A Case of Glioblastoma Masquerading as an Affective Disorder

To the Editor: Brain tumors can produce psychiatric symptoms, particularly if malignant[1] and fast growing.[2] Among gliomas, growth rate seems to be particularly relevant for the occurrence of mental disturbance, with symptoms in up to 80% of glioblastomas and only 25%–35% of lower-grade astrocytomas.[1] We report a case of glioblastoma multiforme, a very fast-growing brain tumor, initially presenting as acute mania.

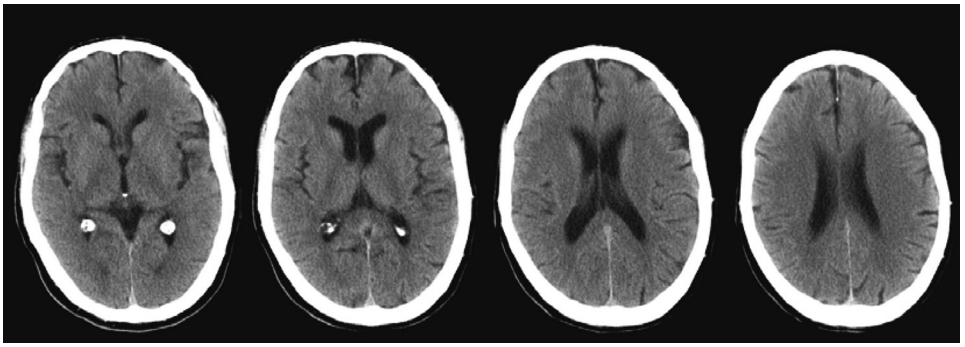
Case report. Mr A, a 76-year-old white man, was admitted to our psychiatric inpatient ward with euphoric mood, increased sexual activity, excessive money spending, and overvalued ideas of grandiose capacity starting 2 months prior. Results of physical and neurologic examination and cognitive evaluation (Mini-Mental State Examination[3,4] [MMSE] score: 30/30) were normal, as were brain computed tomography (CT) scan (Figure 1A), electrocardiogram, and chest radiograph results. Blood and urine analyses, including toxicology screening, revealed only mild leucocytosis. Mr A had a 12-year history of treatment-resistant depression (*DSM-IV-TR* criteria). During the last depressive episode, a neurologist considered the possibility of Parkinson's disease and dementia and started Mr A on selegiline (5 mg/d), donepezil (10 mg/d), amitriptyline (25 mg/d), and perphenazine (2 mg/d). Depression symptoms remitted 1 year prior to the current episode, leading to discontinuation of amitriptyline and perphenazine. In addition, Mr A had a history of hypertension, benign prostatic hypertrophy, glaucoma, gastric ulcer, and degenerative lumbar disc disease, and, at the onset of the current episode, was also taking telmisartan (40 mg/d) and tamsulosin (0.4 mg/d).

On the basis of a working diagnosis of acute mania (*DSM-IV-TR* criteria), Mr A was started on valproic acid (1,000 mg/d), risperidone (2 mg/d), and flurazepam (15 mg if needed). Selegiline and donepezil were discontinued, with no adverse consequences. There was a gradual improvement, leading to full symptomatic remission, with no significant side effects, and he was discharged after 1 month with a diagnosis of bipolar disorder (*DSM-IV-TR* criteria). At his first follow-up consultation 1 month later, Mr A showed marked sedation and significant cognitive deficits (Montreal Cognitive Assessment[5,6] score: 18/30; MMSE score: 23/30), prompting reduction of risperidone to 1 mg/d and replacement of flurazepam with lorazepam. At subsequent evaluations, Mr A remained sedated, and his cognitive function further deteriorated, leading to requests for an electroencephalogram, which was normal, and brain magnetic resonance imaging (MRI). Four months after being discharged, Mr A developed left-side hemiparesis and was referred to our emergency department, where a repeat brain CT scan (Figure 1B) revealed a large right frontal lobe tumor, confirmed by the MRI scan and later diagnosed "postoperatively" as glioblastoma.

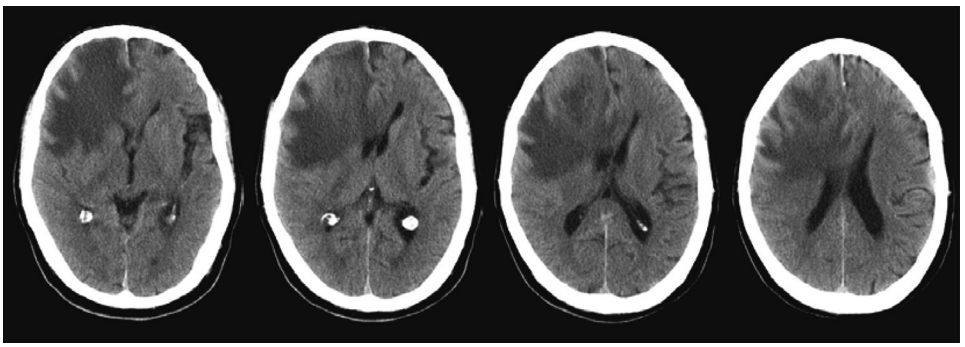
In late-onset bipolar disorder, there is a higher likelihood of underlying organic causes meriting, as exemplified here, extensive diagnostic testing.[7,8] In this patient, while an iatrogenic cause could be considered on initial presentation,[9,10] the subsequent follow-up highlights the need for careful longitudinal investigation. We note that a brain CT, concomitant with an inaugural presentation of mania, was normal, and the same examination performed 5 months

Figure 1. Mr A's Initial and Follow-Up Computed Tomography (CT) Scans

A. Initial Unenhanced Axial Brain CT Scan[a]



B. Follow-Up Unenhanced Axial Brain CT Scan (approximately 5 mo later)[b]



[a]Shows no lesion.
[b]Shows a large infiltrative lesion within the right frontal lobe, with necrotic/cystic center, measuring 63 × 44 mm and associated with significant white matter vasogenic edema, extending to the lateral ventricle, and causing midline shift.

later revealed a large tumor in the right frontal lobe. Frontal brain tumors can present symptomatically as mood disorders,[11–13] with right hemisphere tumors more frequently associated with mania-like syndromes and left hemisphere tumors with depression-like syndromes.[11,14] Similar laterality trends have been described for cerebrovascular lesions.[15] In Mr A, the use of brain MRI at presentation could possibly have allowed for an earlier diagnosis of the lesion.[7] Nevertheless, it is tempting to speculate that the inaugural manic episode was the first expression of a tumor developing in the right frontal lobe, even prior to structural evidence of the lesion, raising interesting possibilities regarding the mechanisms mediating this association.[14]

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