



# Secondary Mania From Cerebral Embolization With Nonfocal Neurologic Findings

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THE CARDINAL FEATURE of an affective disorder is a disturbance of mood with core target symptoms that are not due to any other physical or psychiatric disorder.<sup>1</sup> The target symptoms of a manic episode consist of a predominantly elevated, expansive, or irritable mood with hyperactivity, excessive talkativeness, and inflated self-esteem.<sup>1</sup> As emphasized by Krauthammer and Klerman,<sup>2</sup> it is critical to differentiate primary (or "functional") mania from secondary (or "organic") mania. This differentiation is especially important in general hospitals where preexisting medical problems in older patients are evaluated. Reliance on "hard" neurologic signs to diagnose an underlying organic cause for the affective syndrome is problematic because affective syndromes can be associated with drug-induced, metabolic, or infectious conditions. However, in the case of mania due to focal brain lesions, lateralizing neurologic findings usually provide an early clue to its organic etiology.<sup>3,5</sup>

We believe the following case report is the first to describe bihemispheric infarcts causing secondary mania (organic affective disorder) with non-localizing neurologic findings and a normal electroencephalogram.

## CASE REPORT

A 64-year-old black man came to the emergency room of the New Orleans VA Medical Center with a three-week history of change in personality. His wife reported that about three weeks earlier he had had extreme stress from a major argument with his daughter over a financial issue, after which she had stated that she never wanted to see him again. The patient was saddened by this rejection, became withdrawn and quiet, sat in his chair all day, and had crying episodes. About

a week before admission, he became not only more talkative and animated, but also hyperreligious and grandiose, believing that he was the "Messiah." When his wife could no longer tolerate his behavior at home, she brought him to the VA Medical Center. On initial evaluation, the patient appeared highly agitated, with continuous pacing interrupted only by brief episodes of restless sitting. He demonstrated a labile affect manifested by alternately friendly, smiling behavior and agitated, hostile behavior. His speech was fluent and nondysarthric, but also pressured and rambling, with flight of ideas. He repeatedly indicated that he was the Messiah and that he would "save a place in heaven for others."

Past medical history was significant for chronic obstructive pulmonary disease, clinical mitral valve insufficiency, multifocal atrial arrhythmias, congestive heart failure, left cerebrovascular accident two years earlier (with CT documentation of a "small left frontal lobe infarct" and normal cerebral arteriogram), hypertension, a history of "heavy alcohol abuse" without recent ingestion, and a 75 pack/year history of cigarette smoking. He had no previous history of psychiatric illness.

Physical examination showed BP of 152/100 mm Hg, pulse 96/min, respiratory rate 20/min, and temperature 98.6 F (37 C). The most pertinent positive finding was a 2/6 systolic murmur best heard at the apex and radiating to the axilla. Results of neurologic examination were normal except for a slightly wide-based freestyle gait, blunting to pinprick distal to the knees, and 3+ reflexes throughout.

The patient was initially admitted to the Medicine service for evaluation of a possible toxic/metabolic encephalopathy, since he was taking procainamide (500 mg q6h), digoxin (0.25 mg/day), furosemide (40 mg/day), isosorbide dinitrate (40 mg tid), and triamterene (50 mg/day). Laboratory testing revealed a negative urine toxic screen, procainamide level of 2.9 µg/ml (normal therapeutic level 4 to 10), *N*-acetyl metabolite 1.6 µg/ml (normal 10 to 30), and digoxin 1.4 ng/ml (normal 0.7 to 1.7). Thyroid function studies, SMA-18, and CBC with differential all yielded normal results. No ethanol was detected. The CSF showed an elevated protein level of 64 mg/dl and a glucose value of 71 mg/dl; there were no cells, and bacterial and fungal screens were negative, as were results of the CSF VDRL and serum ANA tests.

Immediately after admission, the patient was treated with haloperidol, receiving a total of 7 mg IM over two hours, which caused him to fall asleep. Oral haloperidol therapy (2 mg/day) was then instituted, and the patient was transferred to the psychiatric unit. By the fourth day of hospitalization, he was no longer psychotic, and conversed fluently in a calm

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FIGURE 1. CT scan shows right occipital lobe infarct (arrow).



FIGURE 2. CT scan shows infarcts in borderzone between right and left hemispheres (arrows).

and cooperative manner. On day 7, when the haloperidol therapy was stopped, he was oriented to person, place, and time, and there was no return of manic or psychotic behavior. A Holter monitor recorded occasional PACs and PVCs; an echocardiogram revealed only calcific aortic stenosis, and results of carotid Doppler testing were normal. Lastly, an EEG was normal but a CT scan of the brain (Figs 1 and 2) revealed a right occipital infarct, a left posterior parietal lobe borderzone infarct, a left frontal borderzone infarct, a right frontal borderzone infarct, a left subcortical infarct, and a left cerebellar infarct (not shown in Figures), and an enlarged calcific pineal gland. When discharged, the patient was taking digoxin (0.25 mg/day), procainamide (500 mg q6h), isosorbide dinitrate (40 mg tid), and furosemide (40 mg/day). In the absence of intracardiac thrombi on echocardiogram, his suspected cardiac embolization was treated with aspirin and dipyridamole.

