Use 'E-MANIC' for secondary mania workup

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ania can be classified as "primary"-often associated with bipolar disorder-or "secondary"—which can have many underlying causes. Secondary mania is more common than primary mania in children and patients age ≥40.1

Older adults in particular are at risk for developing mania associated with increased medical comorbidities and neurologic changes. In a study of 50 patients age ≥65 with mania, 14 (28%) were hospitalized for a first manic episode, and 10 of these 14 patients (71%) had comorbid neurologic disorders.2

Suspect secondary mania in patients:

- who do not have a personal or family history of bipolar disorder
- with an atypical clinical presentation
- presenting with conditions with unexplained neurologic findings.3

Although acute treatment of primary and secondary mania may be similar, appropriate long-term treatment of secondary mania requires identifying and addressing its many causes. The E-MANIC mnemonic1-4 could help you identify causes of secondary mania (Table).

Table

E-MANIC: Is it secondary mania?

Endocrine Medications Abuse of alcohol or illicit drugs **N**eurologic Infections Cardiovascular causes

Endocrine. Thyroid dysfunction can disrupt mood, and mood disorders can impair thyroid function. The direct physiologic effects of thyroid dysfunction can cause mania. Hyperthyroidism can cause secondary mania and trigger restlessness, hyperactivity, insomnia, and irritability. Patients with mixed states of bipolar disorder have an increased risk of hypothyroidism and other medical comorbidities that can slow recovery.5 Some studies suggest thyroid diseases can cause rapid-cycling bipolar disorder,6 although most rapid-cycling patients have normal thyroid function tests. Nevertheless, low thyroid hormone blood levels are more common among individuals with rapid cycling than among bipolar patients in general.

Increased glucocorticoid activity associated with Cushing's disease can cause secondary mania. Contributors can include pituitary adenomas, adrenal adenomas or carcinomas, and ectopic production of corticotropin-releasing hormone or corticotropin. Cushing's disease symptoms include:

- worsening obesity
- new-onset hypertension
- skin changes such as easy bruising, striae, poor wound healing, facial plethora, hirsutism, and acne
- muscle weakness and wasting
- peripheral edema
- neuropsychiatric changes such as depression or mania.

Medications. Corticosteroids, dopaminergic agents-especially L-dopa and bromocriptine—and antidepressants can

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Vol. 7, No. 2 87

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Pearls

continued from page 87

cause secondary mania. Other culprits include bronchodilators, phenytoin, sympathomimetics, amphetamines (including methylphenidate), disulfiram, captopril, hydralazine, opiates, baclofen, bromide, procarbazine, yohimbine, cimetidine, and isoniazid. Over-the-counter agents-especially phenylpropanolamine and herbal preparations—also have been implicated in secondary mania.

Abuse of alcohol and illicit drugs—such as cocaine, amphetamines, phencyclidine (PCP), lysergic acid diethylamide (LSD), inhalants, opiates, cannabis, caffeine, anabolic steroids, and methylenedioxymethamphetamine (MDMA/Ecstasy)—could cause a patient's secondary mania.

Neurologic. When diagnosing secondary mania, look for traumatic brain injury, seizures, neoplasms—especially diencephalic and third ventricle tumors—normal pressure hydrocephalus, multiple sclerosis, idiopathic basal ganglia calcification, tuberous sclerosis, Kleine-Levin syndrome (episodic periods of excessive sleep and overeating followed by amnesia of these episodes), Huntington's disease, and headaches.

Infections. Assess for neurosyphilis, meningitis, influenza, enteric fever, Q fever, cholera, tetanus, posttyphoid immunization, herpes encephalitis, St. Louis encephalitis, HIV, and AIDS.

Cardiovascular causes, cerebrovascular accidents, and collagen vascular disease—as in cases of systemic lupus erythematosus could cause secondary mania.

Patients presenting with secondary mania require a thorough physical evaluation. Base decisions regarding more extensive laboratory and neuroimaging studies on clinical findings of psychiatric, medical, and neurologic examinations.^{4,7}

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