Case report

A case of suspected gliomatosis cerebri: diagnostic and therapeutic challenges in a resource-poor setting.

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Abstract

We present a case of a 70-year-old male with gliomatosis cerebri (GC), who initially presented with behavioural changes and amnesia, which progressed to extrapyramidal and cortical dysfunction. Neuroimaging revealed possible extensive cerebral gliomatosis and brain biopsy showed reactive gliosis. Despite treatment with levodopa-carbidopa, the symptoms worsened, and he succumbed after 18 months. This case highlights the challenges in diagnosing and managing GC in a resource-poor setting.

Keywords: Gliomatosis cerebri, Extrapyramidal dysfunction, Cognitive dysfunction, Diffuse glioma

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Introduction

Gliomatosis cerebri (GC) is a rare, poorly-understood and aggressive form of diffuse glial tumour infiltration pattern of at least three lobes of the cerebral hemispheres, resulting in progressive neurological dysfunction [1]. GC presents with various clinical manifestations, making it challenging to diagnose [2]. Here, we report a case of possible GC in a 70-year-old male who initially presented with transient behavioural changes and subsequently developed extrapyramidal and cortical dysfunction. His neuroimaging was supportive of GC, but his brain biopsy was inconclusive. We discuss the diagnostic and management challenges associated with this rare disease entity in a resource-poor setting.

Case presentation

A 70-year-old male with a history of coronary artery bypass grafting for dual-vessel coronary disease and bladder neck stenosis following open prostatectomy two years earlier, and on a long-term suprapubic catheter and admitted to our medical unit with transient behavioural changes and amnesia lasting six hours, accompanied by visual obscuration and severe early morning generalised headaches over the previous two weeks. His regular medications included aspirin and atorvastatin, and he had a history of smoking (10 pack-years). Upon admission, vital signs were near-normal, oriented in time, person, and place, and had a Glasgow Coma Scale score of 14/15, bilateral disc oedema and generalised hypertonia with no other focal neurology.
A non-contrast CT scan revealed diffuse symmetric white matter hypodensity in bilateral cerebral hemispheres (Figure 1). Mannitol and 3% sodium chloride were administered. Subsequent CT scans confirmed similar findings (Figures 2 and 3), and a cerebral angiogram only showed anatomical variations in the right anterior cerebral artery (Figure 4). Electrocardiogram changes and elevated troponin I levels indicated a non-ST elevation myocardial infarction. Antiplatelets, anticoagulation, intravenous ceftriaxone, and acyclovir was commenced for suspected urinary tract infection and viral meningoencephalitis. A lumbar puncture revealed clear cerebrospinal fluid with a high opening pressure of 400 mm H₂O, normal protein, 51 red cells and absent white cells, xanthochromia, glucose drop or organisms. EEG had generalised cerebral dysfunction with no epileptic activity. Laboratory analyses indicated elevated white blood cell count, inflammation markers, and creatine phosphokinase levels. The patient was discharged with improving laboratory values.

Figure 1: Non enhanced CT brain shows extensive diffuse bilateral symmetrical hypodensity involving the white matter of both cerebral hemispheres, the thalami and midbrain with mild mass effect.
One month later, the patient's condition deteriorated, characterised by escalated behavioural changes, aggression towards relatives, gait issues, and increased motor symptoms. These included limb rigidity, bradykinesia, and tremors in both hands. While muscle power was generally normal, proximal lower limbs exhibited weakness (3/5), and lower limb reflexes were brisk with upgoing plantar reflexes. The patient experienced allodynia but no sensory loss or cerebellar signs. A repeat NCCT brain scan showed previously described changes. Levodopa-carbidopa was initiated for predominant extrapyramidal symptoms, with subsequent dose adjustments.

Figure 2: NCCT brain at 48 hours, the persistence of diffuse cerebral hypodensity, with cerebellar sparing

A follow-up MRI and MRS performed three months later showed T2W and FLAIR hyperintensities involving frontal, temporal, and parietal lobes, consistent with gliomatosis cerebri or diffusely infiltrating astrocytoma (Figures 5 and 6). A stereotactic brain biopsy revealed oedematous reactive gliosis only (Figure 7). Patient refused a repeat brain biopsy.

The patient was referred to the neurosurgical and oncological teams for further care. But he had missed the follow-ups, had a progressively deteriorating extrapyramidal syndrome while on levodopa, and succumbed suddenly from a presumed myocardial infarction 18 months after the initial presentation. The family members did not consent to a pathological postmortem owing to religious reasons.

