

Multiple gliomas

A case review



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BACKGROUND: *Multiple gliomas, although a rare finding, can present with a clinical and radiological picture similar to that of metastatic disease, abscesses, lymphoma and demyelination.*

CASE REPORT: *We report a rare case of multiple gliomas located in the left cerebral hemisphere, with a complex presentation emulating other possible differential diagnoses.*

CONCLUSION: *Multiple gliomas should be taken into consideration as part of the differential diagnosis of multiple parenchymal brain lesions. Certain imaging modalities and findings can be extremely valuable with obtaining a diagnosis, and the subsequent formulation of a therapeutic strategy.*

KEY WORDS: Glioblastoma Multiforme, Imaging, Multiple glioma, Treatment.

Case Report

In August 2010, a 62 year old man from the small island of Gozo, with a history of diabetes mellitus, presented with otalgia and a high fever. He was admitted and treated for otitis media with antibiotics and analgesia. After 2 weeks he developed an expressive dysphasia and left-sided intermittent headaches. He also had a left-sided hemiparesis, with normal tone, no clonus and brisk reflexes. Plantars were downgoing bilaterally. Sensation was grossly intact. Cranial nerves and visual fields were intact.

His WCC was $12.0 \times 10^9/L$ and a normal CRP. Blood cultures were negative. A chest X-ray was normal. Contrast-enhanced CT brain demonstrated a number of ring-enhancing lesions with necrotic centre and surrounding oedema in the left cerebral hemisphere. No midline shift was noted. The medical team and radiologist considered the clinical and radiological findings as suggestive of metastases. Tumour markers were normal. A contrast-enhanced CT of the thorax and the abdomen showed right-sided adrenal hyperplasia and prostatic hyperplasia but otherwise no other significant abnormalities.

A contrast-enhanced MR brain showed four ring-enhancing lesions in the left temporo-parietal region, the largest measuring 4.5 x 3.1cm (Fig. 1, 2). There was significant oedema but minimal displacement of the midline. Given the history of otitis media and diabetes, and the absence of any primary lesion, the diagnosis of multiple cerebral abscesses was considered.

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A biopsy of the largest lesion was performed and the histology was reported as anaplastic astrocytoma Grade III. However, in view of the imaging and the inability to biopsy the necrotic core because of significant intra-operative oedema, the overall clinical impression was that of a Grade IV GBM.

Post-op the patient developed complete expressive aphasia. He was discharged for further rehabilitation and oncological follow-up.

Discussion

The presence of multiple cerebral space occupying lesions is usually due to metastatic disease. The differential diagnosis also includes cerebral abscesses, multiple lymphomas, vascular or demyelinating lesions, including tumefactive multiple sclerosis and brain tumours of glial origin. Multiple gliomas usually involve one or more lobes, of one or both cerebral hemispheres. They were first described in 1896 by Gower¹⁹ and are uncommon. Their incidence ranges from 0.5 to 20% of all gliomas^{4,9,14,29,30}. Some authors have reported an association with neurofibromatosis type 1^{16,29,34} and multiple sclerosis^{16,28}.

Budka, Batzdorf and Malumid^{3,5} made a clear distinction between multifocal and multicentric lesions.

Multifocal lesions include those lesions which disseminate via an established route such as commissures, CSF channels or local metastases, whereas multicentric lesions are widely separated and their occurrence cannot be attributed to any of the former pathways. The distinction between multifocal and multicentric gliomas is, however, of limited practical value. They were also classified by Lafitte et al¹⁹ according to the time of initial diagnosis, with synchronous lesions being those where lesions appear early at diagnosis, or metachronous lesions, where the multiple lesions appear at a later time from the initial diagnosis.

