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Post-Stroke Mania: A Case Series in A Rural, Community Hospital

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ABSTRACT

Background and Purpose: *Post-stroke mania is thought to be rare, and has been described after lesions in the territory of the left medial cerebral artery, biparietal cortex, and the left putamen.*

Methods: *Case-study methodology was used to identify similarities and difference among six cases of post-stroke mania in a rural, community hospital over 1 year.*

Results: *All patients had pre-existing moderate levels of small vessel occlusive disease and two had confirmed lacunar infarcts in the basal ganglia, while one had a small left sided fronto-parietal infarct consistent with the dysarthria-clumsy hand syndrome. Stroke was not initially recognized among these patients due to the absence of acute Computed Tomography (CT) findings. Patients without pre-existing psychiatric diagnoses responded to low dose quetiapine. Two patients with pre-existing diagnoses of depression and anxiety, required higher doses.*

Conclusion: *Post-stroke mania may be under-appreciated due to the subtle neurological findings inherent to basal ganglia and/or lacunar infarcts in other locations. Acute CT is not reliable enough to confirm the diagnosis of stroke which may allow many of these cases to be missed.*

Keywords

Post-stroke mania, Small vessel disease, Cerebrovascular disease, Lacunar infarcts, Basal Ganglia.

Key Points

- Mania following stroke in older patients may be more common than is currently thought.
- Mania following stroke among patients without pre-existing anxiety or depressive disorders tends to respond to low-dose antipsychotic medications.
- Patients with pre-existing diagnoses of anxiety and/or depression may be more difficult to treat and may require

higher doses.
- Post-stroke mania may be under-appreciated due to the subtle neurological findings inherent to basal ganglia and/or lacunar infarcts in other locations.

Introduction

Mania rarely occurs for the first time in late life [1]. A systematic review found only 74 reported cases of adult stroke patients with mania symptoms in the last 50 years, suggesting that mania is a rare consequence of stroke [2]. When it does occur, it often presents atypically with a mixture of manic, dysphoric, and cognitive symptoms and less euphoria than is seen in younger,

more typical cases [3]. Increased cerebral vulnerability due to stroke or head trauma play a stronger role than life events in precipitating late-onset mania among the elderly [3,4]. The most relevant findings on imaging in late onset mania are silent cerebral infarctions and subcortical lesions [5]. Secondary mania has been documented in 17 to 43% of manic cases in the elderly and has been associated with a higher prevalence of cerebral organic disorders [6] especially cerebrovascular disease [7], dementia [8], space occupying lesions, infections, and head injuries. Post-stroke depression is the most common psychiatric disorder following stroke, but mania has been reported [9].

Lee, et al. reviewed 23 reported cases with imaged lesions that caused mania in patients without a prior history of bipolar disorder, finding that mania-causing lesions selectively disrupt networks that include the orbitofrontal cortex, dorsolateral prefrontal cortex, and temporal lobes [10]. When they compared these patients to patients previously diagnosed with bipolar disorder and currently manic (n = 26) or euthymic (n = 21), they found strong, significant, and specific disruption in network communication between the above regions and regions implicated in bipolar pathophysiology, namely the amygdala and the ventrolateral prefrontal cortex.

Materials and Methods

We reviewed 6 cases of mania in elderly patients followed cerebrovascular events from our geriatric medicine consultation service over the course of 1 year. We summarize the similarities and differences among these cases and with others reported in the literature using the case report methodology of Kratochwill and Levin [11].

Results
Case 1

A 79-year-old female was calling 911 repeatedly from her hospital room, multiple local police departments with requests for action on their part, and multiple family members all night long. This was new behavior. The hospital operator had turned off her extension to prevent further calling. She had been treated for depression and anxiety, but never for bipolar disorder. She had known arteriosclerotic cardiovascular disease, hypertension, and hypercholesterolemia. She met DSM-5 criteria for mania. She was highly irritable with pressured speech. She had difficulty listening and launched into a new topic before her prior topic could be addressed. She was angry that family members were avoiding her, and that her rights had been violated by the operators' turning off her telephone. She thought a conspiracy was preventing the police from doing her bidding.

