

# Multiple Myeloma Presenting as Secondary Mania

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## ABSTRACT

*Medical conditions that can cause new onset of mania may be overlooked, leading to treatment delays. The authors seek to increase awareness of multiple myeloma as a possible cause of secondary mania. The authors report on new-onset mania in a 59-year-old woman who after further medical investigation was found to have stage III multiple myeloma. Palliative treatment for multiple myeloma resulted in a decrease in the patient's manic symptoms and stabilization of the medical condition. Recognition of multiple myeloma as a cause of secondary mania will facilitate proper treatment and prevent advancement of the disease.*

## INTRODUCTION

A manic episode is defined by a distinct period during which there is an abnormally and persistently elevated, expansive, or irritable mood. This period of abnormal mood must last at least 1 week, or less if hospitalization is required.<sup>1</sup> Mania is usually thought of as part of bipolar disorder, but it can have a vast array of causes. It is then called secondary mania. The *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision,<sup>1</sup> requires exclusion of other reasons such as medications, drugs of abuse, or medical illnesses before ruling it “primary mania,” which is part of bipolar disorder. Some of the common causes of secondary mania are listed in the Table.<sup>2-4</sup>

## FOCUS POINTS

- Psychosomatic manifestations of multiple myeloma have been described in the literature.
- Multiple myeloma can be a cause of secondary mania and mania can be one of the first presenting symptoms.
- Causes of mental status changes in patients with multiple myeloma include hypercalcemia, renal failure, infections, hyperammonemia, and hyperviscosity syndrome.
- Multiple myeloma should be included in the differential diagnosis in patients presenting for the first time with recent onset of mania.
- Recognition of multiple myeloma as a cause of secondary mania will facilitate proper treatment and prevent advancement of the disease.

Multiple myeloma is a malignant plasma cell disorder that accounts for 10% of all hematologic cancers and 1% of all cancers. Multiple myeloma is incurable, but remissions may be induced with steroids, chemotherapy, thalidomide, and stem cell transplants. Median survival is 3 years, but the introduction of novel treatments in the past decade have improved this prognosis to 50–55 months.<sup>5,6</sup>

Mania occurring in the course of multiple myeloma has not been reported in the literature, and the mechanism by which this psychiatric complication happens remains unclear. Conditions that are known to cause mania that are also a common occurrence during the course of multiple myeloma, such as hypercalcemia<sup>7</sup> and steroid use, were not present when the patient described in this case report had her first two manic episodes.

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Off-label disclosure: This article includes discussion of the following unapproved medications for mood disorder due to multiple myeloma with manic features: risperidone, quetiapine fumarate, and valproic acid.

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## CASE REPORT

Mrs. F. is a 59-year-old Hispanic woman with no previous psychiatric history, who was brought to a university medical center by her family due to progressively worsening bizarre behavior. The patient had been talking to herself, became increasingly paranoid, had not slept for 36 hours prior to admission yet showed no decrease in energy, and tried several times to leave the house at night. The patient was admitted to the psychiatric ward and on examination her behavior was restless and guarded, and she appeared to be responding to internal stimuli. She smiled inappropriately and threw kisses in the air as well as tried at times to hug and express her love to staff members. Her mood was irritable and her affect was labile and elevated. Her speech was disorganized and sometimes pressured. Her thought process revealed flight of ideas and she frequently expressed paranoid ideations such as "Someone is trying to do some stuff to me." Physical examination showed no focal neurologic deficits. On admission, laboratory values revealed elevated levels of blood urea nitrogen (BUN=43 mg/dL) and creatinine (Cr=2.6 mg/dL), high-normal calcium and albumin levels (calcium=10.3 mg/dL, albumin=3.6 g/dL), and a normal ammonia level (ammonia=44 µg/dL). The unexplained high Cr and BUN levels along with a history since 2004 of unexplained aches in her chest, hips, and knees suggested a diagnosis of multiple myeloma. After she was stabilized, the patient was transferred to the general medical floor to investigate the reason for her azotemia. Bone marrow biopsy confirmed the diagnosis of multiple myeloma. Her  $\beta_2$ -microglobulin level was 8.95 mg/L, which reflects stage III multiple myeloma according to the new International Staging System.<sup>8</sup>

On admission the patient was started on risperidone 0.5 mg every 12 hours, which was later increased to 1 mg while she was in the psychiatric unit, along with quetiapine fumarate 25 mg at bedtime. This regimen seemed to partially control some of her symptoms. On day 7 on the medical floors, the patient became more labile and showed increased pressured speech and unstable behavior. Valproic acid was added to the regimen at 500 mg every 12 hours and risperidone was increased to 2 mg every 12 hours. The patient responded well to the treatment and became more approachable, which allowed for further investigation. After multiple myeloma was diagnosed, dexamethasone treatment was started and shortly thereafter the patient's general medical condition and psychotic symptoms showed substantial improvement. The patient was discharged and was followed up on an outpatient basis by the oncology department as well as by the psychiatrist. Lenalidomide was started on an outpatient basis and continued with the dexamethasone. The patient remained on valproic acid (500 mg every 12 hours) on discharge.

After being stable for ~8 months, the patient experienced another psychotic episode. She had stopped taking her valproic acid and was still on chemotherapy and steroids. Her family brought her in because she was becoming paranoid again and

reported visual and auditory hallucinations. She was seeing "spiders" and a "man with a snake" and seemed anxious and agitated at times. It was not clear whether her symptoms were a side effect of chemotherapy and steroids or represented residual problems due to multiple myeloma and the abrupt stopping of the valproic acid. After brief hospitalization, however, she became stable again and was discharged.

