

CASE REPORT

A case of adult-onset diffuse midline glioma diagnosed by histone H3K27M immunostaining after death, which required differentiation from brainstem encephalitis and myelitis

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Abstract

H3K27M-mutant diffuse midline glioma is a malignant glioma that was newly added to the World Health Organization classification in 2016. In diffuse midline glioma, the H3K27M-mutant sometimes develops sub-acutely and requires a differential diagnosis from encephalomyelitis. Here, we report a case of adult-onset diffuse midline glioma that was diagnosed by immunostaining for histone H3K27M after death. The present case required a differential diagnosis of autoimmune cervical myelitis and brainstem encephalitis.

KEYWORDS

adult onset, diffuse midline glioma, H3K27M-mutant, long cord lesion

1 | CASE REPORT

A 26-year-old Japanese man presented with the back of the neck pain and right arm weakness for 5 days. He had no significant past medical or family history. Cranial magnetic resonance imaging (MRI) on day 7 of onset showed hyperintensity lesions from the medulla oblongata to the cervical cord on T2-weighted MRI, and MRI findings on day 13 of onset showed partially enhanced images on gadolinium-enhanced T1-weighted MRI (Figure 1A–E).

The patient was tentatively diagnosed with inflammatory demyelinating disease. Despite immunotherapies with steroids, intravenous immunoglobulin (IVIg), and plasmapheresis, the symptoms progressed rapidly at 2 months after the onset, and he needed

mechanical ventilation. Therefore, he was transferred to our hospital 4 months after the onset.

MRI findings showed that the hyperintensity lesion in the medulla oblongata had gradually expanded at 4 months from the onset. Moreover, 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed upregulation of the signal intensity in the medulla oblongata lesion (Figure 1I). The patient underwent a biopsy of the medulla oblongata lesion and external decompression surgery for hydrocephalus 5 months after the onset.

The medulla oblongata lesion biopsy revealed increased glial cells, perivascular lymphocyte infiltration, as well as a small number of large cells observed with hematoxylin–eosin (HE) staining (Figure 1J). Immunohistochemistry revealed the absence of

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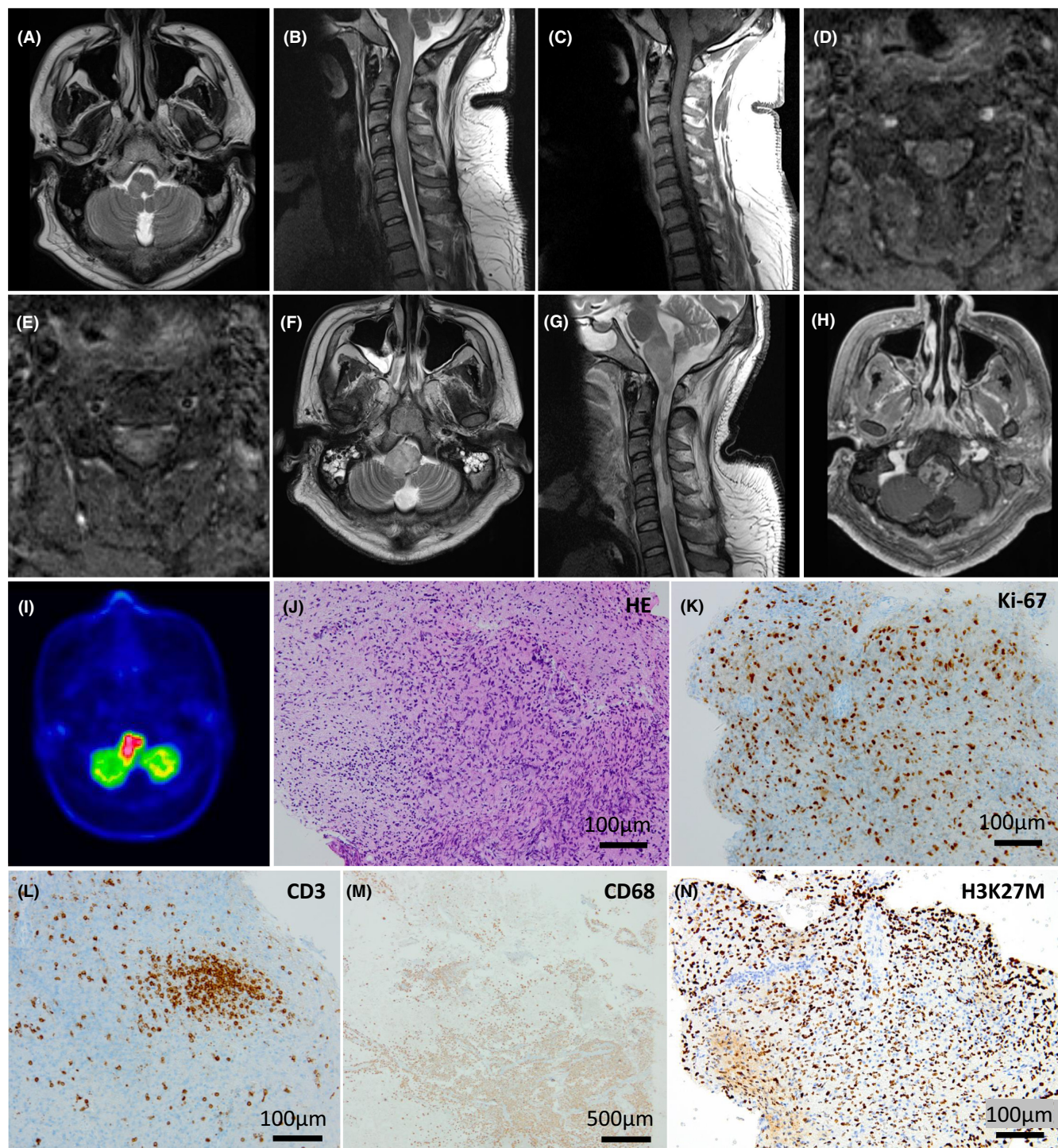


