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Letter to the Editor

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Recurrent mania associated with repeated brain injury

To the Editor:

Mood disorders and disinhibition syndromes have been associated with lesions in specific brain regions. Early studies of poststroke depression have revealed increased rates of depression following left-sided hemispheric strokes [1,2]. Mania that occurs as a consequence of toxic, metabolic or neurologic disturbance has been termed *secondary mania* [3]. Secondary mania due to brain injury has been associated primarily with lesions in the orbitofrontal and basotemporal cortices of the right hemisphere [4]. The reported etiology of these lesions has included traumatic brain injury (TBI), cerebrovascular accidents (CVA) and brain tumors [5]. The relationship between specific lesion location and affective disturbance however remains controversial. We present a patient who developed a recurrence of secondary mania with a left frontal subdural hematoma (SDH) 18 months after an initial episode of mania following TBI.

1. Case report

1.1. Circumstances of admission

Mr. P., a 69-year-old White male, was admitted to the Internal Medicine Service from the Emergency Department after presenting with an acute personality change. According to his primary care physician and the staff at the assisted-living facility, who had known the patient for the prior year, the patient has been doing well until the day of admission. He has been living in his own apartment at the assisted-living center, visiting the dining room for meals and engaging in regular social activities. On the day of admission, the patient awoke with extremely rapid and pressured speech. He intrusively confronted the staff and peers at the assisted-living facility with tangential thoughts and delusions. No auditory, olfactory or visual hallucinations were reported. The assisted-living staff were unaware of any psychiatric history and had not observed any confusion or cognitive decline over the last year. No medication changes were recently undertaken. Mr. P.'s presentation represented a distinct change in personality. Psychiatric consultation was requested for further diagnostic evaluation.

1.2. Previous medical and psychiatric history

Eighteen months before the current presentation, Mr. P. was struck by a car and sustained LeForte I facial fractures and TBI. Computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain revealed bifrontal SDHs and punctate parenchymal hemorrhages involving the right posterior temporal and occipital lobes. Medical records indicate that after initial medical stabilization, psychiatric consultation was done for evaluation of rapid and pressured speech, cognitive dysfunction, distractibility and irritability. There was no prior personal or family history of psychiatric illness. A diagnosis of "dementia secondary to head trauma" was assigned. Psychiatric follow-up at 6 months revealed that the cognitive disturbance had resolved, but speech remained rapid, mood was euphoric and the thought process was described as tangential. A diagnosis of secondary mania was then assigned, and the patient was treated with valproate. Response to treatment was not documented because the patient failed to attend subsequent appointments and was lost to follow-up.

1.3. Physical examination and mental status

Mr. P.'s vital signs were stable, and physical examination was without evidence of trauma. He was well nourished and appeared to be his stated age of 69. Psychiatric assessment revealed that the patient was alert and oriented in all spheres. His speech was pressured and hyperverbal, to the point of being unintelligible at times. He described his mood as "good." Affect was irritable and slightly elevated. Thought process was tangential and difficult to redirect at times. There were no delusions or hallucinations present at the time of psychiatric consultation. Mr. P.'s insight and judgment were impaired. The patient was quite cognitively intact, scoring a 28/30 on the Folstein Mini-Mental Status Examination [6], having lost one point on delayed recall and another point on sentence repetition.

1.4. Laboratory and imaging investigations on admission

Electrolytes, complete blood count, liver function tests and cardiac enzymes were all within normal limits. Chest radiograph and urine did not reveal evidence of infection.

