



Case Report

Diffuse midline glioma H3K27M mutation in adult: A case report

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ABSTRACT

Introduction: Diffuse midline glioma with H3 K27M mutation is a new tumor entity from 2016 which is highly aggressive and classified as a WHO Grade IV tumor regardless of histopathologic features. DMG is an aggressive tumor with a poor prognosis, predominating in children and rarely in adults. The clinicopathologic features in adults remain poorly characterized.

Case presentation: Herein we report a case of a 28-year-old female with diffuse midline glioma with pathology confirmation of histone H3 K27M mutation presenting predominately with left upper and lower limb weakness for 3 weeks followed by an event of loss of consciousness and suspicious mass in MRI Brain/CT Brain. It was confirmed by immunoreactive H3K27M with a score of 4+ in neoplastic cells, which revealed Diffuse midline glioma, H3K27M mutant.

Clinical discussion: Diffuse midline glioma with histone H3–K27M mutation recently classified CNS tumor with grade IV, including both morphologic and molecular features for diagnosis and associated with poor prognosis.

Conclusion: We report a case of adult diffuse midline glioma with H3K27M. The prognosis of diffuse midline glioma is poor and depends solely on H3K27M irrespective of its grade and characteristics. A comprehensive study of diffuse midline glioma on clinical, radiographic, and demographic features in adult is needed.

1. Introduction

Diffuse midline gliomas are primary Central Nervous System (CNS) tumors. It is a rare subtype of glial tumors. World Health Organization 2016 classification of central nervous system tumors, defines diffuse midline gliomas (DMG) with the histone H3 K27M mutation as a distinct Grade IV glioma, regardless of histological features [1]. DMG is an aggressive tumor with a poor prognosis, predominating in children. The exact frequency of these mutations in adults is unknown [2]. This case report has been reported in line with the SCARE 2020 criteria [3].

Herein we report a case of a 28-year-old female with diffuse midline glioma with pathology confirmation of histone H3 K27M mutation presenting predominately with left upper and lower limb weakness for 3 weeks followed by an event of loss of consciousness and suspicious mass in MRI Brain/CT Brain. It was confirmed by immunoreactive H3K27M with a score of 4+ in neoplastic cells, which revealed Diffuse midline glioma, H3K27M mutant.

2. Case presentation

A 28-year-old female presented with a history of loss of consciousness 1 episode, of sudden onset lasting for approximately 15–20 minutes, without abnormal body movement followed by dizziness, severe on sitting up or walking with difficulty in walking, due to loss of balance. She had left upper and lower limb weakness for 3 weeks followed by an event of loss of consciousness with the inability to raise the left upper limbs, inability to grasp any object, difficulty in walking, blurring of vision of the right eye with associated double vision and associated eye pain with drooping of the right eyelid.

MRI Brain (Fig. 1) and CT Brain (Fig. 2) examination showed swollen right half of the midbrain with a well-defined, smoothly outlined, intra-axial lesion measuring about 2 * 2.5 * 1.7 cm in the right half of the midbrain with no abnormal enhancing areas in the lesions or the surrounding area in contrast-enhanced (CE) images. Swollen right half of the Thalamus with a focal area measuring 2.7 * 2 * 1.8 cm showing faintly hypointense signal in T1W and hyperintense signal in T2W and

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FLAIR sequence in the right Thalamus adjacent to the lesion in the right half of the midbrain with no restricted diffusion in the lesion in DWI/ADC map images and no abnormal enhancing areas in the region or surrounding area in CE images were seen along with hydrocephalus with dilated lateral ventricles. Corpus Callosum, Lt Thalamus, hypothalamus, and basal ganglia/internal capsule complex is normal.

Mini frontotemporal burr hole/craniotomy was done, dura reflected and cystic tumor with capsule was removed. The midbrain specimen was sent for histopathological examination.

The sections showed low cellularity and the cells were predominantly elongated with elongated with fibrillary cytoplasm. The nuclei were elongated and mild hyperchromatic. Some areas showed mildly increased cellularity and round to oval cells. Few cells were large and hyperchromatic and occasional multinucleated cells were also seen. Edema was also observed in some areas. Rosenthal fibers, necrosis, granuloma, microvascular proliferation, and mitotic figures were not seen.

On Immunohistochemistry (Fig. 3), P53 and OLIG-2 were immunoreactive and score 3+ in neoplastic cells, Ki-67 was immunoreactive in 15–20% in neoplastic cells. H3K27M was immunoreactive with a score of 4+ in neoplastic cells, which revealed Diffuse midline glioma, H3K27M mutant.