FIGURE 1 At 7 days after the onset, the T2-weighted axial image showed hyperintensity at the right medulla oblongata (A), and the sagittal image showed hyperintensity at the C1-C5 spinal cord (B). At 13 days after the onset, gadolinium-enhanced T1-weighted sagittal image showed partial enhancement at the C3-4 spinal cord (C) and gadolinium-enhanced T1-weighted axial images at the C3-4 spinal cord (D-E). At 6 months after the onset, the T2-weighted axial image showed heterogeneous hyperintensity and expanding lesion at the medulla oblongata (F), the sagittal image shows an enlarged spinal cord lesion and atrophied spinal cord (G), and gadolinium-enhanced T1-weighted axial image (H). Head 18F-fluorodeoxyglucose positron emission tomography shows upregulation of the signal intensity on the medulla oblongata lesion (I). Hematoxylin-eosin staining (J), immunostaining with Ki-67 (K), CD3 (L), CD68 (M), and H3 K27M-mutant-specific antibody (N).

IDH-1R132H mutation. Ki-67 was also positive in cells other than lymphocytes (Figure 1K); however, p53 was negative and ATRX was retained.

Conversely, CD3-positive T cells were observed around the perivascular area in the medulla oblongata lesion (Figure 1L), and the main infiltrating cells were CD68-positive histiocytes in the biopsy

tissue obtained from a tumor in the fourth ventricle (Figure 1M), while CD20-positive B cells were absent. Based on these pathological findings, a diagnosis of autoimmune brainstem myelitis was made.

On neurological examination at 6 months after the onset, he had right abduction nerve palsy; weakness of the right facial muscle; loss of muscle contraction in the neck, trunk, and limbs; loss of deep tendon reflex; Babinski reflex on the left; sensory impairment on both sides below the neck. The routine laboratory tests revealed an abnormal cerebrospinal fluid (CSF) protein concentration of 518.9 mg/dL.

Proceeding MRI scans at 6 months after onset showed that the medulla oblongata and spinal cord lesions were further enlarged (Figure 1F–H). At 7 months after onset, a urinary tract infection led to septic shock and the patient died 2 days later. No consent for autopsy was obtained.

Shortly after the patient's death, an antibody against the H3K27M-mutant, which is highly specific for H3K27M-mutant diffuse midline glioma (DMG), became available on a commercial basis. The biopsied sample was considered positive for the H3K27M-mutant-specific antibody (Figure 1N). Based on the immunohistochemistry results, we finally diagnosed the patient with DMG.

2 | DISCUSSION

Though rarely, cases of DMG in adults have been reported.¹ Recently, immunostaining with the H3K27M antibody can specifically and simultaneously detect multiple K27M mutations in histone H3. The H3K27M mutation is specific for DMG. A previous study reported that the K27M-mutant caused a global reduction in trimethylation level in H3K27.² Immunostaining with the H3K27M antibody can specifically and simultaneously detect K27M mutations in histone H3.

The lesions usually occur in the pons in cases of pediatric patients. However, in adults, the tumor site is mainly in the thalamus and less frequently in the medulla oblongata and spinal cord.^{1,3}

On imaging examinations, DMG usually demonstrates a non-uniform hyperintensity on T2-weighted images. The characteristics of gadolinium enhancement vary from ring enhancement to the absence of enhancement.³

In clinical situations, subacute onset with long cord lesions requires a differential diagnosis between DMG and inflammatory diseases.

Neurologists should consider that the H3K27M antibody is not always available in clinical situations, as this antibody is not used routinely in clinicopathological examinations. Given the clinical and pathological features of DMG, neurologists should seek more detailed pathological consultation if they suspect the presence of DMG.

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Not applicable.

CONFLICT OF INTEREST STATEMENT

Authors declare no Conflict of Interest for this article.

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