Case Report: Psychiatric comorbidity in the setting of encephalomalacia and gliosis

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Case Report

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Abstract

Background

We report a case of an adult female with a history of multifocal encephalomalacia and gliosis following multiple strokes confirmed by magnetic resonance imaging, who presented with neuropsychiatric symptomatology. Encephalomalacia and gliosis of the brain are pathological changes in brain tissue associated with cerebral vascular and traumatic injury, and can present with a variety of symptoms ranging from cognitive decline to psychosis. Neurological manifestations following a stroke are well-documented, but there are few reports of adults with psychiatric symptomatology in the setting of encephalomalacia and gliosis in the caudate nucleus following stroke. Herein we discuss the psychiatric symptom profile and management associated with this lesion, while emphasizing the importance of brain imaging to gain a deeper understanding of its correlation with psychiatric manifestations.

Case presentation

A 64-year-old female with a history of multiple strokes and psychiatric history of generalized anxiety disorder was admitted to an inpatient psychiatry unit due to a 3-month history of worsening anxiety, depression, and functioning. Brain imaging revealed a new-onset focus of encephalomalacia and gliosis of the body of the left caudate, consistent with a transient ischemic attack diagnosed 3–4 months prior to psychiatric hospitalization. While admitted, the patient was treated with risperidone, sertraline, trazodone, gabapentin, and lorazepam with improvement in symptoms of anxiety, mood, and functioning.

Conclusions

Brain imaging in psychiatry is typically used to differentiate organic or structural causes of psychiatric symptoms from functional disorders, but lesions in specific areas of the brain and their clinical correlates are not well-characterized. This case in particular provides support for the involvement of the caudate nucleus in the development of neuropsychiatric symptoms, and is important for understanding the psychopathology of neuropsychiatric disorders with potential to guide treatment for these patients.

Background

Encephalomalacia is the softening or loss of brain tissue as a result of cerebral infarction, ischemia, infection, or traumatic injury, and is often accompanied by surrounding gliosis, characterized by the fibrous proliferation of glial cells in response to central nervous system damage (1). The most common causes of encephalomalacia and gliosis are stroke and trauma, giving way to loss of tissue and impedance of neuronal functioning resulting in symptoms consistent with neurologic and/or seizure disorders (2). Neuropsychiatric symptoms seen in poststroke patients include progressive cognitive

decline, depression, anxiety, apathy, decreased problem solving ability, impaired memory, abstract thinking, and psychosis (3, 4).

Injury to several brain regions including the prefrontal cortex, thalamus, striatum, basal ganglia, midbrain, and brainstem have been implicated in the development of psychiatric symptoms in poststroke patients. The frontal-subcortical circuits mediate motor activity, behavior, working memory, learning and emotion, and structural and functional alterations to these circuits are involved in the pathogenesis of neuropsychiatric disorders such as depression, obsessive-compulsive disorder, and schizophrenia (5). Patients with injury to the caudate nucleus in particular exhibited decreased cognitive functioning, features of psychosis, and behavioral dysfunction including disinhibition, disorganization, and apathy (1, 3, 4, 6, 7). We herein report a case of an adult female who developed acute worsening neuropsychiatric symptomatology in the context of encephalomalacia and gliosis of the body of the left caudate. This case supports the idea that alterations in brain structure and function underlie the development of neuropsychiatric disorders, and highlights the impairment of the frontal-subcortical circuits as a key component in the pathogenesis of neuropsychiatric symptoms in poststroke patients.

Case Presentation

We present a case of a 64-year-old female with a psychiatric history of generalized anxiety disorder, tobacco use disorder, alcohol use disorder, and non-adherence to medical treatment, who was brought to the Emergency Department by Emergency Medical Services with a three-month history of ongoing depression and hopelessness. One month prior, the patient had been brought to a different Emergency Department by a friend due to suicidal ideation but was discharged the same day without clear psychiatric follow-up. The patient also had a past medical history of thalamic pain syndrome secondary to stroke 12 years prior and Stage IIIB adenocarcinoma of the lung in remission status post chemotherapy and radiation completed seven years prior. Scheduled home medications included sertraline, buspirone, and gabapentin. Upon initial evaluation, the patient was expressively depressed and difficult to engage in conversation. The patient's history was limited due to her refusal to engage with the team; however, she admitted that she felt particularly hopeless due to having recently put her dog up for adoption in the context of a recent decline in function and ability to care for the dog. As a result, the patient was admitted to inpatient Psychiatry for further evaluation and management.

