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Case Report

Primary spinal cord glioblastoma: A rare cause of paraplegia

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ABSTRACT

Background: Primary spinal glioblastomas are extremely rare neoplasms and account for only 0.2% of glioblastoma cases. Due to the rare incidence of spinal cord glioblastoma in the literature, its natural history/outcome remains undetermined. The present article describes the clinical presentation, radiological/pathological characteristics, and outcome of the primary spinal cord glioblastoma.

Case Description: Two young patients initially presented with paresis that rapidly progressed to paraplegia. Nondermatomal sensory deficits were also noted, mainly affecting the lower limbs. Neuroradiological imaging revealed an extensive intramedullary spinal cord lesion, with no evidence of concurrent intracranial space-occupying lesions. Thoracic laminectomy, followed by tumor debulking and/or biopsy, was performed. The histomorphology was suggestive of glioblastoma, the World Health Organization grade 4 (Isocitrate Dehydrogenase-wild type). They were discharged in stable condition and were started on chemoradiotherapy, with clinicoradiological follow-up. One patient passed away after 9 months of initial presentation. The other patient was alive at 6-month follow-up.

Conclusion: Primary spinal glioblastoma is a rare and challenging tumor. Patients commonly present with a progressive paresis, resulting in paraplegia, regardless of the surgical resection extent, and received adjuvant chemotherapy. Therefore, primary spinal cord glioblastoma should be considered in patients reporting a rapid lower limb weakness with neuroradiological evidence of extensive, exophytic intramedullary lesion of the spine. A biopsy-proven histopathological diagnosis is of indisputable importance to establish the final diagnosis and plan treatment options.

Keywords: Cervicothoracic, High-grade glioma, Intramedullary, Paresis, Weakness

INTRODUCTION

Glioblastoma is a highly malignant neuroglial tumor. Intracranial glioblastomas are considered the most prevalent primary brain tumors in adults, accounting for 54% of gliomas and 16% of primary intracranial tumors with an incidence rate of 3.19/100,000 persons in the United States.[11] On the other hand, primary spinal glioblastomas are extremely rare neoplasms and account for only 0.2% of glioblastoma cases and 1.5% of all primary spinal cord tumors, as was demonstrated in a population-based study in Norway.[4] A recent study reported a higher prevalence, constituting 9% of gliomas and 2.5% of all neuroglial intramedullary tumors.[3]

Due to the rare incidence of spinal cord glioblastoma in the literature, its natural history/outcome remains undetermined. The present cases describe the clinical presentation, radiological/pathological characteristics, and outcome of the primary spinal cord glioblastoma.

CASE DESCRIPTION

Patient 1

Clinical presentation

A 37-year-old male, intellectually-challenged, presented to the emergency department with a 10-day history of progressive paresis, associated with low back pain and urinary incontinence, following a fall. Initially, the patient was able to ambulate freely with the left hip pain. However, the weakness progressed over the following days limiting his ability to ambulate independently, resulting in paraplegia. The weakness was associated with bilateral numbness and shooting, electrical-like sensation radiating from the hip to the knee. There was no history of fever, rigors, night sweats, fluctuating fatigability, or upper respiratory tract infection.

Physical examination

The patient was alert with a baseline intellectual disability. The muscle power was 5/5 in the upper limbs. Lower limb examination was limited due to excruciating pain. However, the muscle power in the lower limbs was 0/5. Sensation was decreased to pinprick in the lower limbs, especially on the left side, with no specific dermatomal distribution. Apart from a preserved left patellar reflex (+2), the lower limb reflexes were absent. Plantar reflexes were equivocal bilaterally.

Neuroradiological imaging

Thoracolumbar MRI with contrast revealed an intramedullary high T2-signal lesion at T3-T7 level [Figures 1a-d]. Brain MRI was unremarkable [Figures 1e and f]. Given the clinical data and radiological features, the presumptive differential diagnoses included transverse myelitis, demyelinating disease, central nervous system lymphoma, and intramedullary astrocytoma with cerebrospinal fluid (CSF) seeding.

Surgical intervention

The patient underwent upper thoracic laminectomy and tumor debulking. Intraoperatively, a biopsy was obtained from the exophytic part of the lesion and was sent for frozen section and permanent pathology. The biopsy revealed a high-grade glioma. The patient tolerated the surgery well with no complications.

