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CASE REPORT

Delirium masquerading as depression

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ABSTRACT

Objective: Despite the high prevalence of delirium in palliative care settings, this diagnosis is frequently missed, particularly in patients with hypoactive delirium. These patients are also commonly misdiagnosed with depression because of the overlap in symptoms between the two diagnoses. Failure to promptly diagnose delirium can have significant ramifications in terms of delirium reversal, subsequent patient involvement in end-of-life decision making, and the recognition and treatment of other symptoms.

Method: We report a case of a 63-year-old French-speaking woman admitted to our inpatient palliative care unit with colorectal cancer and a history of depression. This case report highlights the major challenges associated with making the diagnosis of delirium in a patient with a complex medical history, including depression.

Results: The patient presented with symptoms of depressed mood and fluctuation in psychomotor activity, but failed to respond to an increase in her fluoxetine treatment in addition to methylphenidate and treatment of her hypothyroidism. A psychiatric assessment in her own language detected features of inattention and confirmed a diagnosis of delirium that was multifactorial, secondary to a combination of posterior reversible encephalopathy syndrome (PRES), hypothyroidism, hepatic dysfunction, and medication.

Significance of Results: Subsyndromal delirium may present with mood lability, and as delirium and depression can coexist, clinicians should perform a delirium screen for all patients presenting with symptoms of depression, preferably in the patient's first language. Cognitive testing can be particularly helpful in distinguishing delirium, especially hypoactive delirium, from depression.

KEYWORDS: Delirium, Depression, PRES

CASE REPORT

A 63-year-old French-speaking woman was initially diagnosed with stage III B colorectal cancer in 2005 and treated with a right hemicolectomy and adjuvant chemotherapy. A solitary hepatic metastasis was excised in February 2008, and following a diagnosis of metastatic lung nodules in May 2008 the patient had further chemotherapy. In late 2008, she was started on low molecular weight heparin for a left femoral deep venous thrombosis. During a hospitalization in November 2009, repeat imaging revealed peritoneal and right iliopsoas muscle metastases, and right-sided hydronephrosis that required a nephrostomy. In January 2010, she was hospitalized with a delirium. During the admission, her opioid was switched from hydromorphone to fentanyl with documentation of an associated resolution of her delirium. She then developed a partial small bowel obstruction, which was managed conservatively and resolved. Prior to

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discharge in late January 2010, she had palliative radiation to her right hemipelvis for right iliopsoas and pelvic metastases. At discharge she was mobile and functionally independent in her activities of daily living. Apart from her cancer, she had a history of hypertension, non-insulin-dependent diabetes mellitus, hypothyroidism, and chronic kidney disease secondary to ischemic nephropathy. She also suffered from depression, and her last major depressive episode, which was associated with a suicide attempt, occurred in 2007.

In March 2010 she was again hospitalized, on this occasion with a 3-day history of four generalized tonic–clonic seizures, one of which was witnessed by her family physician. On admission she was initially aphasic, at times unresponsive, and hypertensive with a systolic blood pressure of 180–200 mm Hg. MRI of the brain showed bilateral subcortical and cortical regions of vasogenic edema, and she was diagnosed with posterior reversible encephalopathy syndrome (PRES). A radiological diagnosis of cerebral metastases could not be excluded, as the patient's renal disease precluded the use of a contrast-enhanced MRI.

A neurological consultation suggested that the primary causative factor of the PRES was hypertension, and an aggressive regimen of antihypertensive agents was initiated. Dexamethasone and phenytoin were also started at this time. The patient's level of consciousness returned to normal, her aphasia gradually resolved, and she scored 21/30 on the English version of the Mini-Mental State Examination, which was performed in early April 2010. She was documented as having decreased mood, psychomotor retardation, and repeated wishes to die. A psychiatric consultation recommended optimizing her antidepressant therapy with methylphenidate in addition to increasing her dose of fluoxetine from 40 to 60 mg daily. It is of note that throughout this admission the patient inadvertently had not been treated for her hypothyroidism. She was then transferred to our palliative care unit in April 2010.

