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Poster Presentation

Molecular Plot Twist: H3 G34V Mutation and MET Amplification in a Diffuse Hemispheric Glioma

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ABSTRACT

Introduction. Diffuse hemispheric glioma, H3G34-mutant (DHG-H3G34m) (CNS WHO grade 4), is a rare, recently characterized subtype of pediatric high-grade glioma. This is the first histopathologically and molecularly confirmed case of DHG-H3G34m in the Philippines, underscoring the rarity of the tumor and the growing capacity for molecular neuropathologic diagnostics in the country.

Case Description. This is a case of a 16-year-old male with a right fronto-parietal tumor. MRI and CT scan shows a large, lobulated, contrast-enhancing mass. Histologic examination reveals a hypercellular neoplasm with sheets of pleomorphic cells with hyperchromatic nuclei, irregular nuclear membranes, and moderate amphophilic cytoplasm. Foci of multinucleated giant cells, microcalcifications, microvascular proliferation, and necrosis are seen. Immunohistochemical studies (IHCs) with GFAP and H3 G34V reveal diffuse positivity. There is loss of expression of OLIG2 and ATRX. Molecular analysis revealed alterations in H3-3A G34V, TP53, ATRX, and an ST7::MET fusion leading to MET amplification.

Discussion. The working diagnosis prior to IHCs was High Grade Neoplasm with differentials of epithelioid glioblastoma, glioblastoma with giant cell features and anaplastic ependymoma. The IHC and molecular findings support the diagnosis of DHG-H3G34m. DHG-H3G34m are caused by mutations in the H3-3A gene which alter the 34th amino acid in the H3.3 histone. Usually a glycine-to-arginine (G34R) mutation is found, but in few instances such as in this case, there is a glycine-to-valine (G34V) mutation. These have poor prognosis with no known targetable treatment; however, the MET fusion found in this case may possibly be treated with MET-tyrosine kinase inhibitors.

Conclusion. This is a case of diffuse hemispheric glioma, H3G34-mutant (CNS WHO grade 4) with a rare H3 G34V mutation and MET amplification in a 16-year-old male, the first histomorphologically and molecularly confirmed case in the Philippines.

Key words. *diffuse hemispheric glioma, brain neoplasms, high-grade glioma, pediatric*