On admission, the patient’s mental status exam was pertinent for withdrawn attitude and downcast eye contact. The patient was minimally responsive and had rapid, monotone speech. She exhibited thought blocking and her thought content consisted of preoccupations and ruminations about her hopelessness. She showed evidence of impaired insight and judgement. Brain magnetic resonance imaging (MRI) was ordered to assess for brain metastasis of primary lung adenocarcinoma and organic etiology for her presentation. However, the patient continued to refuse interviews with care teams, and refused to consent to the brain MRI. On day 4 of admission, risperidone 0.5 mg twice daily was initiated for rigidity of thought, although the patient continued to intermittently refuse treatment and refused to engage with treatment teams. With the patient’s power of attorney in agreement, treatment over objection (TOO) was

granted on day 11 of admission, which permitted the administration of medications and a brain MRI. The patient's sertraline dose was down-titrated to 50 mg daily due to the patient's previous inconsistent use and trazodone 50 mg nightly was started for patient-reported insomnia. Despite this management change, the patient remained evasive, isolative from peers and staff, and ruminative on her hopelessness.

On day 12, a brain MRI was obtained and did not show any evidence of metastases, but demonstrated evidence of new-onset encephalomalacia and gliosis in the left body of the caudate nucleus, compared to previous imaging obtained seven years prior, and consistent with small vessel disease related to persistent smoking (Fig. 1).

These findings were indicative of a stroke that likely occurred more than three months prior to admission. By day 15, the patient was taking risperidone 1 mg twice daily, trazodone 100 mg nightly, sertraline 50 mg once daily, and gabapentin 200 mg three times a day without noticeable improvement. In the following days, the patient's risperidone dose was increased to 1.5 mg and sertraline was increased to 100 mg with intent to precipitate symptomatic improvement, but was unsuccessful in doing so. On day 19, risperidone was increased to 2 mg and electroconvulsive therapy (ECT) was considered due to acute worsening of refractory symptoms; however, the patient never received ECT due to later improvement with other interventions. On day 20, the patient received a single dose of alprazolam with improvement in her symptoms of anxiety. In order to maintain this improvement in symptoms, lorazepam was added to her regimen. The patient's improvement was demonstrated by further engagement with the treatment team, improved mood, wider range of affect, and more interaction with peers in the therapeutic milieu of the inpatient unit.

Given the patient's new sustained improvement, discharge discussions were initiated with the patient's power of attorney and a close friend. At this time, they were concerned about the patient performing her activities of daily living (ADLs). They particularly noted a concerning incident where the patient had "blacked out" in the shower about four months prior. They stated that this incident was diagnosed as a transient ischemic attack (TIA). Upon further questioning, it was discovered that the patient's acute psychiatric decline occurred shortly after this incident. The patient further confirmed this incident upon questioning. The timeline of these events corresponded to the brain MRI findings previously discussed.

For the remainder of the hospital course, the patient's lorazepam dose was optimized to maintain improvement in her mood with minimal sedation. Once optimized, the patient was stable enough to discontinue trazodone and reduce her dose of gabapentin by half. By that time, the patient was also stable for discharge home with adequate social work follow-up, medical follow-up, and a social support system in place. On mental status exam at discharge, the patient was calm and cooperative without signs of psychomotor agitation, and she maintained good eye contact with coherent speech and euthymic mood.

Discussion and Conclusions

Our patient presented with new-onset behavioral disturbances characterized by severe anxiety and depression with hopelessness and helplessness bordering on existential Nihilism. Given the patient's history of lung cancer, other differential diagnoses included paraneoplastic neurologic syndromes and brain metastasis, both of which can present with symptoms that overlap neuropsychiatric disorders, including seizures, personality changes, and mood disturbance (8). Since the changes seen in paraneoplastic neurologic syndromes are potentially reversible with treatment of the primary tumor, it was important to obtain a brain MRI to further assess for organic causes of the patient's psychiatric symptoms (9). However, the patient's brain MRI did not exhibit metastatic or malignant disease, but revealed a new focus of encephalomalacia and gliosis in the body of the left caudate nucleus, with unchanged previous foci of encephalomalacia and gliosis. Given the patient's history of multiple strokes, and sudden worsening of psychiatric symptoms that started shortly after a diagnosed TIA, it is reasonable to consider that her symptoms were due to the ischemic changes of the left caudate.

