368P

Characteristics of deleterious germline mutations in glioma patients

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Background

Glioma is the most common primary central nervous system (CNS) tumor with the highest incidence rate and mortality. The genetic basis of glioma has been found in somatic genomics research, but the characteristics of germline mutations have not been fully elucidated. Here, we reported an analysis of genomic features in 35 glioma patients (pts) with autosomal-dominant inheritance of germline mutations.

Methods

We retrospectively analyzed the next-generation sequencing data of 9,287 pts in a Chinese CNS tumor cohort. The germline mutation features and correlation with somatic IDH1/2 mutations (sIDH1/2m) were analyzed.

Results

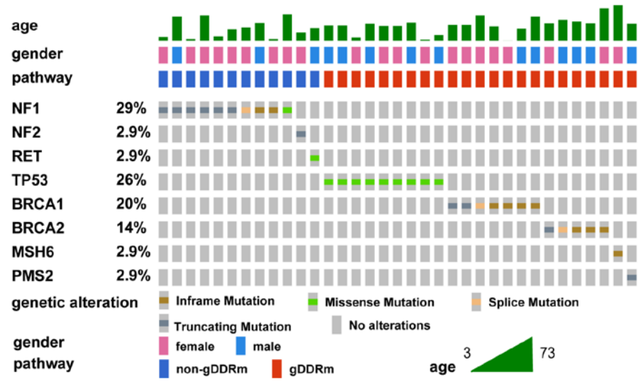

Figure 1. Germline gene mutations and clinical characteristics of glioma patients.

Results

A total of 35 (0.37%) cases with germline mutations were detected, of which 9 pts carried TP53 mutations, 11 pts had NF1/2 mutations, 12 pts had BRCA1/2 mutations and the other three cases harbored mutation in RET, MSH6 and PMS2 respectively. We observed that 65.71% (23/35) of pts' germline mutations occurred in DNA damage response (DDR) genes (TP53, BRCA1, BRCA2, MSH6 and PMS2), while the other 12 pts (34.29%) carried non-DDR gene (NF1, NF2 and RET) mutations. There was no gender and age difference between germline DDR mutation (gDDRm) positive and negative groups.

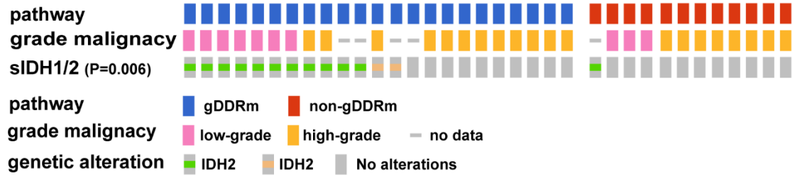

Figure 2. Characteristic of somatic IDH mutations in patients with germline DDR mutations and non- germline DDR mutations .

Besides, gDDRm can occur in both high-grade and low-grade gliomas pts (P=0.7). In addition, 56.5% (13/23) of pts with gDDRm have coexistent sIDH1/2m, which is a marker of good prognosis for glioma, while only 8.3% (1/12) of pts with non-gDDRm carried sIDH1/2m (P=0.006).

Results

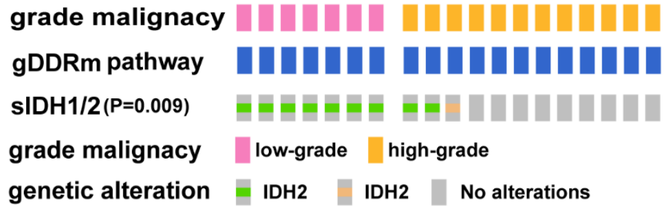

Figure 3. Distribution of somatic IDH mutations in patients with low-grade and high-grade gliomas carrying germline DDR mutations.

We further found that low-grade gliomas pts with gDDRm are more likely to carry sIDH1/2m than high-grade gliomas pts (P<0.001), indicating that this population may have a better prognosis.

Conclusions

In summary, we comprehensively analyzed the characteristics of deleterious germline mutations in pts with glioma, which may be helpful to elucidate the mechanism of glioma, and prompt the prognosis of the disease.

The authors declare no conflicts of interest.

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