Histopathological and molecular features

The histopathological sections showed a hypercellular malignant glioma [Figure 2]. There was pseudopalisading necrosis and endothelial proliferation. The tumor cells were arranged in sheets. The tumor cells appeared pleomorphic with a high nuclear/cytoplasmic ratio. Mitotic figures were readily identified. The immunohistochemistry of Isocitrate Dehydrogenase 1 (IDH1 R132H) expression was negative. The ATRX immunohistochemistry revealed an intact nuclear expression. The p53 expression had a diffuse and strong nuclear positivity. Therefore, a diagnosis of glioblastoma World Health Organization grade 4 (IDH-wild type) was rendered.

Outcome and follow-up

The patient continued to have persistent flaccid paraplegia with lower limb hypotonia. He was discharged in stable condition with regular clinical and radiological follow-up. Two months after discharge, the patient developed an episode of seizure. A repeat brain MRI demonstrated cerebral dissemination of the spinal tumor [Figure 3]. He was enrolled in an intensive rehabilitation program with a goal of achieving adequate neurological recovery to avoid prolonged immobility complications. Nine months after the initial presentation to the emergency department, the patient passed away at home.

Patient 2

Clinical presentation

A 26-year-old female, not known to have any medical illness, was referred from another facility due to a progressive right lower limb paresis for 3 months. The weakness limited her ability to ambulate independently. Three days after the initial presentation, the patient started to complain of bilateral lower limb paresis and numbness, with a sensory level reaching the nipple, associated with urinary urge incontinence. Furthermore, the patient reported a 2-week history of neck pain radiating to the right shoulder, with no specific dermatomal distribution. There was no history of fever, rigors, night sweats, fluctuating fatigability, upper respiratory tract infection, or trauma.

Physical examination

The patient was alert, attentive, and oriented. The muscle power in the upper limbs was 4/5 bilaterally. Sensation in the upper limbs was intact through all dermatomes (C5-T1). Reflexes were +2 bilaterally in the upper limbs. Lower limb examination revealed a muscle power of 3/5 on the right and 4/5 on the left. The reflexes were +3 on the right and +2 on the left lower limbs. The muscle tone was increased on the

