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References

1. Jorge RE, Egan JE, Wolf SS: Neuropsychiatric aspects of traumatic brain injury, in Comprehensive Textbook of Psychiatry, 7th edition, edited by Sadock BJ, Sadock Virginia, 2000, pp 273–285
2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th edition. Washington, DC, American Psychiatric Association, 1994
3. Silver JM, Hales, RE, Kupfer DJ: Neuropsychiatric aspects of traumatic brain injury, in The American Psychiatric Press Textbook of Neuropsychiatry, 3th edition, edited by Stuart C. Yudofsky, M.D., Robert E. Hales, M.D., 1997, pp 521–561
4. Taylor CA, Jung HY, et al: Disorders of mood after traumatic brain injury. Semin Clin Neuropsychiatry 1998 ; 3:224–231
5. Jorge RE, Robinson RG, Starkstein SE, et al: Secondary mania following traumatic brain injury. Am J Psychiatry 1993; 150:916–921
6. van Reekum R, Bolago I, Finlayson MA, et al: Psychiatric disorders after traumatic brain injury. Brain Inj 1996; 10:319–327
7. Mitrovic D, Misic-Pavkov G, Ivanovic S, et al: A manic syndrome after cerebral trauma:case report. Med Pregl 1997; 50:391–393
8. Lim LC: Mania following left hemisphere injury. Singapore Med J 1996; 37: 448-450
9. Yassa R, Cvejic J: Valproate in the treatment of posttraumatic bipolar disorder in a psychogeriatric patient. J Geriatr Psychiatry Neurol 1994; 7:55–57
10. Zwil AS, McAllister TW, Cohen I, et al: Ultra-rapid cycling bipolar affective disorder following a closed-head injury. Brain Inj 1993; 7:147–152
11. Starkstein SE, Fedoroff P, Berthier ML, et al: Manic–depressive and pure manic states after brain lesions. Biol Psychiatry 1991; 29:149–158
12. Deb, Lyons I, Koutzoukis C, et al: Rate of psychiatric illness 1 year after traumatic brain injury. Am J Psychiatry 1999; 156:374–378
13. Blumberg HP, Stern E, Martinez D, et al: Increased anterior cingulate and caudate activity in bipolar mania. Biol Psychiatry 2000; 48:1045–1052
14. Stoll AL, Renshaw PF, Yurgelun-Todd DA, et a: Neuroimaging in Bipolar Disorder: What have we learned? Biol Psychiatry 2000; 48:505–517

Of Illusions, Hallucinations and Creutzfeldt-Jakob Disease (Heidenhain's Variant)

SIR: Sporadic Creutzfeldt–Jakob disease (CJD), a rare progressive neurodegenerative disorder whose classic features include dementia, ataxia, and myoclonus can initially present with nonspecific psychiatric symptomatology such as fatigue, anxiety or a change in personality in about one third of cases, sometimes leading to erroneous diagnoses of depression or psychosis, as has been described in single patient reports. [1] In contrast to the above psychiatric symptoms, the presence of visual perceptual abnormalities such as illusions and hallucinations observed at the onset of a patient's clinical course is usually more likely to be viewed as indicative of a medical, ophthalmologic or neurologic illness rather than of psychiatric etiology.[2] We present a case of an elderly female with an initial presentation notable for the acute manifestation of visual illusions followed by visual hallucinations, but whose complicated medical course led to a variety of psychiatric diagnoses prior to her ultimate diagnosis of CJD.

Case Report

The patient is a 75-year-old female with a past medical history significant for coronary artery bypass surgery, hypertension, arthritis, noninsulin dependent diabetes and hypercholesterolemia. Personal and family history of psychiatric illness, substance abuse, dementia or cognitive decline was denied. She was functioning well as a housewife until a few weeks prior to admission when she became more anxious, presumably over a home reorganization project. Two days prior to admission, she began to experience visual distortions which were described as changes in the furniture : the china closet was tilted, the table had shrunk and the chair legs had been cut off. As the patient was sleeping poorly and becoming more agitated, the family brought her to a local emergency room where her vital signs were stable, and her physical and neurological examinations were unremarkable. On mental status examination she was alert, with fluent coherent speech and no evidence of fluctuation in consciousness. She denied psychotic symptoms, and cognitively her exam was significant only for not knowing the exact date and missing one item out of three in recall. A complete blood count, electrolyte panel, chest x-ray, electrocardiogram and brain computed tomography (CT) were all unremarkable. Her urinalysis revealed white blood cells (10–25) and moderate leucocyte esterase, but this was not treated pending culture results. The patient was admitted to the medicine service with a diagnosis of acute change in mental status. Further evaluation the next day included an ophthalmologic consult who addressed the patient's blurred vision and diagnosed blepharitis. An electroencephalogram (EEG) revealed mild to moderate generalized slowing. Subsequently, the patient had complaints of foot pain and was found to have a right fifth metatarsal fracture of unclear etiology, which was casted. She received oxycodone with acetaminophen for pain relief and then began experi-

