Primary central nervous system lymphoma presenting with psychiatric symptoms: A case report

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SUMMARY

Primary central nervous system lymphoma (PCNSL) is an uncommon type of non-Hodgkin lymphoma confined to the central nervous system, presenting with diverse clinical manifestations, including neuropsychiatric symptoms. This case report describes the diagnostic process of PCNSL in a 76-year-old patient with bipolar disorder type II, who had been in long-term remission, presenting with a depressive episode accompanied by rapidly progressive cognitive impairment and psychotic symptoms following a sudden and traumatic personal loss. The case highlights the challenges in diagnosing PCNSL when psychiatric symptoms dominate the clinical presentation. Additionally, potential risk factors for PCNSL, the association between tumor characteristics and neuropsychiatric symptoms, as well as current insights into prognosis, have been reviewed to facilitate the planning of a multidisciplinary treatment approach.

Key words: Brain tumor, primary central nervous system lymphoma, psychiatric symptoms, neuroimaging

INTRODUCTION

Brain tumors are rare diseases that account for approximately 1.6 percent of all other tumors. Brain tumors usually present with non-specific (headache, weight loss, nausea, dizziness etc.) or focal neurological symptoms (motor deficits, seizures, urinary incontinence, ocular impairments etc). Focal neurological symptoms arise from the compression or destruction of normal brain tissue. Generalized non-specific symptoms occur as a result of increased intracranial pressure, edema or disruption of the blood-brain barrier. Cognitive impairments also can be attributed to alterations of brain connectivity due to tumor (1). Various studies have reported psychiatric symptoms in 50–90% of brain tumor cases. However, the occurrence of brain tumor patients presenting exclusively with psychiatric symptoms is rare, accounting for approximately 20% of cases (2). The mean duration between the onset of psychiatric symptoms and the diagnosis of a brain tumor was 2.6 years, with a range spanning from 1 week to 27 years. Notably, only 7.9% of patients received a diagnosis within 30 days of the initial presentation of psychiatric symptoms (1,3).

The aim of this case report is to illustrate the diagnostic complexity of PCNSL when presenting predominantly with psychiatric symptoms, in the absence of focal neurological deficits. By documenting this rare and diagnostically challenging presentation, the report seeks to raise clinical awareness and underscore the importance of considering underlying organic etiologies in late-onset or atypical psychiatric conditions. This case contributes to the literature by highlighting the neuropsychiatric dimensions of PCNSL and emphasizing the need for timely neuroimaging in such clinical scenarios.

Case report

A 76-year-old male retired chemical engineer who had worked in a refinery for many years, presented to the emergency department following a suicide attempt involving the ingestion of multiple lithium doses. The patient's serum lithium level at the time was measured at 1.61 mg/dL. Gastric lavage was performed and he was monitored in the internal medicine inpatient unit for three days. Psychiatric examination conducted by the psychiatrist revealed

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depressed mood, anhedonia, impaired attention, suicidal ideation, insomnia, reduced libido, low energy and loss of appetite. Upon stabilization of his general medical condition, he was transferred to the psychiatric inpatient unit due to persistent depressive symptoms.

The patient's initial psychiatric symptoms, such as depressed mood, anhedonia, suicidal ideation, insomnia, decreased energy, reduced libido, loss of appetite and psychomotor retardation first appeared in 2004. He was diagnosed with major depressive disorder. Since then, he has experienced a total of five depressive episodes. He had received sertraline and escitalopram at different dosages over time. Upon further exploration of the patient's psychiatric history, it was revealed that he had experienced hypomanic episodes since his early 30s, occurring 1–2 times per year. These episodes, which typically lasted less than a week, were characterized by increased self-confidence, enhanced sexual interest, reduced need for sleep, increased psychomotor activity and pressured speech. Consequently, his diagnosis was revised to bipolar disorder type II in 2006 and lithium was added to his treatment regimen. He had maintained prolonged remission lasting approximately 11 years with a treatment regimen of lithium (600 mg/day) and venlafaxine (37.5 mg/day). However, his recent depressive symptoms, which began one month ago following the traumatic and sudden death of his son, showed rapid progression. During his hospitalization, forgetfulness, disorientation, negativism, paranoid delusions and visual hallucinations were additionally detected. Bipolar disorder type II depressive episode with psychotic symptoms, grief, post-traumatic stress disorder, dementia and delirium were considered as possible diagnoses. In 2017, he underwent transurethral prostatectomy for benign prostatic hyperplasia. In 2023, he was diagnosed with prostate adenocarcinoma (acinar type, Gleason score: 6/10) and subsequently received radical radiotherapy. Despite the brain magnetic resonance imaging (MRI) performed seven months earlier yielding normal results, the possibility of cancer recurrence and brain metastasis was also included in the preliminary diagnoses.