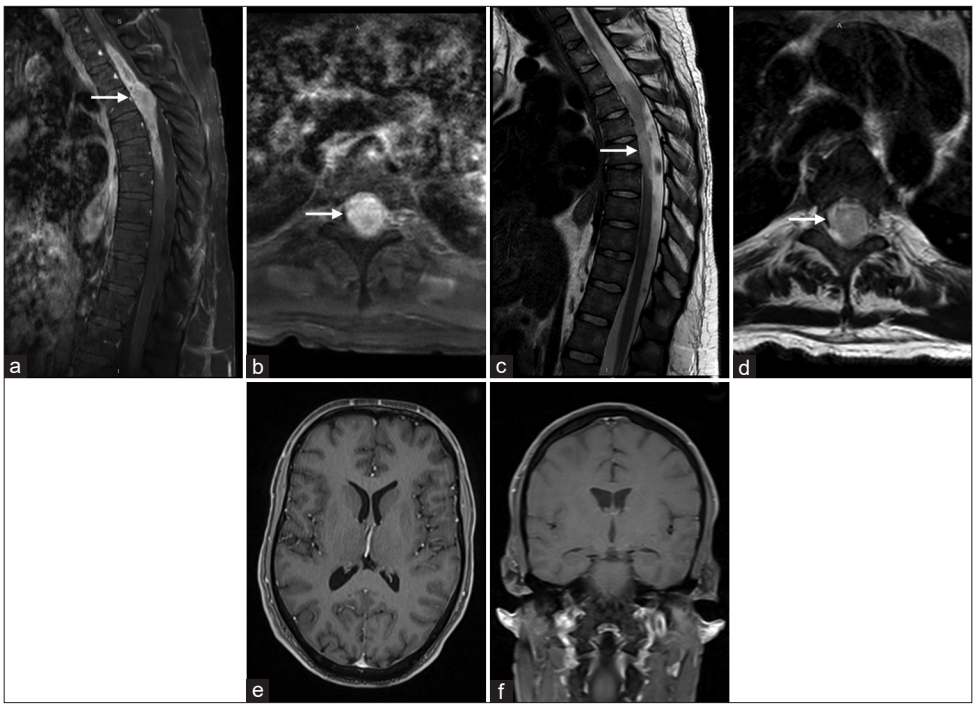

Figure 1: (a and b) Sagittal and axial T1-weighted MRI with contrast of the thoracic spine. (c and d) Sagittal and axial T2-weighted MRI of the thoracic spine. (e and f) Axial and coronal brain MRI with contrast. (a-d) The images demonstrate a T3–T7 intramedullary lesion with heterogenous peripheral enhancement (Arrow). The lesion measures 10.6 × 1.3 cm in craniocaudal and anterior-posterior diameters, respectively. (e and f) The brain MRI shows no evidence of intracranial space-occupying lesions.

right with clonus and upgoing plantar reflex. Sensation was decreased to pinprick and light touch on the left lower limb up to the level of T4 dermatome. The patient was bradykinetic, spastic, using a cane for ambulation, and leaning to her left leg more frequently.

Neuroradiological imaging

Whole spine MRI with contrast revealed a large heterogenous intramedullary lesion of the spinal cord extending from C3 to T9, with nodular enhancement involving the exiting nerve roots [Figure 4].

Surgical intervention

Due to the infiltrative nature of the tumor and the preserved muscle power (3-4/5) in the lower limbs, a T4–T5 laminectomy and biopsy of the intramedullary lesion were performed to establish the diagnosis. Intraoperatively, the frozen section was in favor of glioma. The patient tolerated the surgery well with no complications. Postoperatively, the patient had an unchanged neurological examination.

Histopathological and molecular features

The histomorphology was typical of glioblastoma [Figure 5] with microvascular proliferation, and a very high proliferation index (30–40%) by Ki-67 immunostaining. This was confirmed by a positive immune reaction for the glial markers GFAP (clone 6F2) and Olig2 (clone 211F1.1). The tumor cells reacted negatively for the immunostain IDH-1. However, the IDH-status required further molecular testing of both IDH-1 and IDH-2 which were not possible in this case.

Outcome and follow-up

Three weeks after the surgery, the patient progressed to have bilateral paraplegia, associated with urinary and stool incontinence. The patient underwent radiation of the entire neuroaxis, craniospinal irradiation, followed by concomitant chemotherapy using Temozolomide. The patient is currently wheelchair-bound. She was discharged in stable condition with radiotherapy, oncology, neurosurgery, and rehabilitation follow-up. The patient was alive at 6-month follow-up. However, she travelled outside the country and was lost to follow-up.

DISCUSSION

Primary spinal cord glioblastoma can either originate as primary grade 4 astrocytoma or progress from a lower grade astrocytoma. In addition, they share similar histological features as supratentorial glioblastomas, including nuclear atypia, mitotic figures, palisading necrosis, microvascular