After her vitals were stable, she was discharged with oral medication Levetiracetam 500 mg. Her disease condition was well explained to the patient’s party and was advised for regular follow-up.

3. Discussion

In 2016, WHO reclassified tumors of the Central Nervous System incorporated molecular parameters into the classification. Diffuse midline glioma with histone H3–K27M mutation recently classified CNS tumor with grade IV, including both morphologic and molecular features for diagnosis and associated with poor prognosis [1]. Lesion mainly affects the pediatric age group and is found infrequent in an adult population. Due to the lack of adequate literature, classification,

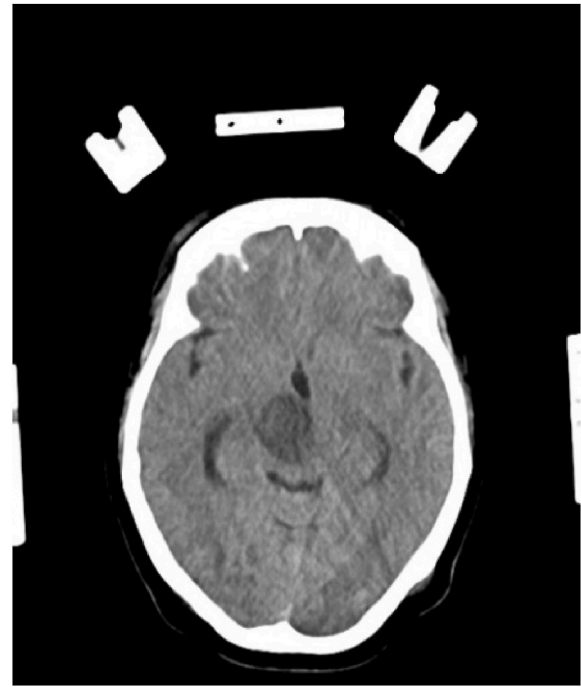


Fig. 2. Showing CT of Brain.

epidemiologic, radiographic, and clinical characteristics remain unclear, especially in adults [4].

H3K27M mutant diffuse midline glioma is most common in the pons and the thalamus. Pons and thalamic midline glioma are common in the pediatric population and spinal cord tumors are mostly in adults [5]. David et al. reported that H3k27M mutant gliomas occurred frequently in children and thalamus and spinal cord tumor in adults [6].

