ASIDE Case Reports

Case Report

Neuropsychiatric Decline in a Patient with Extensive Cerebral Metastases: An Overlooked Case of Antidepressant Discontinuation Syndrome

Laiba Kayani[1,*], Naymal Sheikh[2]

1-Oncology Department, Nottingham City Hospital, Nottingham, United Kingdom
2-Department of Psychiatry, Pilgrim Hospital Boston, Boston, United Kingdom

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ABSTRACT

Acute behavioural changes in patients with newly discovered cerebral metastases are often attributed to disease progression, corticosteroid-induced psychosis, or oncological treatment-related toxicity. However, withdrawal of psychotropics such as Trazodone can cause similar neuropsychiatric symptoms, complicating the diagnostic evaluation of behavioural changes in oncology patients. This case highlights the challenge of distinguishing antidepressant discontinuation syndrome (ADS) from neurological deterioration in a patient with extensive cerebral metastases.

A 56-Year-old man with stage IIIC scalp melanoma (BRAF V600E positive) presented with an acute headache, nausea, and left-sided facial weakness. An MRI head with contrast revealed 16 new cerebral and cerebellar metastases, with the largest lesion (7 cm) in the right parieto-temporal region causing vasogenic oedema and midline shift. This patient had a history of depression with suicidal ideation, well controlled with 6 months of Trazodone 100mg OD. During admission, Trazodone was discontinued due to polypharmacy concerns and Trazodone's sedative nature masking neurological deficits. Within 48 hours, he exhibited irritability, blunted affect, and anhedonia, initially attributed to neurological decline and steroid-induced mood disturbance. Despite initiation of Encorafenib and Binimetinib, his neuropsychiatric symptoms persisted. Following liaison psychiatry consultation, Trazodone was reintroduced with slow-upward titration, resulting in clinical improvement of low mood within 5 days. ADS can mimic the clinical presentation of progressive cerebral metastases, though it is importantly reversible in aspects of depressive symptomology. Misattributing these symptoms can lead to unnecessary interventions and delayed psychiatric management, underscoring the need for careful medication reconciliation, gradual tapering, and multidisciplinary involvement.

1. Introduction

Patients with cerebral metastases frequently experience neuropsychiatric changes attributed to tumour progression, raised intracranial pressure (ICP), or corticosteroid therapy. However, pre-existing psychiatric conditions are rarely prioritised in the interplay of oncological-focused treatment and reversal of tumour symptoms, creating a risk of misattributing symptoms. Antidepressant discontinuation syndrome (ADS) is an under-recognised cluster of symptoms - including irritability, anhedonia, sleep disturbance, and affective blunting - which often emerges within 24-72 hours of antidepressant cessation but can mimic neurological deterioration [1]. We present a case of abrupt Trazadone discontinuation in a patient with extensive cerebral metastases, emphasising the importance of medication reconciliation, psychiatric involvement, and multidisciplinary care in neuro-oncology patients.

* Corresponding author: Laiba Kayani, Oncology Department, Nottingham City Hospital, Nottingham, United Kingdom Email: Laibakayani02@gmail.com

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2. Case Presentation

A 56-year-old man presented to the Specialty Receiving Unit (SRU) with focal neurological deficits of left-sided facial weakness, nausea, and a severe headache refractory to over-the-counter pain relief. He had been referred by his general practitioner in the community after a collateral history obtained from his wife revealed acute bouts of dizziness, lethargy, and increased underlying confusion within the last fortnight. His past medical history was significant for stage IIIC BRAF V600E-positive scalp melanoma, previously treated with wide local excision and eight months of adjuvant Dabrafenib (150 mg twice daily (BD)) and Trametinib (2 mg once daily (OD)). Neurological examination revealed a left-sided pronator drift, pupillary asymmetry, slurred speech, left-sided facial droop, and impaired alertness. He was initially triaged for a cerebellar infarct with a differential diagnosis of tumour recurrence or seizure-related post-ictal weakness. Formal cognitive testing (MoCA/MMSE) was attempted, but the patient declined due to a severe headache and distress and hypoactive delirium. Serial structured mental-state examinations were therefore used to monitor orientation, attention, speech, affect, and engagement. An MRI head with contrast revealed at least 16 new metastatic lesions distributed in both cerebral hemispheres and the right cerebellum. A CT head confirmed a 7 cm right parieto-temporal lesion causing vasogenic oedema, a 6mm midline shift, and effacement of the right lateral ventricle. These findings confirmed advanced intracranial metastatic disease, supporting a palliative prognosis.

These findings were unexpected for the patient, as he recently had his scalp-nodular malignant melanoma completely excised (3 months earlier), with only one positive occipital sentinel node discovered. Surveillance imaging revealed stable paratracheal and supraclavicular lymph nodes and a reduction in hilar node size, with no new metastatic deposits. The patient had already completed 8 cycles of Dabrafenib 150 mg BD with Trametinib 2 mg OD - during which he experienced several instances of fatigue, headaches, steroid-responsive nausea, and significant anxiety with palpitations. He developed depression with suicidal ideation, requiring crisis-team involvement. After an inadequate response to Fluoxetine 60mg OD, he was switched to Trazodone 100mg OD approximately 6 months prior to admission with excellent adherence and symptomatic stability (baseline PHQ-9: 4). He remained monitored under the Community Outpatient Psychiatry team to manage his thoughts of social isolation and feelings of vulnerability due to fear of melanoma recurrence. It was due to his ongoing physical and mental health side effects that Dabrafenib and Trametinib were discontinued under the MDT agreement.

