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Letter to the Editor

H3 K27M-mutant glioma: clinical characteristics and outcomes

We have read the publication by David Meyronet et al[1] regarding the clinical characteristics and prognosis for H3 K27M-mutant gliomas where the authors concluded that H3 K27M-mutant glioma was a distinct subgroup of isocitrate dehydrogenase (IDH) wild-type glioma and constantly located at the midline structure of the brain in adult patients. Their findings provide us with a better understanding of H3 K27M-mutant gliomas; however, there are still some questions remaining concerning their article.

Although H3 K27M-mutant gliomas have various histologic types, they are defined as World Health Organization (WHO) grade IV gliomas in the 2016 WHO classification of central nervous system tumors.[2] However, in the Meyronet article we found that 80% of the diffuse gliomas in their comparative group were glioblastomas (grade IV), and the rest were lower-grade (grades II and III) gliomas. The authors compared characteristics and prognoses between 21 cases of H3 K27M-mutant gliomas and 135 cases of diffuse gliomas without IDH mutation and without histone H3 (IDH/H3 wild-type) in adults. In order to have a better understanding of H3 K27M-mutant gliomas, it would have been important for the authors to exclude lower-grade gliomas from those 135 cases of diffuse gliomas from their comparisons.

The authors also reported in their paper no significant difference in overall survival (OS) between H3 K27M-mutant gliomas and IDH/H3 wild-type gliomas ($P = 0.3$), which could be explained by the inclusion of lower-grade gliomas in their comparative group. Prior studies have shown that surgery type was an independent prognostic factor for OS in H3 K27M-mutation glioma.[3,4] Meyronet et al reported that 16 H3 K27M-mutant glioma patients received biopsy, and partial resection was undertaken in 5 patients—however, in their study, the number of patients who received surgical resection or biopsy in the control group was not mentioned. To distinguish the difference in survival between H3 K27M-mutant gliomas and IDH/H3 wild-type gliomas, we suggest the authors could further compare the OS of patients who received surgical resection between these two groups. Moreover, the prognosis of patients who received biopsy should be compared between H3 K27M-mutant gliomas and IDH/H3 wild-type gliomas as well. They also reached a conclusion that H3 K27M mutation was a negative prognostic factor for H3 K27M-mutation gliomas; nevertheless, they found that H3 K27M-mutant glioma patients had better survival than IDH/H3 wild-type glioma patients. H3 K27M mutation was a negative prognostic factor in diffuse midline glioma, which means that patients with H3 K27M-mutant diffuse midline gliomas had a significantly shorter OS than the H3 wild-type counterparts ($P = 0.001$).[4] One reason why their result was inconsistent with their conclusion was that they compared the OS between H3 K27M-mutant gliomas and diffuse gliomas (IDH/H3 wild-type) rather than between H3 K27M-mutant gliomas and diffuse midline glioma. Another is that the tumor location of these 135 cases of diffuse gliomas was not clarified in terms of data on whether those diffuse gliomas originated from the cerebral hemispheres or the intracranial midline structure.

H3 K27M-mutant glioma was a subgroup of IDH wild-type glioma that was consistently restricted to the midline structure of the brain in their study. However, Lopez et al[5] reported occurrence of H3 K27M mutation in one patient with non-midline glioma and came to the conclusion that H3 K27M mutation was not limited to intracranial midline gliomas and spinal cord gliomas. As has been presented previously, we draw a conclusion that wherever gliomas are located, all of the IDH1 wild-type gliomas are likely to occur with H3 K27M mutation, and H3 K27M-mutation gliomas are not confined to the intracranial midline areas and spinal cord.

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