encing visual hallucinations that included a substance oozing from the ceiling and bugs crawling in the room. The psychotic symptoms were attributed to the pain medication, so it was discontinued and haloperidol was prescribed. Magnetic resonance imaging (MRI) of the brain done on the fourth day of admission revealed only mild atrophy and angiopathic disease. Over the next 3 days, the patient's condition worsened as the persistence of visual hallucinations, including bugs and butterflies, was now accompanied by disorientation to time and place.

Quetiapine was then substituted for haloperidol and a second psychiatric evaluation was requested. It was concluded that the patient was in delirium of unclear etiology, but it was recommended that reversible causes of dementia be excluded by checking lyme titers, B12, folate, and rapid plasma reagent, all of which were found to be within normal limits. With no clinical improvement, the urinalysis was repeated and revealed the presence of infection which was treated with levofloxacin. Additionally, the neurology service prescribed donepezil for a presumptive diagnosis of dementia with superimposed delirium. On the thirteenth day of hospitalization she was transferred to an inpatient psychiatric facility at another institution for further treatment of psychosis.

At the psychiatric facility, the patient was admitted with a diagnosis of Alzheimer's disease and was treated with donepezil and low dose quetiapine as needed, but her status did not improve. Lumbar puncture was suggested but the family refused. Six days later, the patient became mute and catatonic, presumably secondary to neuroleptics which were then discontinued, and a course of low dose lorazepam was prescribed for a period of 5 days. As this was minimally effective, electroconvulsive therapy (ECT) was then proposed, but after one treatment she ceased to eat and drink, necessitating transfer to the medical unit to address dehydration.

On the medical ward, the patient was diagnosed with a fungal urinary tract infection which was treated with fluconazole, and for nutrition, a nasogastric tube was placed. The geriatric neuropsychiatry consultant called to provide continuity of care, discontinued all psychotropic medications and reviewed the history with the family again, confirming that there was no evidence to support that the patient had been experiencing progressive cognitive decline prior to admission. Therefore, further evaluation was recommended and included a repeat head CT, which showed atrophy; an EEG to rule out nonconvulsive status, which demonstrated diffuse slowing consistent with encephalopathy; and a repeat MRI to evaluate for a structural lesion to explain her akinetic mutism, which showed no evidence of acute pathology. Two weeks later when the patient had demonstrated no clinical improvement, it was proposed that she be transferred back to the psychiatric unit to continue ECT for catatonia. Prior to the transfer, the geriatric neuropsychiatry consult requested a lumbar puncture to rule out causes of a rapidly progressive dementia. The cerebrospinal fluid (CSF) demonstrated a nonspecific increase in glucose and protein without malignant cells. The 14-3-3 protein was sent for assessment, and in the interim 12 days while awaiting these results, the hospital course was significant for an unsuccessful trial of methylphenidate for akinetic mutism, the development of myoclonus, and placement of a percutaneous endoscopic gastrostomy tube (PEG). When the CSF immunoassay result was remarkable for an elevated level of the 14-3-3 marker protein, a repeat EEG was performed, which demonstrated triphasic waves at one cycle/second consistent with CJD. Ten days later and 2 months after the patient's initial admission to the first acute care hospital, she was transferred to a long term facility.

Comment

One of the clinicopathologic subgroups of CJD known as the Heidenhain variant is characterized by the predominance of visual symptoms that persist throughout the course of the disease and can include disturbed perceptions of objects or colors, optical hallucinations, visual field defects, visual agnosia, or cortical blindness.[3] Clinically, our patient's course was highlighted throughout by the presence of visual symptoms which initially were illusions, specifically distortions in the shape (metamorphopsia), size (micropsia), and axis (tilt) of her furniture, then blurred vision, and subsequently complex hallucinations of insects which is consistent with this Heidenhain classification. Performance of diagnostic studies such as single photon emission computed tomography (SPECT) or positron emission tomography (PET), which may have supported our clinical diagnosis had occipital lobe hypoperfusion or hypometabolism been demonstrated,[4] was omitted to respect the family's wishes. This case serves as a reminder that in the absence of alterations in consciousness, cognitive decline, known impairments in vision, or culprit medications, visual perceptual distortions (illusions and hallucinations) can be due to lesions anywhere along the visual pathway from the retina to the cortex[5] and may herald an underlying medical, ophthalmologic, or, in this case,

neurologic etiology, rather than a psychiatric one.