The pathogenesis of multiple gliomas is still unexplained. A number of hypotheses have been put forward. That by Willis³⁷ suggests a two-stage approach – the first-stage involving a neoplastic transformation of a large area of brain parenchyma, known as the initiation phase and the second-stage being the actual malignant change after exposure to a triggering factor. Cohnheim and Ostertag²¹ hypothesized that the multiplicity of the glioma could be due to the malignant activation of primitive cells scattered throughout the CNS. Zulch⁴⁰ suggested that the multifocal distribution is due to metastatic spread from a CNS primary.

The number of tumours in each patient ranges from 2 to 15^{18, 31}. The location of multiple gliomas is not consistent. In a study by Kyritsis et al,¹⁸ the major-

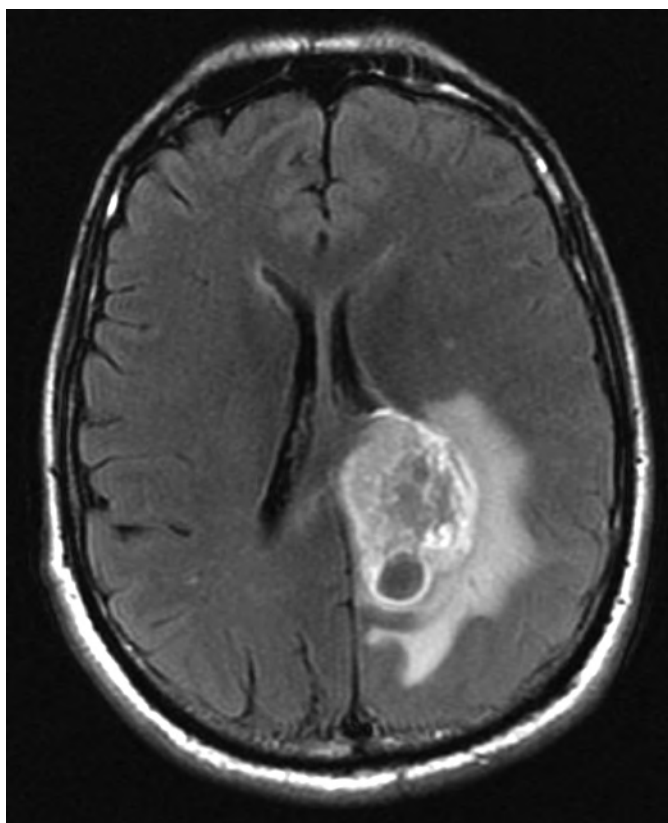


Fig. 1: FLAIR MR Brain demonstrating the largest lesion, measuring 4.5 x 3.1cm at its largest point, with peritumoural oedema.

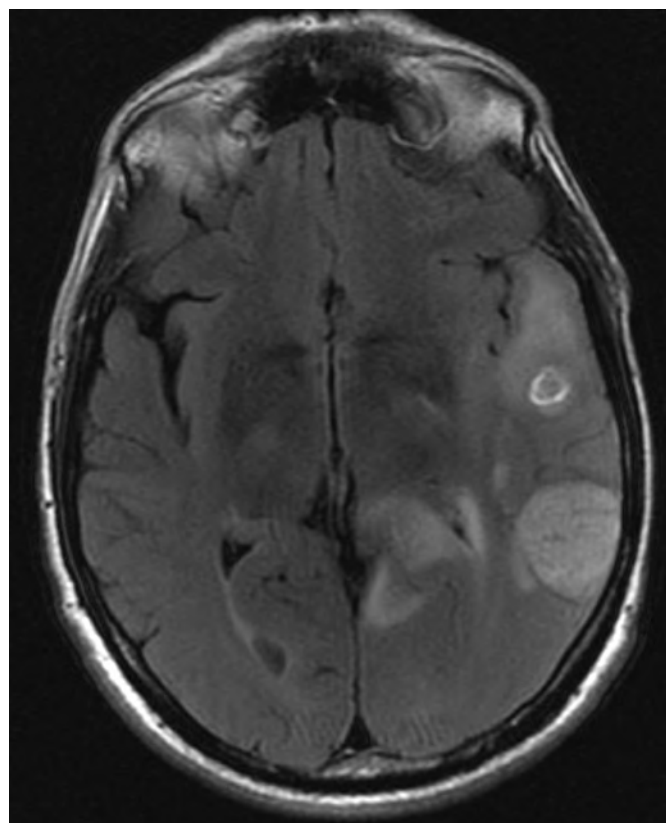


Fig. 2: FLAIR MR Brain showing other synchronous smaller intraparenchymal lesions.