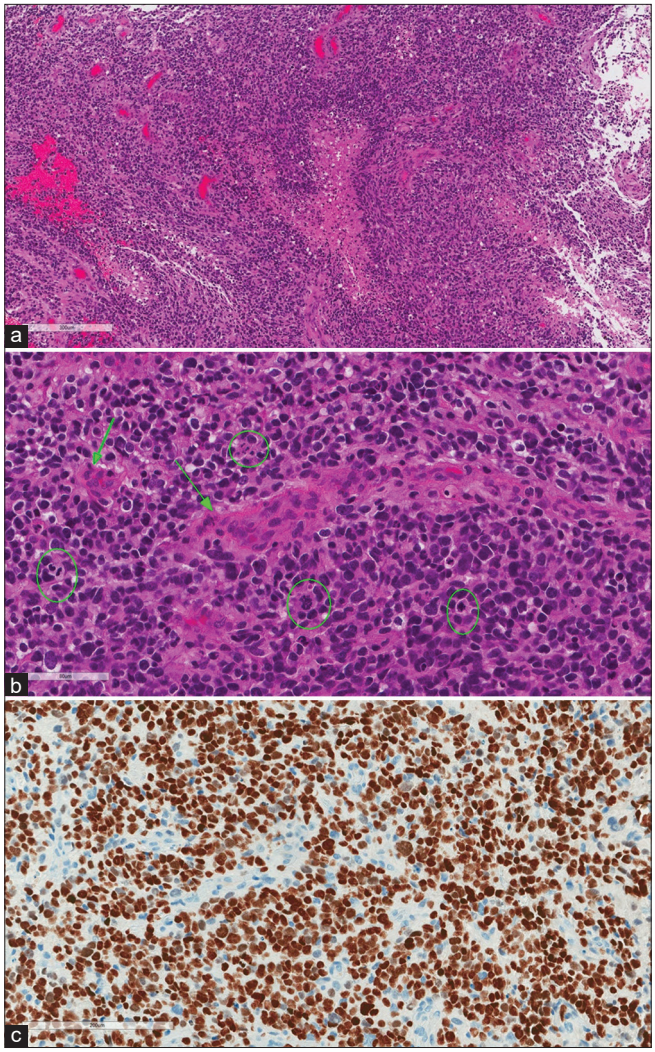

Figure 2: Microscopic images of spinal cord glioblastoma. (a) Low-power micrograph showing high cellularity with palisading necrosis in the middle. (b) Intermediate-power micrograph showing both mitotic figures in green circles and microvascular proliferation (green arrows). (c) Glial differentiation is confirmed by positive nuclear staining for the antibody Olig2 (clone 211F1.1).

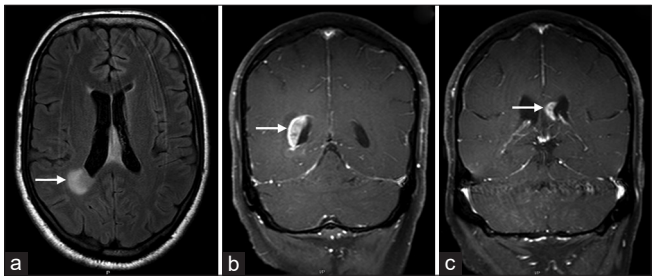

Figure 3: (a) Axial fluid-attenuated inversion recovery (FLAIR) MRI of the brain. (b and c) Coronal T1-weighted MRI with contrast of the brain. (a-c) There are two enhancing subependymal lesions noted in the right peritrigonal region, associated with a high signal in the FLAIR MRI (Arrow). Furthermore, there is a lesion in the inner aspect of the genu and isthmus of the corpus callosum (Arrow).

