

Something smells different

Kristin L. Dawson, MD, and Paula Gibbs, MD



How would you handle this case?

Visit CurrentPsychiatry.com to input your answers and see how your colleagues responded

Ms. D, age 69, has a history of bipolar II disorder and presents with new symptoms, including weakness and increased falls, and smells noxious odors. What could be causing these symptoms?

CASE Depressed and hopeless

Ms. D, age 69, has a 20-year history of bipolar II disorder, for which she is taking citalopram, 30 mg/d. She presents to her outpatient psychotherapist with a chief complaint of depressed mood. The therapist refers her for psychiatric hospitalization and electroconvulsive therapy consultation. Upon admission, Ms. D reports that her depressed mood has worsened over the past 5 weeks after a trip to the Dominican Republic. Ms. D had a negative encounter with airport security that she attributed to her 2 artificial knees and caused her to miss her flight. She endorses poor appetite, loss of energy, anhedonia, difficulty concentrating, poor memory, and feelings of hopelessness.

Ms. D reports increasingly frequent panic attacks as well as intermittent right-sided discomfort, unusual noxious smells, and increased falls. She says the falls likely are a result of new bilateral lower extremity weakness coupled with long-standing imbalance. Ms. D says she has experienced brief occasions of foul-smelling odors while showering without evidence of an offending substance. She also reports a mild, occipitally located headache.

Four years ago, Ms. D was hospitalized for a depressive episode without psychotic features and diagnosed with generalized anxiety disorder, for which she is taking clonazepam, 1.5 mg/d. Her last hypomanic episode was several years ago, and was characterized by in-

creased energy with decreased need for sleep, flight of ideas, increased productivity, and impulsivity. Her medical history includes non-insulin dependent diabetes mellitus, chronic low back pain, hyperlipidemia, arthritis, and gastroesophageal reflux disease; her medications include pioglitazone, 30 mg/d, oxybutynin, 15 mg/d, rosuvastatin, 20 mg/d, losartan, 50 mg/d, and omeprazole, 20 mg/d. She also had bilateral knee replacements 9 years ago and an L4-S1 spinal fusion 11 years ago. She has no history of head injuries or seizures. Ms. D's father had major depressive disorder, her mother died of a cerebrovascular accident at an unknown age, and her brother died of a myocardial infarction at age 52.

Olfactory hallucinations commonly are associated with which region of the brain?

- a) frontal lobe
- b) parietal lobe
- c) temporal lobe
- d) occipital lobe

The authors' observations

A striking aspect of Ms. D's presenting complaints was her intermittent experi-

Dr. Dawson is Child and Adolescent Psychiatry Fellow, University of Kentucky, Lexington, KY. Dr. Gibbs is Assistant Clinical Professor, Department of Psychiatry, University of Utah, Salt Lake City, UT.

Table 1

When to order neuroimaging for psychiatric patients

Patient's age	Most common types of brain tumor	MRI vs CT	Indications to image
≥40 years	Metastases High-grade gliomas Meningiomas	Roughly equivalent for imaging common tumor types. Base on cost, availability, and relative patient contraindications	New-onset cognitive or emotional dysfunction. Patient is not responding to appropriate pharmacotherapy for psychiatric diagnosis
<40 years	Low-grade astrocytomas Oligodendrogliomas	MRI preferred	New-onset cognitive or emotional dysfunction with associated somatic symptoms (headache, nausea, vomiting, papilledema, seizures, or focal deficits). Patient is not responding to appropriate pharmacotherapy for the psychiatric diagnosis

Source: Reference 15

Clinical Point

In psychiatric disorders, olfactory hallucinations often include a delusional belief about the cause of the smell

ence of foul smells. Although olfactory hallucinations can occur with psychotic and affective states, they also may be harbingers of an organic etiology involving the temporal lobe.¹ Olfactory hallucinations associated with a psychiatric disorder often have an accompanying delusional belief regarding the cause of the smell.²

Olfactory hallucinations have been associated with migraines, epilepsy, and Parkinson's disease.¹⁻³ Neoplasms, cerebrovascular events, or traumatic brain injuries that result in focal mesial temporal lobe lesions can present as a partial complex seizure with olfactory or gustatory hallucinations and progress to automatisms.⁴ Characteristic odors in these hallucinations are unpleasant; patients with temporal lobe epilepsy describe the smells as "bad," "rotten," "sickening," and "like burning food."² Ms. D's report of unusual smells warranted consideration of an organic etiology for her mood change and a thorough neurologic examination.

