5-Fluorouracil for Invasive pituitary neuroendocrine tumor

Nelson's syndrome is considered a severe side effect that can occur after total bilateral adrenalectomy in patients with Cushing's disease. It usually presents with clinical manifestations of an enlarging pituitary tumor including visual and cranial nerve alterations, and if not treated, can cause death through local brain compression or invasion. The first therapeutic option is surgery but in extreme cases of inaccessible or resistant aggressive pituitary tumors; the off-label use of chemotherapy with capecitabine and temozolomide can be considered. However, the use of this treatment is controversial due to adverse events, lack of complete response, and inability to predict results. Mirallas et al. present the case of a 48-year-old man diagnosed with Nelson's syndrome with prolonged partial response and significant clinical benefit to treatment with capecitabine and temozolomide [1)].

A survey confirms that TMZ is established as first-line chemotherapeutic treatment of APT/PC. Clinically functioning tumours, low MGMT and concurrent radiotherapy were associated with a better response. The limited long-term effect of TMZ and the poor efficacy of other drugs highlight the need to identify additional effective therapies. [2)].

3: Zacharia BE, Gulati AP, Bruce JN, Carminucci AS, Wardlaw SL, Siegelin M, Remotti H, Lignelli A, Fine RL. High response rates and prolonged survival in patients with corticotroph pituitary tumors and refractory Cushing disease from capecitabine and temozolomide (CAPTEM): a case series. Neurosurgery. 2014 Apr;74(4):E447-55; discussion E455. doi: 10.1227/NEU.0000000000000251. PMID: 24226425.

4: Thearle MS, Freda PU, Bruce JN, Isaacson SR, Lee Y, Fine RL. Temozolomide (Temodar®) and capecitabine (Xeloda®) treatment of an aggressive corticotroph pituitary tumor. Pituitary. 2011 Dec;14(4):418-24. doi: 10.1007/s11102-009-0211-1. PMID: 19960369; PMCID: PMC2891584.

5: McSheehy PM, Port RE, Rodrigues LM, Robinson SP, Stubbs M, van der Borns K, Peters GJ, Judson IR, Leach MO, Griffiths JR. Investigations in vivo of the effects of carbogen breathing on 5-fluorouracil pharmacokinetics and physiology of solid rodent tumours. Cancer Chemother Pharmacol. 2005 Feb;55(2):117-28. doi: 10.1007/s00280-004-0851-9. Epub 2004 Oct 5. PMID: 15592719.

6: Kaltsas GA, Mukherjee JJ, Plowman PN, Monson JP, Grossman AB, Besser GM. The role of cytotoxic chemotherapy in the management of aggressive and malignant pituitary tumors. J Clin Endocrinol Metab. 1998 Dec;83(12):4233-8. doi: 10.1210/jcem.83.12.5300. PMID: 9851756.

7: Kokatsu T, Tsukuda M. Hypopituitarism and hyponatremia in a case with nasopharyngeal carcinoma. ORL J Otorhinolaryngol Relat Spec. 1994 Nov- Dec;56(6):347-51. doi: 10.1159/000276689. PMID: 7838487.

8: Mixson AJ, Friedman TC, Katz DA, Feuerstein IM, Taubenberger JK, Colandrea JM, Doppman JL, Oldfield EH, Weintraub BD. Thyrotropin-secreting pituitary carcinoma. J Clin Endocrinol Metab. 1993 Feb;76(2):529-33. doi: 10.1210/jcem.76.2.8432799. PMID: 8432799.

1)

Mirallas O, Filippi-Arriaga F, Hernandez Hernandez I, Aubanell A, Chaachou A, Garcia-Alvarez A, Hernando J, Martínez-Saez E, Biagetti B, Capdevila J. Aggressive Pituitary Macroadenoma Treated With Capecitabine and Temozolomide Chemotherapy Combination in a Patient With Nelson's Syndrome: A Case Report. Front Endocrinol (Lausanne). 2021 Nov 11;12:731631. doi: 10.3389/fendo.2021.731631. PMID: 34858324; PMCID: PMC8632214.

2)

McCormack A, Dekkers OM, Petersenn S, Popovic V, Trouillas J, Raverot G, Burman P; ESE survey collaborators. Treatment of aggressive pituitary tumours and carcinomas: results of a European Society of Endocrinology (ESE) survey 2016. Eur J Endocrinol. 2018 Mar;178(3):265-276. doi: 10.1530/EJE-17-0933. Epub 2018 Jan 12. PMID: 29330228.