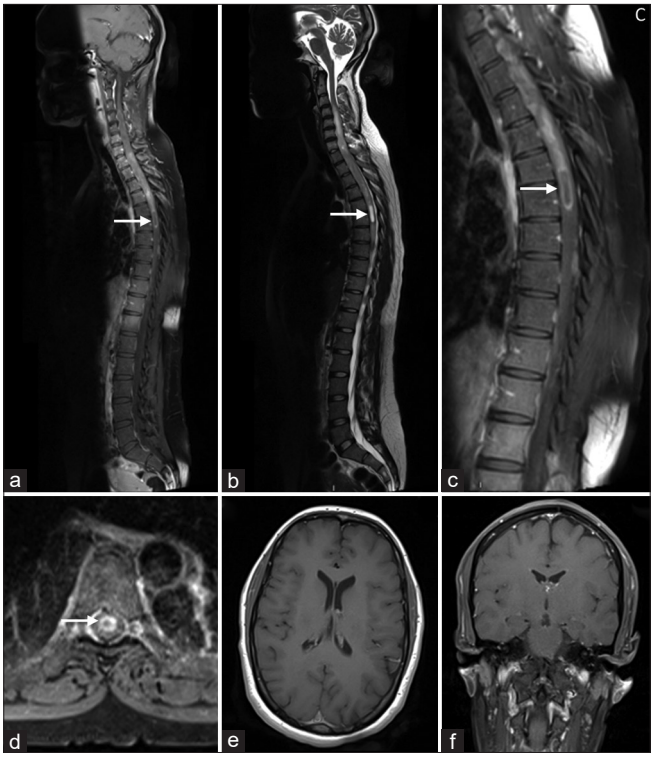

Figure 4: (a-c) Sagittal T1-weighted MRI with contrast and T2-weighted MRI of the spine. (d) Axial T1-weighted MRI with contrast at the level of the cystic component. (e and f) Axial and coronal T1-weighted brain MRI with contrast. (a-d) The images demonstrate a large intramedullary heterogenous lesion extending from the level of C3–C4 until T8–T9. The lesion is causing expansion of the spinal cord, associated with a small cystic and necrotic component mainly at C7 down to T6 (Arrow) with heterogenous enhancement. Furthermore, there are areas of heterogenous enhancement of the exiting nerve roots. (e and f) The images demonstrate no intracranial space-occupying lesions or abnormal parenchymal/meningeal enhancement.

or glomeruloid vascular proliferation, and elevated Ki-67 antigen levels.[3]

Primary spinal cord glioblastoma has mainly targeted younger individuals than intracranial glioblastoma, with a mean age of onset varying between 26 and 40 years among different studies with a slight male predominance.[6,10,13] The clinical presentation depends on the tumor location and expansion within the spinal canal. Thoracic and cervical spinal cord areas were the most frequently affected, followed by the cervicothoracic region, lumbar area, and conus medullaris.[10] Correspondingly, the most common presenting symptom is limb weakness, followed by sensory deficits, in addition to back pain, and bladder/bowel disturbances.[6]

In the present cases, both patients initially presented with paresis that rapidly progressed to paraplegia. Furthermore, the sensory deficits mainly affected the lower limbs in a nondermatomal distribution.