On physical examination, she had subtle weakness of her right hand. She could not resist pressure to bring her outstretched fingers together. She had mild asymmetry of her mouth and nasolabial fold and was slightly dysarthric, which became more apparent the more rapidly she spoke. Balance on the right leg was unsteady compared to the left. Tandem gait was mildly unstable. She demonstrated increased nystagmus on lateral gaze. FLAIR MRI showed diffuse and extensive periventricular small vessel

occlusive disease with a recent lacunar infarct in the left basal ganglia (in our rural setting, we did not have access to DWI MRI studies). Her findings were consistent with the dysarthria-clumsy hand syndrome. Two months prior to the hospital admission, she had experienced increased difficulty with balance and speech, followed seven weeks later (one week prior to admission) by the acute onset of manic symptoms.

Believing that we had encountered a post-stroke mania, we started 25 mg of quetiapine b.i.d., progressively increasing it to 100 mg b.i.d., at which point she no longer wanted to call police departments, family members at odd hours of the night, or to make excessive demands of the nursing staff. She was discharged on a once daily dose of 200 mg. She went to an assisted living facility, at which the staff physician stopped her quetiapine (reason undocumented), and her problematic behavior resumed. She was brought to see us as an outpatient by her family, who believed the quetiapine had greatly helped her and wanted her middle of the night calls to stop again. We resumed the quetiapine at the 200 mg dose and within one week, the problem behaviors had resolved. One year later, she continued on the same dose of quetiapine without the return of these behaviors.

Case 2

An 85-year-old retired nurse was admitted to the hospital after a fall. She was talking rapidly and continually, and not sleeping. She was incoherent. She had been diagnosed with minor neurocognitive disorder (mild cognitive impairment) using the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) three years previously and had managed in her own home on her own with a daughter who lived nearby and checked on her at least every other day. Her daughter helped in managing finances and shopping. She had arteriosclerotic cardiovascular disease, hypertension, and hypercholesterolemia. A head CT from one-year previous revealed moderate small vessel occlusive disease in periventricular areas. No MRI scan was done at that time. Physical examination on admission revealed right-sided hand weakness (weakness in extension of fingers, weak pincer grip, weak grasp) and mild drooping of the nasolabial fold with some stuttering and dysarthria, also consistent with the dysarthria-clumsy hand syndrome. She was unable to hold a cup with her hand or to write or draw. The patient was mildly delirious and appeared to have some difficulty communicating. Because of her nighttime agitation and manic symptoms, we started quetiapine 25 mg P.O. at 6pm.

By the next day, her speech was less pressured, and she had slept four hours during the night. She was no longer talking continually. Two days later, all her neurological findings had disappeared and her delirium was much improved. Her speech was coherent, and she was fully oriented. Her speech was now normal rate and delivery. We continued the quetiapine and she was discharged 6 days after admission to a Skilled Nursing Facility (SNF) for acute rehabilitation. At the SNF, the quetiapine was stopped (reason undocumented) and her pressured, continuous speech returned, along with not sleeping at night. We were consulted again and recommended restarting the quetiapine, after which these problems

resolved. An MRI scan just prior to hospital discharge revealed a new lacunar infarct in the area of the head of the caudate and the putamen. This patient had no previous psychiatric history. This patient had a major CVA six months later and died.

Case 3

A 76-year-old woman was admitted to the hospital after a second fall. Two months previously, she had fallen at home in Florida. Since the first fall, her behavior had been erratic. She gave a distant great-niece, whom she had never seen, $80,000 from the proceeds of the sale of her home. She bought a new Cadillac. She impetuously and impulsively moved back to Maine, where her brother and his wife lived. Just before her second fall, she was preparing to give her distant great-niece another $40,000; to give the Komen Breast Cancer Fund, $10,000; and to give our hospital's cancer center, $25,000. Her brother had learned of these pending transactions and had blocked them using his power of attorney two days before her second fall and admission.