Psychiatric disorders following stroke and traumatic brain injury are well-documented complications of the disruption in neuronal networks, impairment in cerebral metabolism, and axonal injuries as a result of these events (10). Recent research and case reports suggest that frontal lobe dysfunction is heavily implicated in psychiatric disorders, especially as it relates to subcortical structures including the caudate nuclei (4, 5, 7, 11). Based on proposed mechanisms of frontal-subcortical dysfunction by Tekin and Cummings, dorsolateral prefrontal disruptions may present with impaired executive cognitive functioning, orbitofrontal lesions are associated with disinhibition and irritability, and anterior cingulated prefrontal disruptions are associated with apathy (5). As a part of the striatum, the caudate nucleus plays an important role in maintaining function of these circuits, and thus modulates important aspects of human behavior. One recent case study detailed cognitive decline and behavioral changes associated with bilateral caudate lesions including executive dysfunction, disinhibited behavior, impaired verbal and visual information retrieval, and emotional disturbances, underscoring the role of the caudate nucleus in behavioral control (7). Other recent studies support the idea that the etiology of post-stroke neuropsychiatric disorders is multifactorial and includes psychological, social, and biological factors. Psychological and social factors identified in relation to the development of post-stroke depression were previous psychiatric history, poor socioeconomic support, dysphasia, living alone, and female sex (12). Biological factors included organic damage to parts of the brain resulting in interruption of neural circuits and neurochemical pathways, and lesions specifically occurring in the left frontal-striatal circuits and left basal ganglia (including the caudate nucleus) were important factors in the development of post-stroke depression (13, 14). Our patient presented with depression, apathy, and executive dysfunction, which correspond to disruptions in the dorsolateral and/or orbitofrontal circuits maintained by the caudate nucleus (3, 4, 5, 7, 13). Accordingly, we postulate that the patient's neuropsychiatric symptoms were derived from dorsolateral prefrontal and orbitofrontal dysfunction caused by encephalomalacia and gliosis of the left caudate nucleus.

Management of psychiatric disorders after stroke is similar to primary management, with antidepressants, mood stabilizers, antipsychotics, benzodiazepines, and psychotherapy as mainstays of treatment, despite organic origin of symptoms (10, 12). There is growing research that supports the use

of SSRIs in acute poststroke patients for the prevention of poststroke depression and improvement in anxiety and motor and cognitive function, despite somatic origin of psychiatric symptoms (12, 14). In particular, early treatment (within 1–6 months post-stroke) with nortriptyline(12), fluoxetine(12), or citalopram(14) improved survival, mood, cognitive function, and neurological function in patients with post-stroke depression, indicating their role in regulating chemical imbalances and promoting neural mechanisms of stroke recovery. Treatment with antiplatelet agents early after stroke have potential positive effects on cognitive and functional outcomes, and should be considered along with psychotropic medications. As our patient presented with a chronic stroke, psychotropic agents were initiated with improved symptomology in this patient.

Limitations of this study include lack of further investigation into the previously identified lesions found on MRI and their connection to the patient's psychiatric symptoms, and lack of clarity in patient-reported symptomatology, mostly due to difficulties in engaging the patient in meaningful conversation. It is possible that our interpretation of imaging findings and correlation with symptoms underestimated the involvement of other regions of the brain than the caudate nucleus. Despite these limitations, we believe this case adds meaningful insight to the growing evidence of the involvement of the caudate nucleus in the pathogenesis of post-stroke neuropsychiatric disorders.

Encephalomalacia and gliosis are pathological changes in the brain that occur after vascular or traumatic injury and can present with a variety of neuropsychiatric symptoms including cognitive decline, depression, anxiety, apathy, memory impairment, and psychosis. Recent studies have identified particular circuits and regions of the brain that, when damaged, are influential in the pathogenesis of post-stroke psychiatric symptoms (10, 11, 12, 13). Our patient's presentation with severe depression, anxiety, and decline in executive functioning after stroke supports the proposed mechanisms of frontal-subcortical dysfunction and lesions of the caudate nucleus as driving forces of post-stroke neuropsychiatric disorders. This case also highlights the importance of brain imaging in assessing patients with acute psychiatric symptoms in the setting of chronic neuropathological disease such as stroke, traumatic brain injury, or malignancy, which can ultimately help guide treatment and interventions in these patients. Most importantly, this case provides further support for the neurobiological bases of post-stroke psychiatric disorders, while also highlighting potential regions of the brain for further investigation to better understand the pathophysiology of other psychiatric disorders.