EVALUATION Neurologic signs

At the time of admission, Ms. D has a blood pressure of 127/68 mm Hg, heart rate of 74

beats per minute, respiratory rate of 16 breaths per minute, and temperature of 36.5°C. Neurologic examination reveals a left facial droop of unknown duration. Motor strength is weak throughout with left-sided focal weakness. Ms. D's daughter notes that her mother's smile appears "funny" in her admission photograph but is unsure when the asymmetry in her facial appearance began. Ms. D had been ambulatory before admission. Nursing staff observes Ms. D leans toward her left side and exhibits possible left-sided neglect during the first 12 hours of hospitalization.

When asked about her facial droop, Ms. D replies that she had not noticed any change in her appearance lately. She does not appear to be concerned about her worsening ambulation. On hospital day 2, Ms. D seems to have difficulty using utensils to eat breakfast. Ms. D is dismissive of her worsening motor function and asks to be left alone to finish her meal.

What would you do next in evaluating Ms. D?

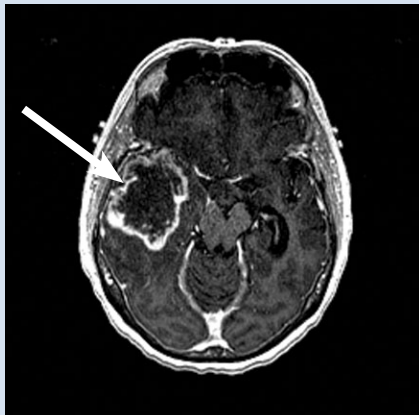
- transfer her to a medical facility for non-emergent brain imaging
- repeat the neurologic examination
- consult with the neurology service
- arrange emergent transfer to a stroke center



Discuss this article at
[www.facebook.com/
CurrentPsychiatry](http://www.facebook.com/CurrentPsychiatry)

Clinical Point

Affective, behavioral, and psychotic symptoms may be the only clinical indicators of brain lesions

Figure**Ms. D's MRI results**

MRI with contrast shows a large right temporal heterogeneous mass consistent with glioblastoma multiforme

The authors' observations

Ms. D's focal neurologic deficits and complaint of a headache on admission were concerning because they could be caused by a cerebrovascular event or space-occupying brain lesion with potential for increased intracranial pressure. Neurologic examination with evaluation for papilledema is indicated, followed by medical transport to the closest medical center for emergent brain imaging. Neither Ms. D nor her daughter could pinpoint the onset of Ms. D's left-sided facial droop, which precluded administering tissue plasminogen activator for a potential acute ischemic stroke.⁵

Ms. D's case prompted us to consider what constitutes timely brain imaging in a patient who presents with psychiatric symptoms. Several neurologic conditions may present first with neurobehavioral symptoms before findings on physical exam. Two series of autopsies conducted >70 years ago at psychiatric hospitals found incidences of brain tumors of 3.45%⁶ and 13.5%.⁷ In a 5-year retrospective study, 21% of meningioma cases presented with psychiatric symptoms alone.⁸ These his-

torical cases suggest that affective, behavioral, and psychotic symptoms may be the only clinical indicators of brain lesions that merit surgery.⁹⁻¹¹

Imaging and radiation exposure

With the advent of CT scans in the 1970s, psychiatrists gained a new method of investigating potential structural CNS pathology in patients presenting with psychiatric symptoms. The dramatic increase in CT scan use in recent years and resulting radiation exposure is responsible for 1.5% to 2% of all cancers in the United States.^{12,13} Certainly, physicians must balance the advantage of early detection of brain lesions with cost-effectiveness and exposure to radiation.¹⁴

There is no consensus regarding use of brain imaging in a patient who presents with new-onset psychiatric symptoms. Certainly, patients with localizing neurologic deficits or symptoms of increased intracranial pressure should undergo brain imaging. As for psychiatric patients without neurologic findings, Filley and Kleinschmidt-DeMasters¹⁵ provide recommendations based on their 1995 case series, and other authors have recommended imaging for patients age ≥ 40 ¹⁶ vs ≥ 50 ^{17,18} who present with atypical mental status changes.