Riassunto

ity were found in the parietal lobe (37%), with the frontal and temporal lobes being involved in 28% and 22% of cases respectively. Either one or both hemispheres can be involved. No hemispheric predilection has since been documented. Multiple gliomas were reported to occur throughout the CNS, with one case report of lesions involving the cervical spinal cord³⁶. As in the presented case, radiological diagnosis is difficult and the working diagnosis of multiple brain lesions is usually metastases. However, some criteria can be used to help distinguish between the two^{1,11,17,20,22,25}. Multiple gliomas are usually seen as iso- or hypo-dense lesions on CT, but are better delineated on MRI. Their size and shape is often different, with minimal surrounding oedema, strong but heterogeneous enhancement with contrast and often indistinct margins. Metastases are often located at the grey/white matter junction, are often of similar size and shape, have significant peritumoural oedema and ring-shaped enhancement. Abscesses may also present as multiple ring-enhancing lesions with a mass effect, and the diagnosis should be especially suspected in the presence of fever and/or immunosuppression. Diffusion-weighted imaging (DWI) can help distinguish tumour necrosis (hypoattenuating) from an abscess (hyperattenuating). Distinguishing between gliomatosis cerebri and multiple gliomas may be difficult as the former contains foci of true malignant glial tissue. However, gliomatosis, in contrast to multiple gliomas, uncommonly demonstrates central tumour necrosis, peritumoural oedema, centrifugal white matter extension and mass effect^{33,38}.

MR spectroscopy can assist with differentiating gliomas from other lesions, in view of differences in metabolic processes and resulting by-products. MR spectroscopy gives a quantitative analysis of metabolites in brain tissue. Normal brain will have a high N-acetylaspartate peak, with lower but equal levels of choline and creatinine. Lipid and lactate concentrations are normally low. In contrast, low-grade gliomas will exhibit a choline peak higher than the N-acetylaspartate peak, with significant levels of lactate. High-grade gliomas display significantly high choline peaks, decreased N-acetylaspartate and high lipid and lactate levels³⁵.

A definitive diagnosis of multiple gliomas and their grading can ultimately only be confirmed with biopsy. Glioblastoma is the most common histotype, but lower grade glial neoplasms have also been reported, including anaplastic astrocytoma and ependymoma^{7,9,10,16,27,34,37,40}. Prognosis of multiple gliomas remains poor, with an average survival of 7.6 months after diagnosis³¹.

Management recommendations vary, with current trends favouring surgical debulking in large lesions with marked mass effect causing intracranial hypertension. On the other hand, smaller lesions causing minimal mass effect or not involving the eloquent cortex tend to be biopsied.^{2,6,13,26,32}

I gliomi multipli, nonostante si tratti di casi rari, possono presentarsi con un quadro clinico e radiologico simile a quello di una malattia metastatica, ad ascessi, al linfoma o a demielinizzazione.

Si riferisce di un caso di gliomi multipli localizzati nell'emisfero cerebrale destro, con una presentazione complessa che emulava altre possibili diagnosi differenziali.

I gliomi multipli devono essere presi in considerazione come parte di una diagnosi differenziale di lesioni multiple del parenchima cerebrale. Certe modalità dell'imaging e certi reperti possono essere estremamente validi per raggiungere la diagnosi, e per prospettare di conseguenza la strategia terapeutica.

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