On admission, Trazodone was discontinued by the clerking doctors due to pharmacologic concerns related to concurrently initiating Dexamethasone 8 mg BD (to reduce ICP). There was concern that Trazodone's sedative properties would mask new or evolving neurological deficits that existed due to his suspected 'stroke' [2]. Over the next 48 hours, he became increasingly irritable, with pronounced anhedonia, affective blunting, and reduced oral intake (PHQ-9:14). He refused engagement with neurorehabilitation services such as physiotherapy and psychological support. These symptoms were initially attributed to neurological deterioration, raised ICP secondary to widespread cranial metastasis, and steroid-induced mood changes. Despite initiation of BRAF/MEK inhibitor therapy for palliative intent (Encorafenib 75mg and Binimetinib 45mg), his neuropsychiatric symptoms and physical symptoms persisted, with only mild improvement in nausea.

Psychiatry reviewed the case and advised that abrupt Trazodone cessation likely contributed to behavioural deterioration. Trazodone was carefully reintroduced, leading within 4 days to marked clinical improvement with stabilisation of low mood, increased verbal fluency, and renewed engagement with support services (PHQ-9: 4). Yet his physical symptoms of dizziness and fatigue remained largely unchanged. Weekly ECG monitoring revealed no QTc prolongation or other abnormalities.

At discharge, antidepressant prescriptions were restricted to weekly, to facilitate close psychiatric follow-up. The patient's functional improvement from a performance status of 3 on admission to 1 following psychiatric stabilisations enabled Brain Metastases MDT (BMMDT) referral for consideration of whole-brain radiotherapy. This was not pursued earlier due to concerns regarding cognitive and psychiatric deterioration, alongside delays from the fortnightly BMMDT backlog. No recurrence of severe behavioural disturbance was reported at the early 4-week outpatient review.

3. Discussion

This case highlights the diagnostic difficulty in differentiating the neurological manifestations of cerebral metastases from neuropsychiatric symptoms related to ADS. Abrupt discontinuation of Trazadone introduced the possibility of withdrawal symptoms such as agitation, anhedonia, irritability, and nausea [3]. These symptoms overlap with raised ICP and corticosteroid-related neuropsychiatric effects. Upon admission, Trazodone was withheld for clinically justifiable reasons, given its sedative potential to mask evolving focal neurological deficits. However, this decision created diagnostic ambiguity. Differential diagnoses included paraneoplastic syndromes, non-convulsive seizures, metabolic encephalopathy, and progression of intracranial metastatic disease-causing neuropsychiatric symptoms.

Though the patient had decision-making capacity and consented to Trazodone withdrawal, rapid transfer between emergency and specialist oncology services meant that formal psychiatric risk mitigation strategies were not adopted at the time of discontinuation. This represents a limitation and key learning point from this case. Corticosteroids, while critical in reducing ICP, can contribute to agitation and emotional lability [4], complicating the primary driver of his behavioural change. ADS was not initially considered, despite a temporal relationship between abrupt Trazodone cessation and behavioural decline. Gradual tapering and proactive mental-health planning remain essential in oncology patients who are vulnerable to both physiological stress and psychological distress.

There are no specific guidelines addressing antidepressant management in patients with acute intracranial pathology, forcing clinicians to rely on general antidepressant switching guidelines [5] and multidisciplinary judgement, tailored to the patient's individual risk. This case highlights a gap in neuro-oncology and psychopharmacology, emphasising the need for guidance on safe antidepressant management in patients with acute neurological compromise.

4. Conclusion

This case highlights the complexity of behavioural alterations in neuro-oncological patients. ADS can mimic the presentation of progressive cerebral metastases and steroid-induced neuropsychiatric sequelae, though it is importantly reversible in aspects of emotional blunting, irritability, and anhedonia. Misattributing these symptoms to disease progression can lead to unnecessary interventions, delayed psychiatric management, and avoidable distress.

Conflicts of Interest

All the authors declare no conflict of interest.

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None.

Informed consent

We have obtained the patient's consent mentioned above. The decision to discontinue Trazodone was made by the admitting medical team during an acute presentation of stroke-like symptomology, with the intention of preventing oversedation and the masking of evolving neurological deficits. The patient and his family were informed of the rationale and agreed to the medication change. IRB approval: Not applicable.

Large Language Model

The authors did not use generative AI or large language models in preparing this manuscript. The authors reviewed and verified

all content, and they take full responsibility for the integrity and accuracy of the manuscript.

Authors Contribution

LJK contributed to conceptualization, formal analysis, investigation, writing, drafting the article, and revising it. NS contributed to literature research and editing of the final draft.

Data Availability

All data generated or analyzed during this case report are included within the published article. No additional datasets were generated or analyzed. Due to the nature of a single-patient case report and to protect patient privacy, no raw or identifiable data are publicly available. Any further information is available from the corresponding author upon reasonable request and subject to ethical and privacy considerations.

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