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References

1. Moellentine CK, Rummans TA: The varied neuropsychiatric presentations of Creutzfeldt-Jakob disease. Psychosomatics 1999; 40:260–263
2. Norton JW, Corbett JJ: Visual perceptual abnormalities: Hallucinations and illusions. Semin Neurol 2000; 20:111–121
3. Mathews D, Unwin DH: Quantitative cerebral blood flow imaging in a patient with the Heidenhain variant of Creutzfeldt-Jakob disease. Clin Nucl Med 2001; 26:770–773
4. Kropp S, Schulz-Schaeffer WJ, Finkenstaedt M, et al: The Heidenhain variant of Creutzfeldt-Jakob disease. Arch Neurol 1999; 56:55–61
5. Kolmel HW: Visual illusions and hallucinations, in Balliere's Clinical Neurology: International Practice and Research, vol 2, no 2: Visual Perceptual Deficits, edited by Kennard C. London, Bailliere Tindall, 1993, pp 243–264

Peripheral Circulatory Disturbance Induced by Milnacipran

Sir: Milnacipran is a novel selective serotonin and norepinephrine reuptake inhibitor (SNRI) with no neurotransmitter receptor binding affinity.[1] Spencer and Wilde[2] reported that milnacipran is as effective as tricyclic antidepressants (TCAs) and that it is tolerated as well as selective serotonin reuptake inhibitors (SSRIs) and placebo. Milnacipran is reported to have little adverse effect on cardiovascular function and may be safe in cases of overdose.[1] To our knowledge, there has been no report of peripheral circulatory disturbance induced by milnacipran. We describe here a patient who experienced such disturbance during milnacipran treatment for major depressive disorder.

Case Report

The patient was a 37-year-old Japanese man. He had no previous history of peripheral circulatory disturbance, cardiovascular disease, or hypertension. He visited our Department of Psychiatry because of depressive symptoms—difficulties in concentration, lassitude, decreased appetite, insomnia, depressive mood, and notions of suicide. He was diagnosed with major depressive disorder and admitted upon his first visit to our department. Milnacipran 50 mg/day (bid) was started to treat the major depression. Physical examination and laboratory studies, including thyroid-stimulating hormone, free thyroxin tests and blood pressure, were normal. Brotizolam 0.25 mg/day was used to treat the insomnia, and sound sleep was achieved. Three days after the start of milnacipran, the patient felt slight coldness in his feet. After 7 days, the milnacipran was titrated up to 100 mg/day (bid). His feet appeared cyanotic, and the feeling of coldness was so severe that he was unable to sit still. No vascular abnormality of the feet was found upon physical examination by a cardiac surgeon, and the patient was diagnosed with peripheral circulatory disturbance. Even though the patient's depressive symptoms had decreased with the drug, milnacipran was stopped 10 days after it was started. He was started on fluvoxamine 50 mg/day (bid), and the fluvoxamine was titrated up to 150 mg/day (tid) within 2 weeks. The peripheral circulatory disturbance disappeared within one week after the cessation of milnacipran. The depressive symptoms ameliorated completely, and the patient was discharged 5 weeks after admission. No changes have been made to the medical regimen since that time, and peripheral circulatory disturbance has not recurred.

Comment

The milnacipran was apparently responsible for the peripheral circulatory disturbance, since the symptoms were alleviated by its withdrawal. The patient tolerated the fluvoxamine (an SSRI) well. Because fluvoxamine has a negligible effect on norepinephrine reuptake and no receptor binding affinity,[3] the pharmacological difference between the two drugs may lie mainly in the inhibiting effect of milnacipran on norepinephrine reuptake. Intra-arterial administration of norepinephrine in rats has been reported to stimulate peripheral vasoconstriction and induce vasospasm.[4] It is likely that milnacipran enhances norepinephrine neurotransmission, causing the peripheral circulatory disturbance we observed in our patient. If peripheral circulatory disturbance is observed in patients treated with milnacipran, it may be useful to change the medical regimen from milnacipran to an SSRI. Nevertheless, it should be noted that with milnacipran the risk of an adverse cardiovascular effect is low.

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References

1. Kasper S, Pletan Y, Solles A, et al: Comparative studies with milnacipran and