



Is Psychiatric Depression a Presenting Neurologic Sign of Meningioma? A Critical Review of the Literature with Causative Etiology

Remi A. Kessler, Joshua Loewenstern, Karan Kohli, Raj K. Shrivastava

Key words

- Depression
- Meningioma
- Resection

Abbreviations and Acronyms

BDI: Beck Depression Inventory
HADS-D: Hospital and Anxiety Depression Scale-Depression
HRSED: Hamburg Rating Scale for Emotional Disturbances
SSRI: Selective serotonin reuptake inhibitors
WHO: World Health Organization

Department of Neurosurgery, Icahn School of Medicine at Mount Sinai, New York, New York, USA

To whom correspondence should be addressed:
 Remi A. Kessler, B.A.
 [E-mail: remi.kessler@icahn.mssm.edu]

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INTRODUCTION

Meningiomas are the most common type of central nervous system tumor, representing approximately 37% of all primary central nervous system tumors.¹ Although the vast majority are benign solitary intracranial neoplasms typically located in the skull base or over the convexity of the brain, their position can result in significant morbidity and mortality.^{2,3} The World Health Organization (WHO) classifies meningiomas into 3 categories by tumor differentiation and mitotic activity: benign (WHO grade I), atypical (WHO grade II), and anaplastic/malignant (WHO grade III).⁴ Population-based studies approximate that 80%–90% of meningiomas are WHO grade I.^{5,6} Many meningiomas are extremely slow growing and are asymptomatic or minimally symptomatic. As such, diagnosis is often made via an incidental finding on neuroimaging or at an autopsy; a systematic review and meta-

■ **BACKGROUND:** Benign meningiomas constitute 80%–90% of all meningiomas and represent the most common type of central nervous system tumor in adults. The vast majority of meningiomas are minimally symptomatic or asymptomatic early in their onset and thereby can often result in delayed diagnosis. Early diagnosis of meningioma is critical, as it can maximize treatment options and improve outcomes and survival. Although seizures and focal neurologic deficits are considered to be the most prevalent symptoms, depression also may be an important and significant sign. A subtle neurologic depression may be an even early presenting sign of meningioma and may precede more traditional presenting symptoms.

■ **METHODS:** We performed a comprehensive literature review that analyzes the results of prospective studies and case reports on this topic.

■ **RESULTS:** Our findings show evidence to suggest that depression may be correlated with meningioma presentation. Its prevalence is possibly increased with an anterior location of the tumor.

■ **CONCLUSIONS:** For patients who exhibit nuances of depression without a history of psychiatric illness, an index of suspicion for meningioma may be warranted.

analysis of incidental findings on brain magnetic resonance imaging in approximately 20,000 patients found meningioma to be the most common incidental tumor, identified on 0.29% of magnetic resonance imaging.^{7,8} For those that are symptomatic, the mass's location and the period of time over which the tumor grows primarily influence the symptoms at presentation.⁹ Early identification of meningioma before clinical progression is essential to maximize treatment options and efficacy, and it is often critical to avoid serious neurologic deficits and improve survival.^{10,11}

Early diagnosis of meningioma is challenging as so few tumors are initially symptomatic. Signs and symptoms that are typically viewed as consistent with meningioma presentation are seizures and focal deficits to include visual changes, loss of hearing or smell, mental status changes, and extremity weakness.^{11–13} It is well-documented that psychiatric signs are common complications of brain tumor

progression and that depression is the most common in patients with meningioma, impacting more than 20% of patients.^{14,15} It also has been found that larger tumor volumes, frontal location, and left/dominant hemisphere are predictors of possible neurocognitive deficits, with specific emphasis on depression and anxiety.¹⁶ However, in rarer cases, patients may present initially and primarily with psychiatric signs, notably depression. These presentations of depression are often treated with traditional antidepressant regimens to include selective serotonin reuptake inhibitors (SSRIs) and/or other classes of antidepressant medications, as well as psychotherapy, to which these patients are treatment-refractory.¹⁷ A subtle initial presentation of depression, preceding classic symptoms such as headache, visual disturbances, and focal deficits, could be an early sign of meningioma and may warrant a heightened sense of awareness on the part of the clinician. As