On admission, the patient presented with depressed mood, and described feelings of guilt, lack of interest in activities, and disturbed sleep. She was oriented to person, place, and time. Methylphenidate was titrated over a week to 15 mg twice daily, and thyroid replacement was initiated, all associated with minimal improvement in her symptoms. Interestingly, her level of psychomotor activity fluctuated daily from a low, almost catatonic-like state, during which times she communicated little and refused personal care, to periods of improved alertness, communication, and interaction. She was pleasant with staff and able to express sadness at her condition and the finality of her life. She did not have any periods of agitation, perceptual disturbances, or aggression. Assessing the patient in French two weeks following admission, a consultant psychiatrist noted that she had a short attention span, reduced ability to sustain attention, thought-blocking, and difficulties in articulating her thoughts, which the patient described as different from in her previous depressive episodes. The psychiatrist diagnosed the patient with delirium, and postulated that this could be multifactorial, secondary to combined contributions from PRES, hypothyroidism, hepatic dysfunction, and medication, most likely hydralazine. On the basis of laboratory investigations, other causes for delirium, including renal impairment, phenytoin toxicity, anemia, infection, electrolyte abnormalities, and hypercalcemia, were ruled out. The patient's fluoxetine and dexamethasone were decreased, and hydralazine was discontinued. Amlodipine was also decreased as the patient's blood pressure normalized. Her thyroid stimulating hormone level decreased from 58.41 to 8.87 IUs.

The patient's level of alertness, psychomotor activity abnormalities, and liability of mood improved for a period of almost 2 weeks, during which she was able to enjoy some quality time with her family. Ultimately, she developed a marked progression of her hepatic dysfunction, sacral skin ulceration, and a resistant pseudomonas urinary tract infection, which were associated with a nonreversible period of agitated delirium prior to her death, 7 weeks following her admission.

DELIRIUM, DEPRESSION AND POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

Delirium is characterized by disturbances in consciousness, attention, cognition, and/or perception, which occur acutely and have a fluctuating course (American Psychiatric Association, 2000). The prevalence of delirium in older patients ranges from 9.6% to 89%, depending on diagnostic criteria, clinical setting and population studied. It occurs in up to 85% of patients with terminal illnesses (Gagnon, 2008; Leonard et al., 2009; Voyer et al., 2009).

Delirium leads to decreased functional and cognitive status and increased morbidity and mortality (Gagnon, 2008; Voyer et al., 2009). Importantly, delirium inhibits patients from being active participants in end-of-life decision making and also makes it more difficult to identify and treat other symptoms or conditions that the patient may have (Spiller & Keen, 2006). Rapid diagnosis is critical so that appropriate management of the underlying cause(s) may be instituted, as delirium can be reversed even in advanced cancer (Spiller & Keen, 2006; Gagnon, 2008).

Although not seen in our patient, several case reports have supported the use of methylphenidate in decreasing the symptoms of hypoactive delirium (Morita et al., 2000; Keen & Brown, 2004; Gagnon et al., 2005).

Whereas hyperactive delirium is more readily identified, the prevalence of delirium among patients in palliative care settings is thought to be much higher than recognized because symptoms of hypoactive delirium are common in these patients and frequently go undiagnosed (Spiller & Keen, 2006). Symptoms of hypoactive delirium include psychomotor retardation, lethargy, confusion, decreased level of consciousness, and reduced awareness of and interaction with the environment (Spiller & Keen, 2006). These patients are frequently thought to be suffering from low mood or fatigue, and unless formal screening for cognitive impairment is performed, the diagnosis of delirium is potentially missed (Spiller & Keen, 2006; Breitbart et al., 2009). In their 2006 study of acute admissions to a specialist palliative care unit, Spiller & Keen found that 29% of admissions had delirium, and 86% of these patients showed symptoms of hypoactive delirium. Other research has shown that patients with hyperactive delirium are diagnosed sooner, and that management is instituted faster than in patients with less active symptoms (Nicholas & Lindsey, 1995; Spiller & Keen, 2006). A study by Meagher et al. (1996) showed that patients with hyperactive delirium were treated more frequently with psychotropic medications and were more likely to receive environmental interventions than were patients with mixed or hypoactive delirium.

