# BRAF V600E mutation in glioneuronal tumor

Glioneuronal tumors (GNTs) are the most common histological type of brain tumors in patients who received epilepsy surgery, and part of them presented with BRAF V600E mutation.

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To evaluate the expression of the BRAF V600E mutated protein and its association with activation of the mammalian target of rapamycin (mTOR) pathway, immunophenotype and clinical characteristics in GNTs, Prabowo et al., investigated a cohort of 174 GNTs. The presence of BRAF V600E mutations was detected by direct DNA sequencing and BRAF V600E immunohistochemical detection. Expression of BRAF-mutated protein was detected in 38/93 (40.8%) gangliogliomas (GGs), 2/4 (50%) desmoplastic infantile gangliogliomas (DIGs) and 23/77 (29.8%) dysembryoplastic neuroepithelial tumors (DNTs) by immunohistochemistry. In both GGs and DNTs, the presence of BRAF V600E mutation was significantly associated with the expression of CD34, phosphorylated ribosomal S6 protein (pS6; marker of mTOR pathway activation) in dysplastic neurons and synaptophysin ($P < 0.05$). In GGs, the presence of lymphocytic cuffs was more frequent in BRAF-mutated cases (31 vs. 15.8%; $P=0.001$). The expression of both BRAF V600E and pS6 was associated with a worse postoperative seizure outcome in GNT ($P < 0.001$). Immunohistochemical detection of BRAF V600E-mutated protein may be valuable in the diagnostic evaluation of these glioneuronal lesions and the observed association with mTOR activation may aid in the development of targeted treatment involving specific pathogenic pathways [1)].

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Data from 35 patients diagnosed with GNTs, including 24 gangliogliomas and 11 dysembryoplastic neuroepithelial tumors, were retrospectively collected. DNA was extracted from GNTs tissues and BRAF V600E mutation was examined by DNA sequencing. The correlations between BRAF V600E mutation and clinical features were analyzed.

Totally, BRAF V600E mutations were detected in 11 patients with GNTs, the rate of mutation were 33.3% and 27.3% in GGs (8/24) and DNTs (3/11), respectively. The probability of BRAF V600E mutation in females (7/12, 58.3%) was significantly higher than that in males (4/23, 17.4%) ($P=0.022$). Moreover, patients with BRAF-mutated GNTs had a significantly wider variety of seizure types compared to GNTs with BRAF wild-type status ($P=0.027$). However, no significant correlation between the BRAF status and certain clinical features, such as age of seizure onset, duration of epilepsy, age at surgery, location of the tumor and postoperative seizure free, were observed.

Zhang et al., demonstrated the presence of BRAF V600E mutation in Chinese epileptic patients with GNTs, which was significantly correlated with gender and multiple seizure types. Large sample studies and long-term follow-up are required for further confirmation [2)].

## Case reports

The patient described here had a desmoplastic infantile astrocytoma harboring a BRAF V600E mutation. After relapse following initial standard chemotherapy treatment, he was successfully treated with the BRAF V600E inhibitor vemurafenib at the age of 3 years 11 months and 5 years 0 months. A rapid response was observed on both occasions. This illustrates the possibility of continuous oncogenic addiction and the therapeutic potential of BRAF V600E inhibitor monotherapy in

LGG, even in very young severely compromised children. BRAF V600E inhibition in LGG and possible (re-)treatment regimens are briefly discussed [3].

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2)
Zhang YX, Shen CH, Guo Y, Zheng Y, Zhu JM, Ding Y, Tang YL, Wang S, Ding MP. BRAF V600E mutation in epilepsy-associated glioneuronal tumors: Prevalence and correlation with clinical features in a Chinese population. Seizure. 2016 Dec 9;45:102-106. doi: 10.1016/j.seizure.2016.12.004. [Epub ahead of print] PubMed PMID: 27984807.
3)
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