OUTCOME Scan, then surgery

Ms. D's head CT reveals a large right-sided temporoparietal low-density lesion with 8-mm left lower midline shift (**Figure**). She undergoes a right temporal craniotomy with resection of the mass, which is confirmed by surgical pathology to be a glioblastoma multiforme World Health Organization grade 4 tumor. Postoperative MRI shows evidence of infarction in the right posterior cerebral artery distribution and residual tumor is identified on follow-up imaging. Ms. D is referred to radiation oncology, where she receives a prog-

Table 2

Frontal lobe syndromes

Syndrome	Characteristics
Dorsolateral	Deficits in executive functioning, including organization and behavior planning
Orbitofrontal	Prominent disinhibition
Medial-frontal	Apathy, abulia

Source: Reference 15

nostic median life expectancy of 14 months with radiation and temozolomide treatment.¹⁹

The authors' observations

Glioblastoma is a rare cancer that comprises 25% of all malignant nervous system tumors.²⁰ It is associated with a poor prognosis, with a <30% relative survival rate for adults at 1 year and 3% at 5 years.²⁰ Headaches, seizures, motor weakness, and progressive neurologic deficits are common symptoms of glioblastoma at diagnosis.²⁰ Ms. D was offered the standard of care treatment for a high-grade glioma, including surgical resection followed by concomitant external-beam radiotherapy and chemotherapy.²¹

Consider structural brain lesions in patients who present with neurobehavioral symptoms, although most of these patients will be diagnosed with a primary psychiatric disorder. Ms. D had a known psychiatric disorder that predated the onset of neurologic symptoms and diagnosis of a rare brain cancer. Before she developed neurologic signs, Ms. D experienced symptoms uncharacteristic of her previous depressive episodes, including olfactory hallucinations, that provided an early indicator of a CNS lesion. Consider brain imaging in patients of any age who do not respond to medications targeting the presumed psychiatric diagnosis to ensure that insidious brain tumors are not missed (*Table 1, page 55*).¹⁵

Compared with cerebrovascular lesions, neoplasms are more difficult to clinically correlate with their anatomic location.

Neurobehavioral symptoms are more frequently associated with tumors originating in the frontal lobe or temporolimbic regions of the brain. The 3 types of frontal lobe syndromes are dorsolateral, orbitofrontal, and medial-frontal (*Table 2*).¹⁵ Temporolimbic tumors may present with hallucinations, mania, panic attacks, or amnesia. A meta-analysis found a statistically significant association between anorexia and hypothalamic tumors.²² Reports of neuropsychiatric symptoms that respond to pharmacologic treatment further confound the clinical picture.¹⁶

It is uncommon for a patient with a long-standing mood disorder to develop a primary brain cancer. However, Ms. D's case serves as an important reminder to consider medical comorbidities in our aging psychiatric population. In particular, a patient who develops unusual symptoms or does not respond to previously effective treatments should be more closely examined and the differential diagnosis broadened.