Differentiating between delirium and depression is also critical, as the management and treatment of each diagnosis is different (Nicholas & Lindsey, 1995; Breitbart et al., 2009). A study by Farrell and Ganzini (1995) found that 41% of patients referred to the psychiatric consultation liaison service for evaluation and treatment of a depressive disorder were in fact delirious. In their study of hospice inpatients, Leonard et al. (2009) found that $> 50\%$ of patients studied were diagnosed with either depression or delirium, and that 50% of patients meeting DSM-IV criteria for depression were also diagnosed with delirium or subsyndromal delirium (SSD). In 1 week follow-up, patients' symptoms of depression and delirium followed a similar course, and the authors postulated that sustained changes in mood may be more common in patients with delirium than is frequently recognized (Leonard et al., 2009). Using the Hospital Anxiety and Depression Scale, Spiller and Keen (2006) also found a significant correlation between severity of depression and severity of delirium. They therefore concluded that an assessment for delirium should be included in any assessment for depression (Spiller & Keen, 2006).

One of the complicating factors in this case was the diagnosis of PRES. PRES is diagnosed in patients who have signs of encephalopathy and a distinct pattern of cerebral vasogenic edema on neuroimaging (Hinchey et al., 1996; Bartynski, 2008a; Mueller-Mang et al., 2009). It has been diagnosed in association with a wide variety of conditions including treatment with chemotherapeutic agents, uncontrolled primary or secondary hypertension, renal disorders, electrolyte imbalances, and tumor lysis syndrome (Mirza, 2006; Bartynski, 2008a). The symptoms of PRES can vary depending upon the location and the extent of cerebral edema, with headache and seizures being most common (Hinchey et al., 1996; Mirza, 2006; Bartynski, 2008a; Mueller-Mang et al., 2009). As the time from symptom onset increases, patients may show signs of confusion, agitation, disorientation, lethargy, somnolence, and coma (Hinchey et al., 1996; Hagemann et al., 2004; Mirza, 2006). The pathophysiology of PRES remains controversial and is thought to be related either to endothelial dysfunction leading to hypoperfusion of the brain, or failed autoregulation with severe hypertension leading to breakdown of the blood–brain barrier (Bartynski, 2008a,b; Mueller-Mang et al., 2009). The treatment of PRES primarily involves blood pressure lowering and treatment of the underlying cause (Mirza, 2006). With prompt therapy, the majority of patients return to their premorbid level of functioning over days to weeks (Mirza, 2006). Some patients, however, develop cerebral ischemia or infarction, or they die (Stott et al., 2005; Mueller-Mang et al., 2009).

DISCUSSION

Our case presentation highlights several challenges associated with diagnosing delirium in a patient with a very complex medical history, including a history of depression. Interestingly, this patient did not present with disorientation or agitation, but did show signs of inattention as well as a fluctuation in psychomotor activity. This fluctuation in psychomotor activity was especially helpful in distinguishing hypoactive delirium from depression, and highlights the importance of considering the diagnosis of SSD or hypoactive delirium in patients presenting with low mood. Cognitive testing would have been valuable in making the diagnosis of delirium as well. The language barrier, when assessing the patient for symptoms of delirium and depression, was also significant and the ability of the psychiatrist to assess this patient in her own language was particularly helpful in making the appropriate diagnosis. Finally,

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recent literature has supported the relationship between symptoms of dysphoric mood and hopelessness and the onset of delirium, even when controlling for demographics, mental status, functional status, and medical comorbidities (McAvay et al., 2007). This case report highlights the importance of recognizing that the symptoms of depression in patients with advanced cancer may herald the onset of delirium.

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