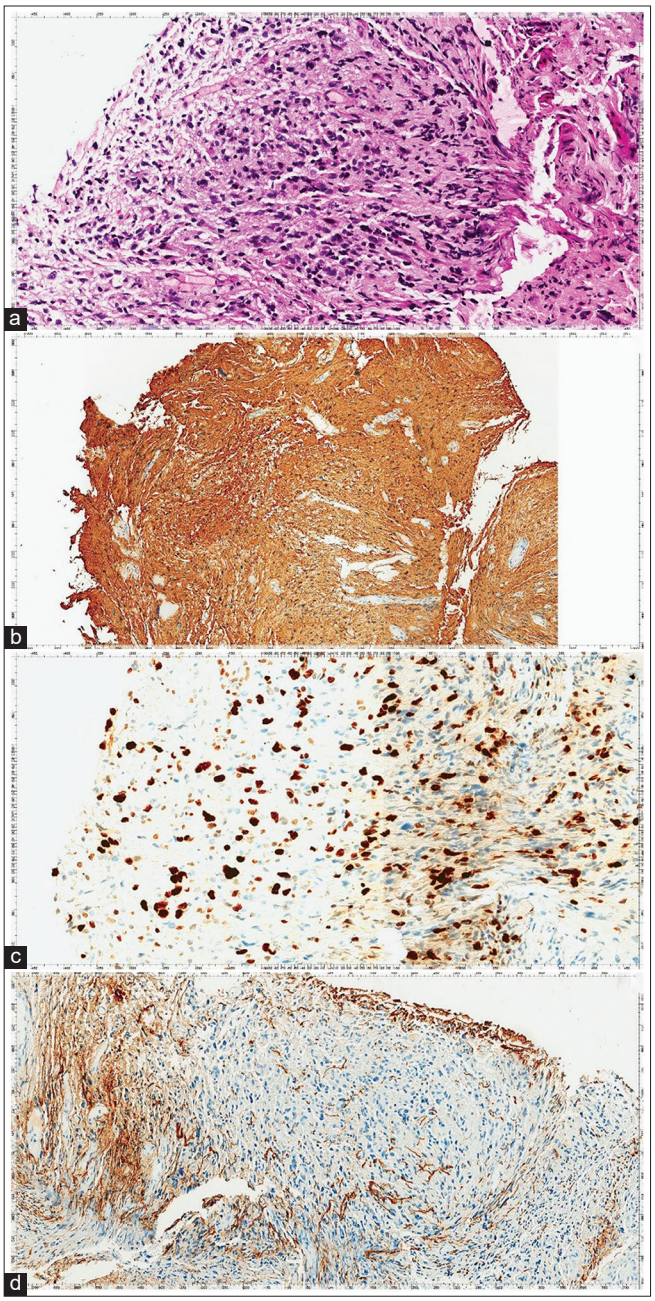

Figure 5: Microscopic images of spinal cord glioblastoma. (a) Hematoxylin and Eosin-stained section shows low-to-moderately cellular infiltrative glioma. There is a focus of endothelial proliferation with no evidence of necrosis. The tumor cells appear round/oval and some are elongated and hyperchromatic. A few mitotic figures are observed. There are no Rosenthal fibers. (b) The tumor cells are immunopositive for GFAP and p53 (Not shown). (c) Ki-67 immunolabeling is estimated to be high (30–40%). (d) Neurofilament immunostain highlights a significant degree of infiltration

Like its intracranial counterpart, primary spinal glioblastoma carries a poor prognosis and high mortality rate. The mean survival rate is estimated to be 14 months.[10,12] Resultant complications include cerebral metastasis, hydrocephalus secondary to CSF dissemination, mass progression, and respiratory paralysis.[6,8]

It is worth mentioning that both patients in the present article had a primary spinal cord glioblastoma, that is, no evidence of space-occupying lesion in the brain. Seeding of intracranial glioblastoma to the spinal cord is present in approximately 25% of the cases; however, seeding of spinal glioblastoma intracranially is rare.[2,5] Spinal glioblastoma was proposed to disseminate through leptomeningeal pathway.[1,2] Intracranial metastases are usually located in the ventricles, subarachnoid space, brainstem, hypothalamus, thalamus, cerebellum, and septum pellucidum.[8] The first patient initially had an unremarkable brain MRI. However, 3 months after, the patient had evidence of cerebral dissemination of the tumor, as demonstrated in [Figure 3].

Due to the scarce reported cases, the optimal management remains controversial. The current treatment options include biopsy, subtotal, or gross total resection, in addition to radiotherapy, and chemotherapy.[10] Results of the benefit of gross total resection on survival are conflicting with multiple studies reporting no significant survival difference primarily due to its infiltrative nature, and in some cases, worse outcomes resulted from total resection.[9,10,12] On the other hand, the extent of resection was not consequential.[10] Similarly, chemotherapy, more commonly temozolomide, and radiotherapy effects and timing are disputed.[10],[12] Conventionally, it is recommended to perform subtotal resection followed by adjuvant radiotherapy.[6,7]

In the present article, the first patient underwent subtotal resection whereas the second patient underwent biopsy followed by concomitant chemoradiotherapy, using temozolomide. Considering their intricate location within the spinal cord, aiming for aggressive surgical resection might have resulted in acute neurological sequelae.

CONCLUSION

Primary spinal glioblastoma is a rare and challenging tumor. Patients commonly present with a progressive paresis, resulting in paraplegia, regardless of the surgical resection extent and received adjuvant chemotherapy. Therefore, the primary spinal cord glioblastoma should be considered in patients reporting a rapid lower limb weakness with neuroradiological evidence of extensive, exophytic intramedullary lesion of the spine. A biopsy-proven histopathological diagnosis is of indisputable importance to establish the final diagnosis and plan the treatment options. Persistent reporting and documentation of such rare cases in the literature are fundamental for the progress of the current knowledge and the contribution to the optimal treatment options.

Authors' Contributions

Bashaer Alharbi: Conceptualization, Writing – Original Draft, Writing – Review and Editing. Hajar Alammar: Writing – Original Draft, Writing – Review and Editing. Ali Alkhaibary: Conceptualization, Investigation – Radiological Images, Investigations – Histopathological images, Writing – Original Draft, Writing – Review and Editing. Ahoud Alharbi: Writing – Original Draft, Writing – Review and Editing. Sami Khairy: Conceptualization, Supervision, Writing – Review and Editing. Ali H. Alassiri: Investigations – Histopathological Features, Writing – Original Draft, Writing – Review and Editing. Fahd Alsufiani: Investigations – Histopathological Features, Writing – Original Draft, Writing – Review and Editing. Ahmed Aloraidi: Conceptualization, Investigations – Surgical Management. Writing – Review and Editing. Ahmed Alkhani: Conceptualization, Investigations – Surgical Management. Writing – Review and Editing. All authors have critically reviewed and approved the final version of the manuscript.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.

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