Discussion

Our patient's clinical course, marked by transient behavioural changes, amnesia, and progressive neurological deficits, illustrates the insidious nature of this condition. Moreover, the initial diagnostic dilemma, supported by definitive neuroimaging findings but confounded by inconclusive biopsy results, highlights the need for a multidisciplinary approach and underscores the importance of considering GC as a potential differential diagnosis in patients presenting with atypical neurological symptoms.

Gliomatosis cerebri, initially described by Nevin in 1938, is an uncommon growth pattern seen in diffuse gliomas, characterised by the rapid proliferation of neoplastic glial cells affecting at least three lobes of the bilateral cerebral hemispheres, and potentially extending to infratentorial structures, corpus callosum, and thalami [1, 2]. The WHO classification now regards it as a growth pattern since 2016, with occurrences across various glioma grades and cell types, though its molecular underpinnings remain elusive [3]. GC can be categorised as primary or secondary, with variations in the mass presence and genetic associations. It primarily manifests as a diffuse infiltration, sparing neurons and resulting in challenges in clinical presentation [2].
Figure 3: Contrast enhanced CT brain does not show any contrast enhancing areas within the cerebral parenchyma. No abnormal leptomeningeal or pachymeningeal contrast enhancement.

Figure 4. CT cerebral angiogram, normal except absent A1 segment of the right anterior cerebral artery
Figure 5: Magnetic Resonance Image sequences, axial cuts. Panel 5A: T1W images show intermediate to hypointense symmetrical cerebral white matter signal alteration, most marked in the frontal lobes. Mild effacement of the lateral ventricles is seen considering his age. The occipital lobe, cerebellum, brain stem, pituitary gland and supra sellar structures are spared. Panel 5B: T2W images also shows corresponding symmetrical hyperintensity involving the white matter of both hemispheres and thalami. Panel 5C: FLAIR images show diffuse hyperintensity symmetrically involving the corresponding white matter of both hemispheres extending from the periventricular region to the juxtacortical region and the thalami. Panel 5D: T1W Post Gadolinium images does not show any contrast enhancing lesions. Panel 5E: Diffusion Weighted images does not show any areas of diffusion restriction. Panel 5F: ADC Maps shows symmetrically increased white matter diffusivity, especially in the frontal lobes. Panel 5G: VEN BOLD does not show any abnormal blooming artefacts to suggest haemorrhage or calcification.
Gliomatosis cerebri's definitive diagnosis requires a tissue biopsy revealing diffusely infiltrating neoplastic cells while maintaining brain structure integrity. Challenges in resource-limited settings include biopsy accessibility, proper sampling, and cost. The superiority of MRI in imaging GC is evident due to superior contrast resolution and detailed anatomical depiction. Distinct features include bilateral hemispheric involvement, lack of mass effect, and enhancement. Advanced MR techniques and MRS assist in differentiating GC from other brain white matter disorders [5]. Elevated Cho/Cr ratio and myoinositol level along with depressed NAA/Cho and NAA/Cr ratios, within hyperintense areas on FLAIR and T2WI, are characteristic [6], as seen in this patient. Treatment-wise, the optimal approach is yet unknown. Surgical intervention is restricted due to its diffuse nature, while survival benefits of radiation therapy are questioned due to toxicity risks from its large field. Primary chemotherapy with procarbazine and lomustine offers some clinical benefits [7]. Challenges in our case encompassed the absence of specialised units and limited experience due to their rarity. The condition's complex nature, variable presentation, and treatment ambiguities demand further research for improved management strategies.

**Conclusion**

Gliomatosis cerebri, an aggressive growth pattern of brain tumor presents with a wide range of clinical
manifestations. Its diagnosis is challenging due to the nonspecific nature of the symptoms and radiological findings. The prognosis is generally poor, and treatment options are limited. This case report highlights the limitations of histological definitive diagnosis in a low resource setting, and the need for further research to improve diagnostic strategies and develop targeted therapies. Early recognition, prompt referral to relevant specialties and multidisciplinary management are crucial to optimise patient outcomes in this rare disease entity.

**Author contributions** – all authors AR, KD, KK were equally involved in preparing the manuscript

**Ethical clearance and consent for participation** – Consent was taken from the patient prior to death, during the initial ward stay, to include clinical information for this case report and for publication.

**References**