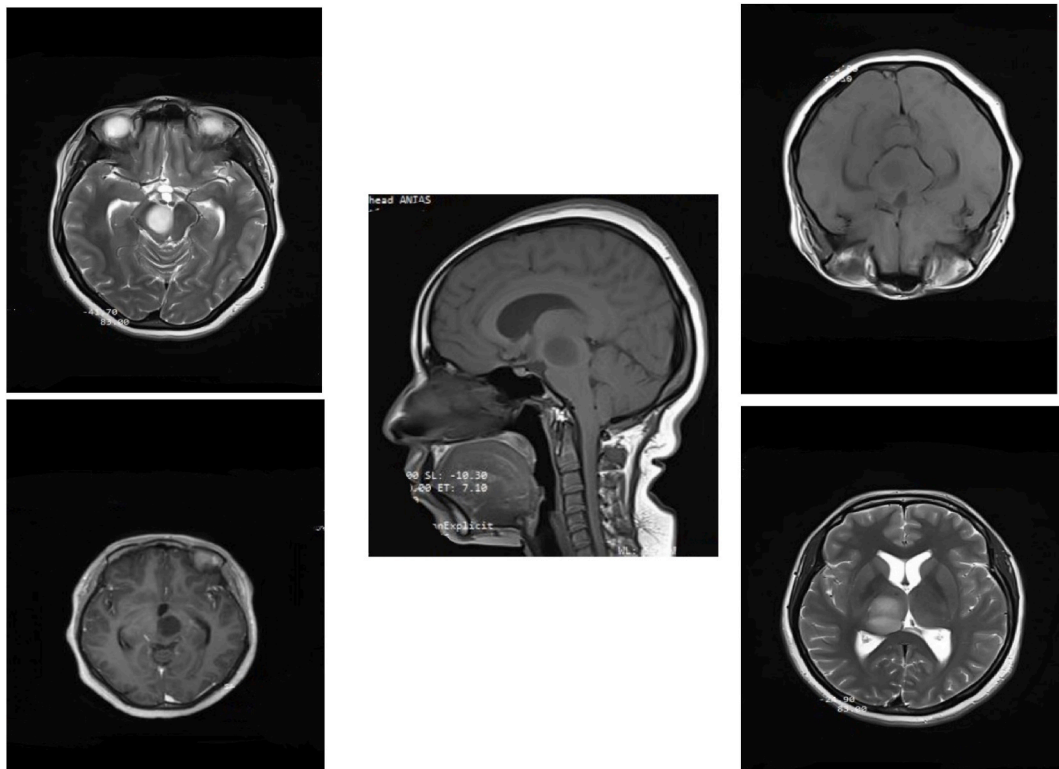


Fig. 1. Showing MRI of Brain.

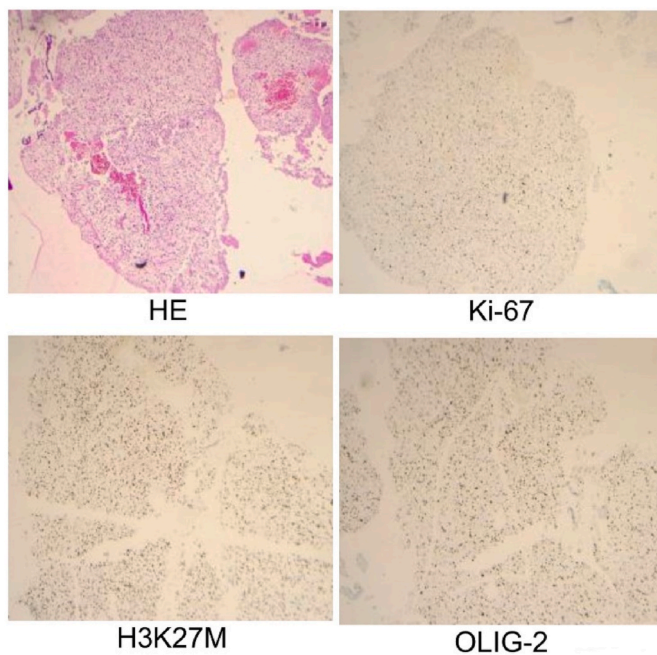


Fig. 3. Showing immunohistochemistry of the section of the midbrain.

Independent of histopathologic grade, testing for H3K27M mutation should be done in all pediatric midline glioma [7].

Macroscopic features were not regularly described in the literature but in general it shares the characteristics features of other infiltrative gliomas including distortion and enlargement of affected structures, with the area of necrosis or discoloration [4]. Characteristics features of this disease are a mutation of H3K27M which is histone 3 (H3) isoforms H3.3 and H3.1, resulting in the substitution of methionine for lysine at residue 27 of the histone H3 N-terminal tail [8]. H3.3 affects gene expression through epigenetic regulations thus participating in cell regulation and differentiation [9]. This case was also histopathologically proven H3K27M mutant.

The majority of cases are managed with surgery, radiation, and drugs. The role of surgery is primarily for diagnosis [5,6] H2K27M mutation has a poor prognosis. Prognosis of H3K27M mutations not related to the extent, location, and grade of the tumor [4].(9) The prognosis of patients occurring in the thalamus is better than the brainstem because the expression of the gene of cyclin-dependent kinase 6 (CDK6) is different in the brainstem and thalamus with H3K27M mutation(9). Mutations in adults do not influence survival significantly [10].

4. Conclusion

Diffuse midline glioma with H3K27M mutation is predominately seen in the pediatric population and can infrequently be seen in an adult population. It is more common in the thalamus and midbrain. The prognosis of diffuse midline glioma is poor and depends solely on H3K27M irrespective of its grade and characteristics. A comprehensive study of diffuse midline glioma on clinical, radiographic, and demographic features in the adult is needed.

Ethical approval

This is a case report, therefore, it did not require ethical approval from ethics committee.

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Author contribution

Author 1: Led data collection, contributed to writing the case information and discussion. Author 2: Contributed to the process of original draft preparation and introduction. Author 3: Contributed to conceptualization, methodology, and discussion. Author 4: Revised it critically for important intellectual content, contributed to review and editing. Author 5: Edited the rough draft into the final manuscript. Author 6: who diagnosed the case, collected the data, and preserved the pictures. Author 7: The resident radiologist, who helped in the diagnosis and supervised throughout the process of manuscript writing.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal on request.

Registration of research studies

Not applicable.

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Declaration of competing interest

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103567>.

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