On admission, she was agitated and angry. On arrival to her room, we met an angry woman who couldn't stop talking about her brother violating her rights and preventing her from using her money as she saw fit. She was grandiose and pressured. She was irritable. She had no idea how much money she had and was unable to do arithmetic. Her neurological exam was positive only for increased lateral nystagmus and difficulty balancing on one leg, in tandem, on heels, or on tiptoes. Her sternal nudge was positive. Neuropsychological testing with the RBANS and subtests of the Wechsler Adult Intelligence Scale (WAIS) revealed minor neurocognitive disorder. Her MRI scan revealed moderate periventricular small vessel disease. A new (in the past two months), small lacunar infarct was noted in the area of the basal ganglia using FLAIR MRI. Minimal brain atrophy was present. Her past medical history was positive for coronary artery disease, hypertension, diabetes, and hypercholesterolemia. She had no prior diagnosis of bipolar disorder, but had been treated for years for anxiety disorder, mostly with benzodiazepines. We agreed that she lacked capacity to manage her finances. The great-niece stopped visiting and would not return our telephone calls. We reported the situation to the Agency on Elder Abuse. Due to her high levels of agitation in the evening, we started quetiapine 25 mg PO bid. This was enough to eliminate her agitation and irritation. She stilled wished to give away her money and believed she had the right to do so, but was not having tantrums about her brother preventing this. She was discharged to an assisted living facility for further acute rehabilitation. The physician in acute rehabilitation stopped her quetiapine (reason undocumented) and her irritability and pressured speech returned. We were consulted again on an outpatient basis, recommended restarting the quetiapine, and eventually titrated it to a dose of 50 mg PO twice daily, which produced less sedation than 100 mg PO at bedtime. This dose kept her from being irritable, pressured, and demanding of her rights to give away her money. She continued to do well on this dose over the next 8 months.

Cases 4 through 6 are summarized in Table 1. Evidence of clinical stroke existed in each of these cases on FLAIR MRI scans. In all three cases, mania came after a definitive neurological event. These six cases emerged from 262 inpatient geriatric consultations, which suggests a more common prevalence than previously appreciated.

Similarities

All six patients had moderately severe small vessel occlusive disease in the periventricular white matter. Four had or developed lacunar infarcts in the area of the basal ganglia. Two had temporal lobe infarcts. None of the patients had a previous diagnosis of bipolar disorder. Four presented with problems with gait and balance. Subtle neurological findings existed on physical examination, which were not appreciated by the ED physician or the admitting hospitalist. The possibility of stroke contributing to these patients' psychiatric symptoms was minimized or denied by their hospitalists in relation to the absence of acute findings on the CT scan. Fall was a common sentinel event that brought these patients to the Emergency Department. While two of the patients had pre-existing minor neurocognitive disorder, none had major neurocognitive disorder.

Differences

Two of the patients had a pre-exiting psychiatric history (depression and anxiety diagnoses) and required higher doses of quetiapine to manage their mania than the others who had no pre-existing psychiatric history.

Discussion

Our findings suggest that post-stroke mania may be more common than the current literature would suggest. Over one year in a rural 192-bed hospital, we encountered six cases (almost 2% of our geriatric consultations), and no cases of new-onset geriatric mania without a preceding neurological event. The neurological antecedents appear to be under-appreciated due to contemporary reliance on CT scanning or MRI to diagnose stroke versus clinical examination. We also noticed a tendency on the part of the hospitalists to not carefully assess gait and balance. The neurological findings may be subtle and transient and represent basal ganglia and/or lacunar infarcts in other locations. Our 6 patients convincingly demonstrated mania occurring after small cerebrovascular events.

Cognitive impairment, dementia, personality change, psychosis, apathy and anxiety all occur after stroke [12]. Lesions in the cerebral hemisphere and limbic structures may produce symptoms suggestive of mania. Right-sided cerebrovascular lesions involving regions connected to the limbic cortex have been implicated in late-onset mania [13]. In addition, secondary mania in right-handed people with dominant left hemisphere involvement is increasingly being recognized [14]. Removal of inhibitory tracks from the pre-frontal cortex to the limbic brain and ventral striatum may unmask mania that was previously kept in check. More attention should be directed to the basal ganglia and to small vessel occlusive disease in explaining new onset, geriatric psychiatric syndromes, and especially the role of basal ganglia lesions in post-stroke mania. The existence and sequelae of cerebral small