On follow-up evaluation one month after discharge, the patient showed delusional ideation, but again responded to haloperidol (1 mg bid). During evaluation two months after discharge, the patient's wife reported that he had lost interest in things and was sleeping excessively. When he stopped taking haloperidol a week before evaluation, he had recurrence of grandiose and paranoid delusions, inability to sleep, and periods of elated mood and irritability.

On examination (by E.A.B.), he was well groomed, alert, and cooperative. His speech was clear, and he insisted that he was "the big man from the North" and that he could "see things before they happened." He was fully oriented, but his mood was labile. His score on the Mini Mental State Examination (MMSE) was 22/30, which indicates mild cognitive dysfunction. Primarily, he demonstrated calculating difficulties and problems in copying diagrams. His score on the Brief Psychiatric Rating Scale (BPRS) was 43/114, with significantly abnormal ratings for depression, conceptual

disorganization, suspiciousness, grandiosity, hallucinations, and thought content.

Twelve months later, the patient was again evaluated by one of us (T.G.) in the VA Behavioral Medicine Clinic. He had had no further manic or psychotic episodes. His Hamilton Depression Scale score was 4, BPRS 14, and MMSE 17/30 with impairment on memory, orientation, calculation, command performance, and constructional testing. Neurologic examination was unremarkable except for impaired upgaze, impaired left-sided rapid alternating hand movement, distal blunting to pinprick, right-sided reflex asymmetry (3+ compared to 2+ on the left side), increased jaw jerk, bilateral grasp reflexes, and a positive snout reflex. An EEG was abnormal, with left hemisphere alpha wave suppression and frontotemporal slowing. Radionuclide ventriculography of the heart revealed a normal ejection fraction of 60%.

## DISCUSSION

This patient initially had a stress-related depressive episode, followed by a manic syndrome. Although the role of stress in precipitating mood changes in the elderly is well known,<sup>6</sup> our patient had no history of a psychiatric disorder before this episode at age 64. Mania is rare after age 60, and when it does occur, it usually is in a patient with a history of depressive episodes before age 50.<sup>7</sup> In our case, the negative psychiatric history in addition to cardiovascular disease and multiple drug therapy made an organic cause more likely.

Management with haloperidol controlled the patient's acute symptoms so that he could be ade-

quately assessed. After one week, there was no recurrence of psychosis when the haloperidol was discontinued, but one month after discharge, haloperidol was required for a recurrent manic episode. Two months later, the BPRS interview (score = 43/114) confirmed an active psychosis, which could have influenced the MMSE score (22/30) since 5 points were lost to attention/concentration problems. Twelve months later, with a much improved BPRS (14/114), his MMSE score had fallen to 17/30, with cognitive impairment more typical of dementia, involving memory, orientation, and command performance. Moreover, he demonstrated numerous cortical release signs, including increased jaw jerk, snout reflex, and bilateral grasp reflexes. He had impaired upgaze but no other cranial nerve abnormalities, and examination showed asymmetry, with right-sided hyperreflexia and impaired left-sided rapid alternating hand movement. The CT scan findings (Figs 1 and 2) combined with the cognitive dysfunction and diffuse cortical abnormalities on neurologic examination were consistent with multiple infarcts. In retrospect, the initial neurologic examination failed to detect a focal abnormality because he had diffuse bihemispheric disease, reflecting involvement of both anterior and posterior circulation (Figs 1 and 2). At this point, multiple-infarct dementia was diagnosed.

In a comprehensive review, Cummings and Mendez<sup>4</sup> concluded that secondary mania resulted from basal forebrain disease involving either the right or left hemisphere. These authors also proposed that degenerative, traumatic, and infectious processes involving the basal ganglia, thalamus, brain stem, and limbic portions of the frontal and temporal lobes may produce secondary mania.

Hence, a dysfunction of subcortical emotional and neurovegetative centers is important in the pathogenesis of organic manic syndromes. Our case suggests that widespread cortical lesions also may produce secondary mania, perhaps due to the release of cortical inhibition on subcortical emotional centers.

#### SUMMARY

We have reported a unique example of an organic affective syndrome in a patient who had focal brain lesions, but whose initial neurologic examination was nonfocal. In retrospect, the only clue to an organic disorder was hyperreflexia in this patient with a history of alcohol abuse and clinical signs of a distal sensory neuropathy. This case emphasizes the importance of pursuing a neurologic work-up (including CT scan) in older patients with sudden mood changes, even in the absence of focal neurologic findings.

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