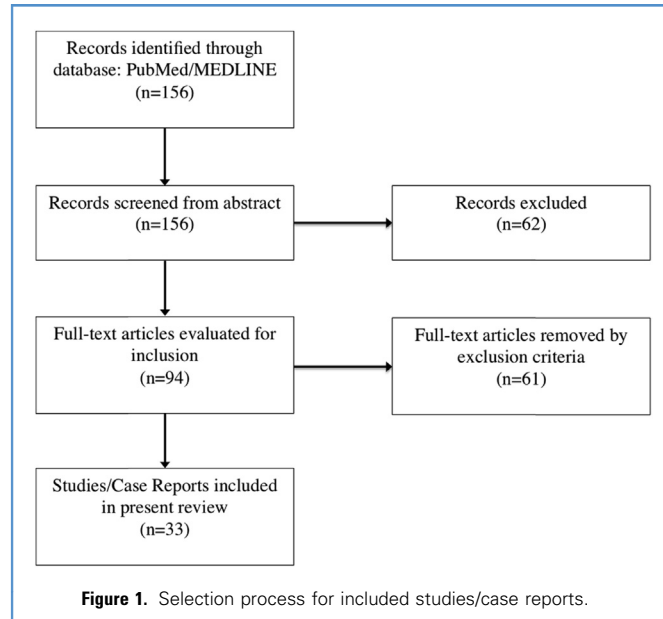
opposed to a secondary depression due to receiving a brain tumor diagnosis or anticipating a neurosurgical procedure, initial depression on presentation may be a premature sign of meningioma. In this study, we explored a potential discernable link between treatment-refractory depression in patients with no previous history of psychiatric illness and identification of meningioma.

METHODS

We conducted a comprehensive literature search through PubMed to identify prospective or retrospective studies, case reports, case series, and literature reviews that address depression and meningioma diagnosis. We selected the terms depression, psychiatric, meningioma, SSRI, and antidepressants. All applicable papers were evaluated for their relevance. Two reviewers independently examined the search results to screen for applicable papers. Exclusion criteria consisted of history of depression before diagnosis of meningioma, postresection onset of depression, cause of depression attributed to other intervention, not meningioma (other tumor type), not depression (other psychiatric illness), veterinary medicine, and non-English language. Only prospective studies that used rigorous criteria to measure depression were included for review. These included the Hospital and Anxiety Depression Scale-Depression (HADS-D), the Beck Depression Inventory (BDI), the Hamburg Rating Scale for Emotional Disturbances (HRSED), the Hamilton Depression Rating Scale, and the EuroQoL-5D. For instance, the HADS-D, a commonly used scale for in-hospital depression screening, is a well-validated index that consists of 7 items discerning symptoms of depression, including interest in enjoyable activities, frequency of cheerful mood, and level of energy or fatigue, which are scored in a Likert scale.¹⁸

RESULTS

The flow chart depicted in **Figure 1** outlines the selection of included studies and case reports. The literature search identified 156 records. There was agreement on 33 articles (14 clinical studies and 19 case reports) that met final inclusion criteria. Of the 14 clinical



studies, 12 were prospective and 2 were retrospective. The included studies and reports represent an aggregate of 1401 patients with an intracranial meningioma. Summaries of the previous clinical studies and cases reports are depicted in **Table 1**^{14-16,19-29} and **Table 2**,^{18,30-48} respectively.

Patients with Depression at Presentation

As depicted in **Table 1**, the number of patients with meningiomas who presented with depression symptoms ranged from 3.7% to 26.0% of their respective samples, with 6 of 8 studies (75%) reporting between 7% and 16% of the sample, for those studies with information available. Mean (or median) depression index scores ranged from 7.9 to 9.8 on the HADS-D, 4.5 on the BDI, and 17.5 and 17.0 for female and male patients, respectively, on the HRSED. In each study, these scores corresponded to a mild depression on the HADS-D, minimal depression on the BDI, and greater-than-normal scores on the HRSED (normal = 10). Of the 8 studies that compared patients with meningiomas with either patients with a different intracranial tumor or healthy controls, 3 (37.5%) reported that patients with meningiomas had greater depressive symptoms than their respective control group(s). Three of the 7 studies that

evaluated postoperative depression measures found that symptoms significantly improved after removal of the meningioma.

Tumor Location and Depression

When data were available, 4 studies reported that the majority of tumors were located in either frontal or anterior skull base regions, whereas 3 categorized tumor locations by other means, and Hendrix et al.¹⁶ restricted their analysis to frontal meningiomas only (see **Table 1**). Of those that conducted a specific analysis, 83% (5/6) of studies found that anteriorly located meningiomas were significantly associated with greater symptoms of depression.

Cases of Meningioma Presenting with Depression

The literature search revealed 19 distinct case reports over the past 50 years, representing 20 patients with meningioma without a significant history of depression who nevertheless presented with depression symptoms and were subsequently diagnosed with an intracranial meningioma (see **Table 2**). The youngest of these patients was a 26-year-old man and the oldest was a 77-year-old woman. Fifteen (75%) of the 20 patients had a meningioma located in either the frontal area or anterior skull base. Common

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