Age and sex	Initial Event	Neurological Findings	Preceding psychiatric history	Time to onset of mania	Result
1. 79 year old female	Fall with confusion and gait instability 8 weeks before admission; similar episode 1 weeks / before admission; similar episode day of admission.	On admission, dysarthria-clumsy hand syndrome x 5 days, plus gait and balance disturbance, and nystagmus	Anxiety and depression	At the time of her second fall, one week before admission	Resolved with 200 mg/day quetiapine; returned on discontinuation; resolved on resumption.
2. 85 year old female	Fall	Dysarthria-clumsy hand syndrome x 2 days; delirium	3 year history of minor neurocognitive disorder	Hours; 7 days after admission MRI showed new lacunar infarct in the area of the head of the caudate and the putamen	Resolved with 25 mg daily quetiapine; returned on discontinuation; resolved on resumption.
3. 76 year old female	Fall 2 months previous and again just before admission	Increased lateral nystagmus with disturbance of gait and balance. MRI showed new small lacunar infarct in the area of the left basal ganglia	No previous psychiatric history	Onset after the first fall with excessive spending and generosity and irritability and suspiciousness	Resolved with 50 mg quetiapine bid; returned on discontinuation; resolved on resumption.
4. 8o year old female.	Acute onset of delirium.	Left, medial parieto-temporal lobe infarct with previous lacunar infarcts in the basal ganglia	No previous psychiatric history	Mania appeared as the delirium resolved.	Resolution with 50 mg/day quetiapine
81 year old male	Acute onset of gait and balance disturbance and hypersexuality with pressured speech loss of memory, and irritability	Left, medial temporal lobe infarct with severe periventricular small vessel disease	Anxiety and Depression	Mania diagnosed from irritability, hypersexuality, and pressured speech.	Improvement but not resolution with 225 mg quetiapine/day and 50 mg sertrailine/day.
90 year old female	Fall	Disturbance of gait and balance and sensory loss in only right arm and leg x 5 days. MRI old basal ganglia lacunar infarcts	No previous psychiatric history	Acute onset of sleeplessness with irritability and strident demands for unnecessary services and items; pressured and loquacious speech, not always understandable; suspiciousness	Substantial improvement with 0.5 mg risperidine per day.

Table 1: Summary of the time course of events of the six patients with post-stroke mania.

vessel disease is only now becoming appreciated [10], especially because the neurological findings are often transient and it may require diffusion tensor imaging to find the lesions to fiber tracts, a technology that most hospitals do not have.

The likelihood of developing a stroke is greater among patients with bipolar disorder than controls, and the all-cause mortality rate is higher among patients with bipolar disorder than controls [15]. Compared with schizophrenia patients, those with bipolar disorder were 19% more likely to have diabetes, 44% more likely to have coronary artery disease, and 18% more likely to have dyslipidemia, after adjustment for other factors [16].

Pathological generosity, as existed in one of our patients, has been described following a left lenticulocapsular stroke with hypoperfusion of several anatomically intact cortical areas [17]. A 49-year-old man developed excessive and persistent generosity as he recovered from a left lenticulocapsular hematoma. His symptoms resembled an impulse control disorder. (99m) Tc-HMPAO SPECT demonstrated hypoperfusion, mostly in the ipsilateral striatum, dorsolateral, and orbitofrontal cortex. This case study adds pathological generosity to the range of behavioral changes that may result from discrete unilateral lesions of the lenticular nucleus and nearby pathways.

In another case report of post-stroke mania, SPECT scan performed during the manic state demonstrated hypoperfusion in the right temporal and frontal regions due to right putaminal hemorrhage [18], the site of lesion for one of our patients. It also showed hyperperfusion in the inferior lateral prefrontal lobe, the temporal lobe, and the medial and lateral parts of the parietal lobe in the left hemisphere. A second SPECT scan performed during the euthymic state demonstrated moderate improvement in the hypoperfusion in the right fronto-temporal regions. The focal hyperperfusion in the anterior insular cortex, inferior lateral prefrontal lobes, and superior-middle temporal gyrus in the left hemisphere had vanished.

Recent research is leading to the understanding that mania results from disrupted connectivity in brain circuits involving the orbitofrontal cortex, the dorsolateral prefrontal cortex, the temporal lobes in communication with the amygdala and the ventrolateral prefrontal cortex, thereby explaining the existence of multiple location of lesions all leading to mania [19].

Treatment of mania with even small doses of antipsychotic medication resolved the symptoms. The differentiation between neurological and psychiatric causation may not affect treatment, but it matters to families and to the care they receive. At least in our region, patients with psychiatric diagnoses are less likely

to be accepted by assisted living facilities and skilled nursing facilities and are stigmatized more than patients with neurological diagnoses. Families also appear to be more comfortable with neurological explanations than that of late-onset bipolar disorder. The other lessons from this case series is the importance of a careful neurological examination after a fall, especially an assessment of gait and balance, and the avoidance of over-reliance on imaging to rule out small strokes in the presence of significant, albeit transient neurological findings.

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