1.5. Hospital course and treatment

The psychiatric consultation service diagnosed the patient as manic, and a workup for potential causes of secondary

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mania was initiated. Laboratory studies including thyroid-stimulating hormone, rapid plasmin reagin, folate and vitamin B12 were normal. A CT of the brain revealed a left-sided frontal "acute on chronic" SDH with mild left frontal mass effect. Specifically, the SDH tracked along the left frontal lobe, with the largest area measuring 7 mm in thickness anterior to the orbitofrontal area of the prefrontal cortex. A subsequent MRI also revealed a left frontal SDH, but also noted gliosis in the left orbitofrontal and left posterior basotemporal lobes along with the right occipital lobe. The gliosis was thought to represent coup and countercoup lesions from the original TBI 18 months prior. An electroencephalogram (EEG) was performed, and the findings were normal, without slowing or epileptiform activity. The psychiatric consultation service assessed the patient's problem as mania secondary to recurrent left-sided frontal SDH, although recurring mania due to prior TBI, which included right-sided lesions, could not be excluded. Olanzapine was initiated at 2.5 mg/day and titrated to 5 mg/day for mood stabilization. Serial neuroimaging revealed no increase in SDH size at 1 week after admission, and no surgical procedure was performed. Mr. P., however, continued to exhibit manic symptoms and was transferred to a psychiatric unit once the medical evaluation was completed.

While on the inpatient psychiatric unit, Mr. P. was started on valproate (250 mg tid), and olanzapine was increased to 7.5 mg/day with good results. The patient was discharged to his assisted-living facility after 2 weeks with a therapeutic valproate level of 72 μg/ml. Psychiatric and neurosurgical follow-up at 1 and 2 month revealed that the patient was doing well and at his prior euthymic baseline. MRI at 1 month revealed stable left-sided frontal SDH. Valproate was continued and a taper of olanzapine was initiated.

2. Comment

The occurrence of disinhibition syndromes and mood disorders related to lesions affecting the frontal lobes or frontal–subcortical circuits have been well described in the literature [7]. The patient presented in this case, however, is unique in that he developed recurrent mania apparently after suffering a recurrence of brain injury. This injury was initially induced by a TBI and subsequently by a left-sided frontal SDH. Mr. P.'s secondary mania was successfully treated with a combination of atypical antipsychotic and antiepileptic medications. Pharmacologic therapy of secondary mania has included case reports of successful treatment with lithium [8], valproate [9], carbamazepine [10] and clonidine [11]. As mentioned previously, multiple case studies have linked mania to right-sided lesions in the orbitofrontal and basotemporal regions [4], along with the diencephalon [12]. Exceptions to this right-sided predominance have been noted but appear rare [13]. A study by Jorge et al. [14] of 66 consecutive patients with closed head injuries found that 9% met criteria for a manic episode with the presence of temporal basal polar lesions associated with secondary mania. A relationship between right-sided lesions and mania was not found due to the presence of bilateral injuries in a majority of the patients. The case presented here is unique in that Mr. P. developed mania twice as a consequence of recurrent brain injury. The first episode of TBI-related secondary mania was consistent with the classical bilateral or right-sided lesions previously reported in the literature. The second manic episode, which occurred 18 months after the first episode, however, appears related to an acute left-sided frontal SDH.

Other possible explanations for the second episode of mania also exist. For example, the second episode of mania may have been a recurrence of mania as a consequence of the first brain injury, which was a TBI, and resulted in multifocal brain damage. However, the suggested temporal relationship between the acute left-sided frontal SDH and the acute occurrence of a second manic episode suggest a causal relationship. An alternative explanation for the second episode of a mania is the occurrence of an ictal event secondary to the initial TBI. An EEG was performed, which did not reveal evidence of seizure activity. However, a single negative EEG does not rule out the possibility of an underlying seizure focus, which may be responsible for Mr. P.'s manic symptomatology. Another potential confounding variable is that orbitofrontal lesions, regardless of lateralization, have been linked to disinhibition syndromes that may be confused with mania [15]. Mr. P.'s symptoms and examination, however, are most accurately described as mania because the primary manifestations were pressured speech, elevated mood and tangential thoughts without significant change in comportment. In summary, this case points to the importance of screening for potential etiologies of secondary mania when the history is atypical for primary mania.

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