gross total resection is not anticipated. Medical therapy is an option for most endocrinologically active adenomas, but nonfunctioning and functional adenomas that do not respond to medical therapy require a multidisciplinary approach. Radiation is often beneficial and can be delivered either as fractionated therapy or in a single dose. Conformal dose planning can be used in most cases to maximize therapeutic benefits. This article reviews the evaluation and treatment of invasive pituitary neuroendocrine tumors and discusses promising new therapies [1)].

Although targeted therapies such as vascular endothelial growth factor, epidermal growth factor and mTOR inhibitors have also been used to treat refractory PAs, the effectiveness of these targeted therapies is still not known due to a lack of data from randomized prospective trials. As a novel therapeutic method, cancer immunotherapy is a promising strategy for the treatment of refractory PAs, but further preclinical research and clinical trials are needed to assess the efficacy of this new approach. In summary, early identification and a multidisciplinary approach are required to treat refractory PAs [2)].

Eighty-three invasive adenomas were analyzed for survival outcomes. Analyzed prognostic factors included age, sex, race, histology, tumor extent, and treatment.

Only non-white race, male gender, and age ≥65 were significant negative prognostic factors for invasive adenomas ($p = 0.013$, 0.033, and <0.001, respectively). There was no survival advantage to radiation therapy in treating adenomas at 5, 10, 20, or 30 years ($p = 0.778$, 0.960, 0.236, and 0.971) [3)].

Ma et al., from the Zhejiang Sci-Tech University, Hangzhou, Zhejiang, China examined associations between DNMTs expression and clinicopathological features or promoter methylation status of tumor suppressor genes (TSGs).

Overexpression of DNMTs was detected in pituitary neuroendocrine tumors. Frequencies of DNMT1 overexpression were significantly higher in macroadenomas, invasive tumors, and grade III and IV tumors. DNMT3A was frequently detected in invasive tumors and grade IV tumors. In addition, DNMT1 and DNMT3A were frequently detected in high-methylation tumors. Furthermore, in multivariate logistic regression, the significant association between DNMT1 or DNMT3A and high-methylation status persisted after adjusting for clinicopathological features.

The findings suggested that tumor overexpression of DNMT1 and DNMT3A is associated with tumor

aggressive behavior and high-methylation status in pituitary neuroendocrine tumors. This data support a possible role of DNMT1 and DNMT3A in TSG promoter methylation leading to pituitary neuroendocrine tumor invasion and suggest that inhibition of DNMTs has the potential to become a new therapeutic approach for invasive pituitary neuroendocrine tumor [4].

Temozolomide for Invasive pituitary neuroendocrine tumor

Temozolomide for Invasive pituitary neuroendocrine tumor.

5-Fluorouracil for Invasive pituitary neuroendocrine tumor

5-Fluorouracil for Invasive pituitary neuroendocrine tumor.

1)
Hornyak M, Couldwell WT. Multimodality treatment for invasive pituitary neuroendocrine tumors. Postgrad Med. 2009 Mar;121(2):168-76. doi: 10.3810/pgm.2009.03.1989. PMID: 19332975.
2)
Dai C, Liu X, Ma W, Wang R. The Treatment of Refractory pituitary neuroendocrine tumors. Front Endocrinol (Lausanne). 2019 May 29;10:334. doi: 10.3389/fendo.2019.00334. PMID: 31191457; PMCID: PMC6548863.
3)
Hansen TM, Batra S, Lim M, Gallia GL, Burger PC, Salvatori R, Wand G, Quinones-Hinojosa A, Kleinberg L, Redmond KJ. Invasive adenoma and pituitary carcinoma: a SEER database analysis. Neurosurg Rev. 2014 Feb 14. [Epub ahead of print] PubMed PMID: 24526366.
4)
Ma HS, Wang EL, Xu WF, Yamada S, Yoshimoto K, Qian ZR, Shi L, Liu LL, Li XH. Overexpression of DNA (Cytosine-5)-Methyltransferase 1 (DNMT1) And DNA (Cytosine-5)-Methyltransferase 3A (DNMT3A) Is Associated with Aggressive Behavior and Hypermethylation of Tumor Suppressor Genes in Human pituitary neuroendocrine tumors. Med Sci Monit. 2018 Jul 13;24:4841-4850. doi: 10.12659/MSM.910608. PubMed PMID: 30002361.