## DISCUSSION

Multiple myeloma is a cancer of the plasma cells affecting black Americans approximately twice as often as white Americans.<sup>9</sup> In the Hispanic population, the incidence rate is 6.4 per 100,000 in men and 4.7 per 100,000 in women.<sup>10</sup> Recent data have shown an increase in incidence and earlier age of onset.<sup>9</sup> The average patient age when symptoms present or the condition is diagnosed is 70 years.<sup>9</sup> Multiple myeloma is more prevalent in men than in women. The most recent data show that multiple myeloma was diagnosed in an estimated 59,000 Americans in 2006.<sup>10</sup> The patient may have no symptoms in the early stages of myeloma, but the most common early signs are pain, usually in the lower back and ribs, and decreased renal function. As renal function deteriorates, patients may also report fatigue, loss of appetite, confusion or difficulty in thinking, muscle weakness, nausea, and vomiting. Several known organic causes are routinely considered for changes in mental status in patients with multiple myeloma, such as hypercalcemia, renal failure, infections, hyperammonemia, and hyperviscosity syndrome.

**TABLE**  
**CAUSES OF SECONDARY MANIA<sup>2-4</sup>**

<i>Medical Conditions</i>	<i>Medications</i>
CNS infection (eg, HIV, neurosyphilis)	Corticosteroids
Multiple sclerosis	Anabolic steroids
Metabolic disturbances (eg, uremia, vitamin B <sub>12</sub> deficiency)	Antidepressants
Epilepsy	Cocaine
Neoplasm	Dextromethorphan
Strokes	Dopamine agonists (eg, bromocriptine, levodopa)
Traumatic brain injury	Isoniazid
Huntington's disease	Stimulants
Hyperthyroidism	Sympathetic amines
Hyperadrenalism	Zidovudine

CNS=central nervous system; HIV=human immunodeficiency virus.

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Hypercalcemia was not thought to be a contributing factor in this patient, because her corrected calcium level of 10.3 mg/dL was in the high-normal range. Hypercalcemia can produce changes in personality and mood,<sup>11</sup> but these changes usually occur in the setting of a serum calcium level >12 mg/dL. Renal failure and azotemia can also cause changes in mental status in patients with multiple myeloma.<sup>12</sup> This patient did have impaired renal function, but her serum creatinine level had already been elevated 1 month earlier, according to studies done at that time, and at her baseline mental status she was functioning well at home and at work. Therefore, it is unlikely that renal failure was the primary cause of her abrupt character alteration. The patient also had no signs of infection, her ammonia levels were normal, and hyperviscosity syndrome was thought to be unlikely because her serum protein level was low and her IgG level was 382 mg/dL.<sup>13</sup>

Psychosomatic manifestations of multiple myeloma have been described in the literature. Silberfarb and colleagues<sup>14</sup> reported the results of physician ratings of global psychological function in 290 patients with a diagnosis of multiple myeloma. Approximately 3% of patients were rated by a psychiatrist to have at least a moderate level of emotional distress. No patients were explicitly noted to have manic or psychotic symptoms as a presenting symptom. Patient-rated surveys from the same study revealed that many of the patients with multiple myeloma experienced tension, depression, and anger. These symptoms, however, were similar in severity and incidence to those in patients with gastric, pancreatic, or lung cancer. In addition, the vast majority of patients in this study were aware of their diagnosis, which diminishes the accuracy of the survey as a pure measure of the psychological manifestation of the intrinsic disease process.

In 1983, Silberfarb and colleagues<sup>14</sup> reported five cases of multiple myeloma on the general medical floors that had psychiatric manifestations. Four of these patients had delirium. In the case we are reporting, nothing suggested delirium at any point with the exception of the patient's second psychotic episode. Her Mini-Mental Status Examination score was 29 and she showed no fluctuation of consciousness at any point during her first admission.

## CONCLUSION

Our patient's initial presentation can be interpreted as mania secondary to multiple myeloma. Secondary mania may occur with several medical problems and may be

induced by certain drugs in patients with no history of psychiatric illness. Krauthammer<sup>15</sup> cautioned in 1978, "Physicians are alerted to the variety of organic dysfunctions that may cause a manic syndrome and are therefore urged to screen for them when this diagnosis is made." Organic causes such as infection (eg, HIV, neurosyphilis), metabolic disturbances (eg, vitamin B<sub>12</sub> deficiency), epilepsy, neoplasm, and medications (eg, corticosteroids) should be considered (Table).<sup>2-4</sup> As this case shows, multiple myeloma can also be a cause of secondary mania, and mania can be one of the first presenting symptoms. Therefore, multiple myeloma should be included in the differential diagnosis in three types of populations as a secondary medical cause of recent onset mania such as young patients without any previous family history of bipolar disorders and/or substance abuse, older patients with a first manic episode with psychosis, and any patient with refractory mania to combination therapy. This case emphasizes the importance of medical investigation in patients with late onset of manic symptoms and the need to include multiple myeloma in the differential diagnosis. This case further suggests that in addition to the known possible causes, factors that are as yet undetermined may contribute to psychosis in patients with multiple myeloma. These unknown factors may be worth future investigation. **PP**

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