Abbreviations

MRI
magnetic resonance imaging
TOO
treatment over objection
ECT
electroconvulsive therapy
ADLs

activities of daily living
TIA
transient ischemic attack

Declarations

- **Ethics approval and consent to participate:** Our institutional review board granted consent for publication of encrypted information.
- **Consent for publication:** Written informed consent for publication of this case report was obtained from the patient's family.
- **Availability of data and materials:** All data generated or analyzed during this study are included in this published article.
- **Competing interests:** The authors declare that they have no competing interests.
- **Funding:** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.
- **Authors' contributions:** WL, PC, and EB obtained relevant patient information through patient interactions. WL wrote the initial draft of the manuscript and performed the research and literature review pertinent to the case. PC provided the information contained in the case presentation and was a major contributor in writing the manuscript. All authors read and approved the final manuscript.
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Figures

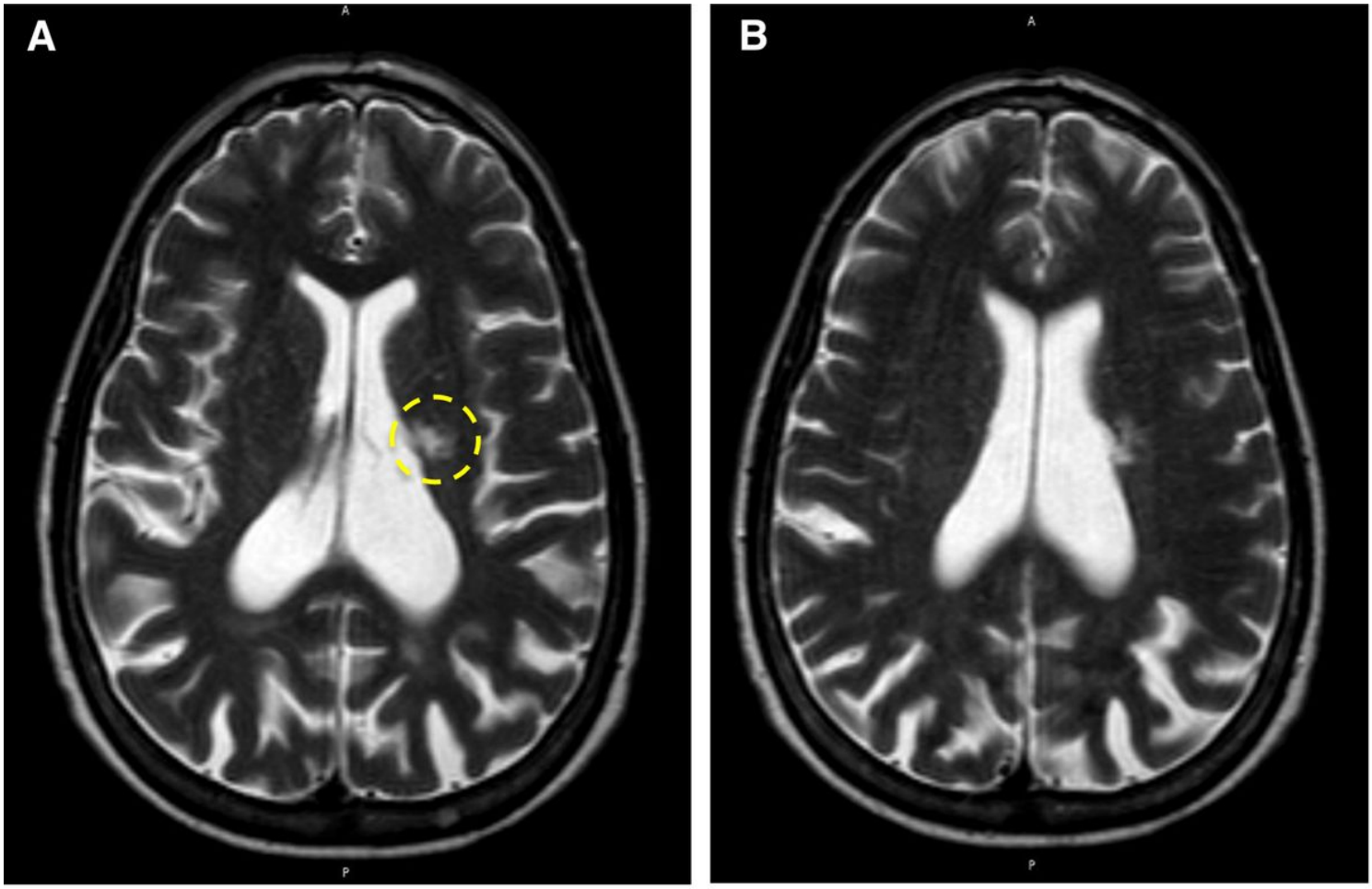

Figure 1

Brain MRI. Axial T2-weighted imaging revealed new-onset encephalomalacia with surrounding gliosis in the body of the left caudate (A, circled). On T2-weighted imaging, encephalomalacia and gliosis both appear hyperintense, with encephalomalacia often causing adjacent ventricular enlargement with “negative” mass effect (A, B).