Hamilton Depression Rating Scale score was 24, The Positive and Negative Syndrome Scale score was 82 and Mini Mental Test score was 21/30 at the first psychiatric examination. No abnormalities were identified in the hemogram, routine biochemistry tests, sedimentation and C-reactive protein levels, serological tests or complete urine analysis. Electrocardiography revealed sinus rhythm and the neurological examination showed no significant findings. A treatment regimen of sertraline 50 mg/day and risperidone 1 mg/day was initiated. During hospitalization, the dose of risperidone was titrated up to 3 mg/day. Brain MRI was performed due to the recent onset of psychotic and neurocognitive symptoms. Contrasted brain MRI showed an intraaxial mass lesion measuring 43x33x43 mm in the left anterior temporal region characterized by regular borders and lobulated contours. It appeared iso-hypointense on T1-weighted imaging (WI), iso-hyperintense on T2WI and marked diffusion restriction with homogeneous enhancement on post-contrast series. There was no hemorrhage signal on susceptibility weighted imaging (SWI) sequence. The findings suggested a differential diagnosis favoring lymphoma or a high-grade glial tumor as the primary consideration. Extensive vasogenic edema was observed in the left temporoparietal region around this lesion. The mass effect resulted in compression of the temporal and occipital horns of the left lateral ventricle and a 4 mm subfalcine shift from the midline to the right was observed (Figure 1 a-e). He was referred to

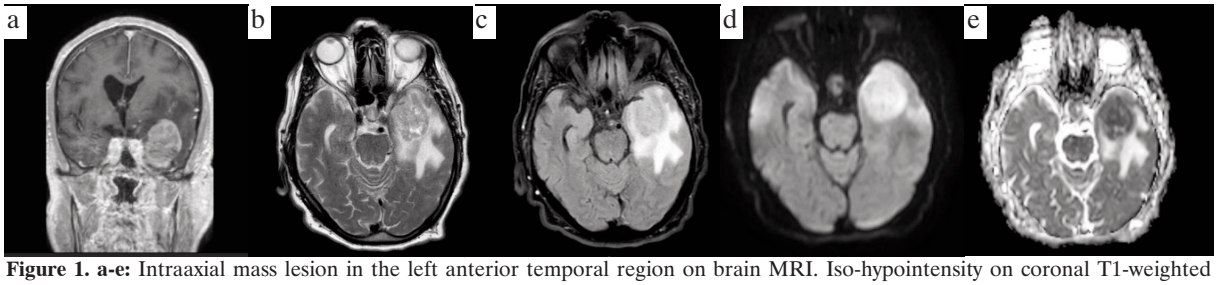

Figure 1. a-e: Intraaxial mass lesion in the left anterior temporal region on brain MRI. Iso-hypointensity on coronal T1-weighted images and subfalcian shift (a). Iso-hyperintensity on axial T2-weighted images (b). Extensive vasogenic edema in the left temporoparietal region on fluid-attenuated inversion recovery (FLAIR) images (c). Hyperintensity on transversal relaxation attenuated by controlled excitation (TRACE) images in diffusion-weighted images (d). Significant diffusion restriction in the apparent diffusion coefficient (ADC) map on diffusion-weighted images (e).

neurosurgery and oncology. Dexamethasone 16 mg/day intravenously was administered to alleviate peritumoral edema and levetiracetam 1000 mg/day orally was prescribed for seizure prophylaxis. After necessary consultations, he was referred to the neurosurgery department and underwent surgical resection. Histopathological examination confirmed diffuse large B cell lymphoma (DLBCL) and his diagnosis was established as PCNSL.

