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# MULTIFOCAL LEUCOENCEPHALOPATHY PRESENTING AS ANTIDEPRESSANT INDUCED MANIA

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*A male patient presented with tricyclic induced hypomania after treatment for chronic depression. On follow up the patient deteriorated towards dementia with multifocal leucoencephalopathy. The possible role of brain lesions in the causation of affective syndromes and the neurobiological hypothesis of bipolar syndromes are discussed. The authors propose that chronic depression should be thoroughly investigated for a probable Axis III diagnosis.*

## INTRODUCTION

Leucoencephalopathy is a descriptive term in which there is selective pathology in the white matter which appear as white patches (Lumsden, 1973). The effects of the various causes of leucoencephalopathy range from immediate death to gross cerebral softening and gliosis which may present later as any neuropsychiatric syndromes. There has been very little research or reports on the psychiatric presentations or manifestations of leucoencephalopathy. Krishnan et al (1988) reported a higher prevalence of leucoencephalopathy in patients with late-onset depression and 25% of younger depressives. They suggested that this encephalopathy may be etiologically related to the occurrence of depression in the elderly; in most cases the etiology is vascular.

Irrespective of the etiology of leucoencephalopathy, many of the patients usually present with depression and anxiety symptoms. They may receive antidepressants for their early symptoms of depression. Antidepressants are well known to induce mania/hypomania (Wehr & Goodwin, 1987) and antidepressant response is considered to be a marker for a family of disorders with this common pathophysiology (Hudson & Harisson, 1990). Hence, antidepressant induced mania/hypomania in a patient who later deteriorated to an organic brain syndrome raises many questions about the possible implication of the various theories of the pathophysiology of affective disorders. In this case, the authors report a patient who presented with antidepressant induced hypomania who was diagnosed to have multifocal leucoencephalopathy after two years.

## CASE REPORT

Mr. A, a 40 year old male presented with a fifteen day history of talking and socializing excessively, making elaborate business plans and excessive cheerfulness. He was spending more money than usual and expressed increased self esteem. Prior to these problems, he did not do his work properly and was sitting alone most of the time. He did not show any initiative and had a reduced appetite and excessive sleep. He expressed weakness and lethargy and was not interested in any pleasurable activities. Occasionally, he expressed ideas of worthlessness and hopelessness and the predominant mood state was sadness.

For all these complaints, which lasted for about two years, he was treated with oral imipramine 50 mg and thioridazine 20 mg. by a private practitioner and developed the presenting complaints. There was no past or family history of mental illness. He was a salesman by occupation, married with 4 children, was premorbidly well adjusted and no abuse of any psychoactive substance was reported.

Mental status examination revealed a young male, well built with normal psychomotor activity and no cognitive impairment. The patient was euphoric with inflated self esteem. A provisional diagnosis of Bipolar Disorder, currently hypomania (probably antidepressant induced) was made and he was advised to continue tablet lithium carbonate 900 mg which he was receiving at the time of consultation. After that the patient did not come for follow up and remained symptomatic. He consulted a number of psychiatrists in the meantime and was treated with varying dosages of antipsychotics and lithium carbonate.

The hyperactive and cheerful mood state came down and he started roaming aimlessly, talking irrelevantly and misidentifying people. Within 2 to 3 months, he was not able to remember things and events; he was again brought to the this hospital in 1992 with all these problems and a 4 day history of aggressive and assaultive behaviour.

Patient was started on 2.5 mg of haloperidol tablet and his EEG and CT scan was done. EEG revealed total absence of alpha activity in the background with slow waves of delta range and focal

slowing over the right temporal lobe. CT scan revealed three small sized low attenuating areas, two of which were symmetrically located in each of the frontal lobes anteriorly and the third in the deep left parietal lobe around the posterior horn of the third ventricle. A radiological diagnosis of multifocal leucoencephalopathy with probable vascular etiology was made.

The patient remained in the hospital for 10 more days and did not show any improvement except in his sleep. He was then refereed to a neurologist. He did not show any further improvement and he gradually needed total supervision in all areas of functioning.

## DISCUSSION

A wide variety of neurological diseases have been implicated in the causation of both depression and mania (Krapthammer & Klerman, 1978; Scott, 1990). Depression can be an early manifestation of a dementing process associated with feelings of fatigue and lack of initiative, and it is not surprising that many cases of dementia receive antidepressants as initial treatment (Strubb & Black, 1988). To the best of our knowledge, we are not aware of any reports of leucoencephalopathy presenting with a full affective spectrum. Our patient presented with tricyclic induced mania and within two years deteriorated to florid dementia. Clinico-pathological evidence suggests that brain disease can produce depressive symptoms or syndromes especially with lesions of the frontal lobe, particularly of the left hemisphere (Strubb & Black, 1988).

An interesting aspect of our case is the development of antidepressant induced mania (AIM). Antidepressants are known to cause mania or worsen the course of affective disorders (Wehr & Goodwin, 1987). The suggested mechanism for AIM is the increase in the neurotransmitter level of norepinephrine and / or dopamine (Bunney et al, 1972). Our patient had a two year long depression which switched to hypomania with antidepressant treatment and later deteriorated to dementia with bilateral anterior frontal lesions on CT scan.

Robbinson (1984) proposed that lesions of the anterior cortex disrupt the noradrenergic innervation of the cerebral cortex and that depression may be the behavioral manifestation of the depletion in the cortical bioamine pathway, with more anterior lesions producing more depletion of bioamines. Though it may be hazardous to speculate on the basis of a single case report, it may be conceptualized that the original white matter lesion in the frontal lobe may have led to norepinephrine depletion and that the short term antidepressant treatment caused a functional increase of catecholamines which behaviorally manifested as mania (Bunney et al, 1972).

Krishnan et al's (1988) finding that the major depression may be etiologically related to leucoencephalopathy also supports our case report. We conclude that major depression of longer duration should be thoroughly investigated as many cases may turn out to have an organic basis (Scott, 1988). The apparent bipolarity revealed by antidepressant therapy should not be an alibi to prevent the clinician from searching the etiology.

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