



## Lithium for bipolar depression with chronic pain

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### ABSTRACT

Chronic pain complaints are common among patients with major depression, and patients with physical pain are more likely to develop major depression. Antidepressants are effective against both pain and the symptoms of depression, but the use of these agents for treating patients with bipolar disorder is problematic because of the significant risk of inducing mania. In the present case, a patient with bipolar depression suffering from chronic pain had been misdiagnosed with major depressive disorder and treated with antidepressants for several years. His pain improved dramatically after the administration of lithium, and he remained free of pain despite the discontinuation of treatment with antidepressants. This suggests that lithium might be more useful than antidepressants for the treatment of bipolar depression with chronic pain. Further research is needed to compare the effectiveness of lithium to that of other mood stabilizers such as valproate, carbamazepine, and lamotrigine in order to identify treatment strategies for patients with bipolar disorder associated with chronic pain.

**Keywords:** *bipolar depression, chronic pain, antidepressants, lithium*

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### INTRODUCTION

Chronic pain complaints are common among patients with major depression [1], and patients with physical pain are more likely to develop major depression [2]. Antidepressants, especially dual-action medications that enhance serotonergic and noradrenergic neurotransmission simultaneously, are effective against both pain and the symptoms of depression [3, 4]. Use of these agents for treating patients with bipolar disorder and chronic pain, however, is problematic due to the significant risk of inducing mania [5].

Here, we report a case of bipolar depression with chronic pain successfully treated with lithium. The patient had been misdiagnosed with major depressive disorder and treated with antidepressants for a long

time. His pain improved dramatically after the administration of lithium, and he remained free of pain despite the discontinuation of treatment with antidepressants. This suggests that lithium might be more useful than antidepressants for the treatment of bipolar depression with chronic pain.

### CASE PRESENTATION

A 64-year-old Japanese man suffered chronic facial pain for 8 years. He had a history of two depressive episodes at the ages of 38 and 55, and had been hypomanic for 6 months after the second depressive episode. At age 56, he began to experience slight facial pain that continued to worsen. Because the treating physician was not aware that the patient had previously experienced a hypomanic episode, the

patient was diagnosed with major depressive disorder and treated with several different types of antidepressants. At the age of 64, he was admitted to our department. His chief complaint was facial pain. In addition, he had a depressed mood, loss of interest and pleasure, decreased concentration, appetite loss, and insomnia; these symptoms had been present for at least 2 weeks. The findings of the physical examination, including blood and neurologic tests and brain computed tomography and magnetic resonance imaging, were normal. Because the patient never mentioned his past hypomanic episode, he was diagnosed with "Major Depressive Disorder, Recurrent," with accompanying chronic pain as one of his symptoms. He was treated with an increased dose of sertraline (100 mg per day), and mianserin (10 mg per day) was added for insomnia due to the pain. After more than 2 weeks at the same doses of sertraline and mianserin, his depressive mood subsided, but he became very irritable and continued to complain of pain. Around the same time, his wife mentioned the 6-month period of hypomania that had occurred after the second depressive episode. He was then strongly suspected of having a bipolar disorder and treated with lithium at 400 mg per day (lithium concentration = 0.41 mEq/L). His pain dramatically improved, and he became talkative and hyperactive. Such hypomanic symptoms disappeared 3 days after discontinuation of the mianserin, and he was discharged. Two months after discharge, he experienced a relapse of slight pain; the lithium dose was increased to 600 mg per day (lithium concentration = 0.66 mEq/L) and the dose of sertraline was concomitantly decreased. Two weeks later, his slight pain had disappeared and he has since remained free of pain despite the discontinuation of the sertraline.

## DISCUSSION

An association between pain and major depression has been reported [1, 2]. Little is known, however, about the prevalence and correlation of pain in bipolar disorder, and one epidemiologic study has reported that moderate or great pain interference was significantly more common among patients with bipolar disorder than those with major depressive disorder [6]. In our case, the patient had suffered chronic facial pain for over 8 years. The patient's mood changed from depressive to irritable while taking antidepressants, and although his pain improved dramatically after the addition of lithium, he became hypomanic. Fortunately, his hypomanic

symptoms disappeared after the discontinuation of mianserin. His pain, however, relapsed slightly after a few months. The combination of lithium and the antidepressants mianserin, which enhances noradrenergic neurotransmission, and sertraline, which enhances serotonergic neurotransmission, was effective for treating his pain. His pain was also improved, however, by increasing the dose of lithium, and he has remained pain-free despite discontinuation of the antidepressants. Lithium alone, and not only lithium augmentation, thus appears to be effective for both bipolar depression and chronic pain. Antidepressant treatment, which is clinically effective for patients with major depressive disorder and pain, was not effective for this patient, indicating that the neural mechanism of bipolar depression with pain might be different from that of major depressive disorder with pain. It is important to consider the possibility of bipolar depression when diagnosing depressive patients with pain. Lithium is frequently used in the treatment of patients with cluster headaches [7]. Additionally, intrathecal administration of lithium has been reported to reduce neuropathic pain responses in a rat model of peripheral neuropathy [8]. Taken together, these observations indicate that lithium alone may be effective for the treatment of bipolar disorder with chronic pain. Lithium augmentation might also be effective for patients with major depressive disorder and pain. To our knowledge, this is the first report of the effectiveness of lithium for chronic pain. Further research is needed to compare the effectiveness of lithium to that of other mood stabilizers such as valproate, carbamazepine, and lamotrigine, which are anti-epileptic medications, in order to identify treatment strategies for patients with bipolar disorder associated with chronic pain.

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