The patient's follow-up has been ongoing at the outpatient psychiatry clinic after the operation. During this period, while his psychotic symptoms subsided, depressive complaints persisted. Consequently, risperidone was gradually tapered and discontinued. The dose of sertraline was increased to 100 mg/day. Due to the persistence of depressive symptoms, lithium was reinitiated, as it had previously been the most effective treatment for the patient. His current treatment regimen consists of lithium 600 mg/day and sertraline 100 mg/day.

DISCUSSION

PCNSL is identified in about 4-5% of all primitive brain tumors (2) and DLBCL represents the most prevalent subtype, comprising more than 90% of cases (4). The incidence of PCNSL was found to be 0.4 per 100,000, rising to 4.32 per 100,000 in individuals aged 70 to 79. The median age at diagnosis of PCNSL is ≥ 64 (5) and age is an independent risk factor for PCNSL (4). Its frequency is higher in men than in women (3). The most significant risk factor for PCNSL has been identified as immune system alterations (immunosuppressant treatments, autoimmune diseases, acquired immune deficiency syndrome (AIDS)) (6).

PCNSL is typically located in the brain parenchyma (92%) as a solitary lesion (65%). It is three times more common in the supratentorial (most frequently in the frontal lobe) than in the infratentorial region (3). The most common clinical manifestation of PCNSL is focal neurological deficits (70%), followed by neuropsychiatric and behavioural changes (43%) (3,5). The most common psychiatric manifestations in brain tumors are mood symptoms. The relationship between tumor size, localization, peritumoral edema, histopathological features and psychiatric symptoms was investigated in patients with brain tumors. While psychiatric symptoms were observed more frequently in patients with tumor sizes exceeding 4 cm, this difference did not reach statistical significance. Only supratentorial localization, the presence of peritumoral edema and malignant histopathological features demonstrated a statistically significant association with the occurrence of psychiatric symptoms (7). Brain tumors located in the left frontal lobe have been frequently associated with depressive symptoms, while those in the right frontal lobe are linked to mania. Tumors in the temporal lobe are commonly associated with psychotic manifestations (8).

Our patient exhibits potential risk factors for PCNSL, including age, gender and immune system alterations potentially induced by radical radiotherapy administered one year ago. He also worked as a chemical engineer at a refinery for 30 years and exposure to harmful industrial chemicals is one of the non-genetic risk factors for brain tumors (1). Tumor diameter greater than 4 cm, malignant character, peritumoral edema and supratentorial location may have created a predisposition to psychiatric symptoms in our patient. The tumor's location in the temporal region, a key component of the limbic system, can lead to the manifestation of depressive and psychotic symptoms in our patient. Recent studies suggest that peritumoral edema disrupts the connections between limbic structures and the cortex, this disruption may play a more critical role than tumor location and size in the development of psychiatric symptoms (7). The extensive peritumoral edema determined in our patient may have accelerated the psychiatric symptoms. Generally, slow-growing tumors tend to remain neurologically silent. In our case, despite the presence of a fast-growing tumor, no focal neurological symptoms were observed.

The 5-year survival rate for PCNSL is reported to be less than 20-30%, with a median survival of 10 to 20 months (6). Early diagnosis and prompt initiation of treatment are crucial for enhancing both quality of life and survival outcomes. Diagnosis can become more challenging in cases where the anticipatory signs are solely psychiatric symptoms. Therefore, brain imaging is recommended in psychiatric conditions with sudden or late onset, poor

treatment response and atypical features (1,7). An integrated and multidisciplinary approach is essential in the management of brain tumors.

PCNSL presents significant diagnostic challenges, particularly when neuropsychiatric symptoms overshadow neurological manifestations. Clinicians should be aware that PCNSL may initially present with purely psychiatric symptoms. Prompt diagnosis and multidisciplinary management, involving neurology, psychiatry, oncology and neurosurgery, are crucial to improving both survival outcomes and quality of life for PCNSL patients. In cases of late-onset, rapidly progressive or atypical psychiatric presentations, particularly those accompanied by cognitive decline or poor treatment response, early neuroimaging should be considered to rule out underlying organic pathology. Further research is warranted to improve the understanding of neuropsychiatric manifestations in PCNSL.

Informed consent: Written informed consent was obtained from the patient and his wife to publish this manuscript.

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