References

1. Assad G, Shapiro B. Hallucinations: theoretical and clinical overview. *Am J Psychiatry*. 1986;143(9):1088-1097.
2. Carter JL. Visual, somatosensory, olfactory, and gustatory hallucinations. *Psychiatr Clin North Am*. 1992;15(2):347-358.
3. Fuller GN, Guiloff RJ. Migrainous olfactory hallucinations. *J Neurol Neurosurg Psychiatry*. 1987;50(12):1688-1690.
4. Chang BS, Lowenstein DH. Mechanisms of disease: epilepsy. *N Engl J Med*. 2003;349(13):1257-1266.
5. Lansberg MG, Bluhmki E, Thijs VN. Efficacy and safety of tissue plasminogen activator 3 to 4.5 hours after acute ischemic stroke: a metaanalysis. *Stroke*. 2009;40(7):2438-2441.
6. Hoffman JL. Intracranial neoplasms: their incidence and mental manifestations. *Psychiatr Q*. 1937;11(4):561-575.
7. Larson CP. Intracranial tumors in mental hospital patients. *Am J Psychiatry*. 1940;97(1):49-58.
8. Gupta RK, Kumar R. Benign brain tumours and psychiatric morbidity: a 5-years retrospective data analysis. *Aust N Z J Psychiatry*. 2004;38(5):316-319.

Clinical Point

Consider brain imaging in patients who do not respond to medications targeting the presumed psychiatric diagnosis

Clinical Point

Temporolimbic tumors may present with hallucinations, mania, panic attacks, or amnesia

Related Resources

- MD Anderson Cancer Center. Brain tumor videos and podcasts. www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/brain-tumor/videos-and-podcasts/index.html.
- Braun CM, Dumont M, Duval J, et al. Brain modules of hallucination: an analysis of multiple patients with brain lesions. *J Psychiatry Neurosci*. 2003;28(6):432-449.

Drug Brand Names

Citalopram • Celexa	Oxybutynin • Ditropan
Clonazepam • Klonopin	Pioglitazone • Actos
Losartan • Cozaar	Rosuvastatin • Crestor
Omeprazole • Prilosec	Temozolomide • Temodar

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

9. Chambers WR. Neurosurgical conditions masquerading as psychiatric diseases. *Am J Psychiatry*. 1955;112(5):387-389.
10. Trimble MR, Mendez MF, Cummings JL. Neuropsychiatric symptoms from the temporolimbic lobes. *J Neuropsychiatry Clin Neurosci*. 1997;9(3):429-438.
11. Uribe VM. Psychiatric symptoms and brain tumor. *Am Fam Physician*. 1986;34(2):95-98.

12. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Engl J Med*. 2007;357(2):2277-2284.
13. Berrington de González A, Mahesh M, Kim KP, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. *Arch Intern Med*. 2009;169(22):2071-2077.
14. Weinberger DR. Brain disease and psychiatric illness: when should a psychiatrist order a CAT scan? *Am J Psychiatry*. 1984;141(12):1521-1526.
15. Filley CM, Kleinschmidt-DeMasters BK. Neurobehavioral presentations of brain neoplasms. *West J Med*. 1995;163(1):19-25.
16. Moise D, Madhusoodanan S. Psychiatric symptoms associated with brain tumors: a clinical enigma. *CNS Spectr*. 2006;11(1):28-31.
17. Bunevicius A, Deltuva VP, Deltuviene D, et al. Brain lesions manifesting as psychiatric disorders: eight cases. *CNS Spectr*. 2008;13(11):950-958.
18. Hollister LE, Boutros N. Clinical use of CT and MR scans in psychiatric patients. *J Psychiatr Neurosci*. 1991;16(4):194-198.
19. Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. *N Engl J Med*. 2005;352(10):987-996.
20. Brandes AA, Tosoni A, Franceschi E, et al. Glioblastoma in adults. *Crit Rev Oncol Hematol*. 2008;67(2):139-152.
21. Chandana SR, Movva S, Arora M, et al. Primary brain tumors in adults. *Am Fam Physician*. 2008;77(10):1423-1430.
22. Madhusoodanan S, Opler MG, Moise D, et al. Brain tumor location and psychiatric symptoms: is there any association? A meta-analysis of published case studies. *Expert Rev Neurother*. 2010;10(10):1529-1536.

Bottom Line

Brain tumors and other neurologic conditions may present with affective, behavioral, and psychotic symptoms. Consider brain imaging for a psychiatric patient with new-onset neurologic symptoms or one who does not respond to previously effective treatments.