CASE REPORT

Prolonged mania in a case of bipolar affective disorder

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Abstract

Bipolar disorder, which often has its onset in adolescence or early adulthood, is characterised by marked variations in mood, ranging from major depressive episodes to manic exacerbations. Compared to depressive episodes, manic recurrences are often brief and usually respond to anti-manic medications within a few weeks. Infrequently bipolar patients get badly affected by protracted manic symptoms that exhibit resistance to the usual anti-manic agents. As mania is a very disruptive condition with severe and adverse consequences for the patient, every effort should be made to bring it under control as soon as possible. Nonetheless, an occasional patient may require prolonged and persistent treatment to attain remission. In a case where manic symptoms are showing resistance, an evidence-based pharmacotherapuetic approach by the treating physician is essential. The provision of psychological and social support to the patient is vital in conjunction with biological measures for optimal management.

Keywords: Bipolar disorder, Treatment-resistant mania, Atypical antipsychotics, Mood stabilisers.

Introduction

The depressive episodes of bipolar disorder are typified by a low mood. In contrast, mania is a state of high energy with elation, grandiose thinking, over-activity, distractibility, decreased need for sleep, racing thoughts, pressure of speech and flight of ideas.[1] Depressive episodes can be of a protracted nature lasting for months. In contrast manic disturbances are briefer and often respond to treatment within weeks.[2] In bipolar patients who get afflicted by severe and prolonged mania there can be adverse physical, psychological and social consequences which underscore the need to quickly bring such exacerbations under control.[3] Rarely mania becomes resistant to usual psychopharmacological interventions and continues unabated in spite of adequate treatment with anti-manic agents.[4] We present here the case of a teenaged girl who had a severe manic exacerbation that persisted for several months with symptoms continuing unabated in spite of optimal drug treatment. Her condition finally resolved with the manipulation of mood-stabilising medications and the therapeutic process was conducted in an informed and evidence-based manner. The whole treatment course was guided by the principles of biopsychosocial model of management.

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Case Report

Miss M, 18, unmarried female was brought to the outpatient psychiatry clinic of Pakistan Railways Teaching Hospital, Rawalpindi, by her father. He said that for the past 12 weeks she was over-active, over-talkative, had severe sleeplessness and was upsetting others by non-stop shouting, repeated banging and thumping and boisterousness. Her medical record showed that she was a known case of bipolar disorder and had been suffering from affective episodes since the age of 14. The present symptoms had progressively got worse over a period of three months, but the family was somehow coping with her condition. The father was informed that her manic exacerbation required that she be admitted and treated with parenteral antipsychotics and sedatives, but he refused to give permission for such interventions. When the possibility of electroconvulsive therapy (ECT) as a treatment of last resort was mentioned, he requested that an initial trial of oral medications be given a chance and if she showed no improvement within a reasonable period, then he would be willing to consider other options.

Systemic physical examination during the initial consultation did not reveal any abnormality. She was five feet, eight inches in height, weighed 55kilogrammes and the body mass index (BMI) was calculated to be approximately 17.75 (underweight). The laboratory assessment, which included complete blood picture, erythrocyte sedimentation rate (ESR), serum electrolytes, urea and creatinine, liver function tests (LFT), thyroid profile and urinalysis, were within normal limits. Treatment record showed that she had a similar but less severe episode about a year ago, and had responded to a combination of oral medications that included haloperidol, divalproex sodium and diazepam on an outpatient basis. However, after remission she had

stopped taking her mood-stabilising medications.

She was prescribed risperidone 6mg, divalproex sodium 1000mg and alprazolam 2mg to be administered in two equal, divided doses daily. The principle used to calculate the dose of divalproex sodium was as per the recommendations of American Psychiatric Association (APA) guidelines for the treatment of acute mania in outpatients, which advises an initial daily dose of 750-1000mg.[5] Expert recommendations that regular clinical evaluation was more important in gauging response in acute mania compared to serum valproate levels which were followed and the latter were not relied upon.[6]

In the outpatient setting, the first week of treatment saw very little change, but decrease in the severity of manic symptoms was noted in the next 3 weeks. No change in pharmacotherapy was made at this point (1 month after the start of medications) and she continued to take the same regimen for a further period of 4 weeks. After 8 weeks of treatment there was significant improvement in her condition as she slept for 6 to 8 hours per day, the speech was no longer pressured and boisterousness was much diminished. However, she continued to show expansiveness, grandiose ideation and distractibility, and manic symptoms seemed to plateau at this stage.

It was decided to replace risperidone with aripiprazole, which was given in a single daily dose of 15mg to control the above-mentioned residual manic symptoms. The amount of alprazolam was halved to 1mg/day, while the dose of divalproex sodium remained at 1000mg/day. During the next 2 weeks she showed a decrease in expansive behaviour, grandiose ideation and distractibility, and became more appropriate socially. However, her elation was replaced with dysphoria and she complained of being keyed up and tense. Concurrently, she exhibited physical symptoms of sweating, trembling and palpitations. To counter this apparent anxiety state she was given gabapentin 300mg three times per day. After a further 2 weeks on this treatment the patient seemed to make a complete recovery with no manifestations of anxiety and displayed a euthymic mood. At this stage of remission (12 weeks after initial presentation) her daily medications consisted of aripiprazole 15mg, divalproex sodium 1000mg, alprazolam 1mg and gabapentin 900mg. She was advised to continue taking these drugs for the foreseeable future to maintain the remission phase of bipolar disorder. The need for periodic follow-ups to monitor the psychiatric and physical status was also stressed to her. In these subsequent visits her weight, menstrual cycle regularity and flow, LFT and blood indices remained unchanged from baseline and within normal limits.

Discussion

This patient exhibited mania for three months prior to the start of the treatment. Even when anti-manic agents were given, there was a period of at least 1 month when there was no significant reduction in her symptoms. However, persistence with a combination medication regimen consisting of an atypical antipsychotic, an anticonvulsant mood-stabiliser and an intermediate acting benzodiazepine resulted in a breakthrough in manic symptoms. This regimen was followed in accordance with the guidance provided by the World Federation of Societies of Biological Psychiatry (WFSBP).[7] An extensive search of published studies since 1980 validated the superiority of combination therapy over monotherapy in the manic phase in terms of efficacy.[8] A review of the literature showed that risperidone in combination with divalproex sodium for controlling acute mania was safe and well tolerated, involved no clinically significant cytochrome p450 interaction, and the drugs did not influence the steady-state pharmacokinetics of each other.[9]

The most recent evidence examining the use of aripiprazole with divalproex sodium revealed that the combination offered an effective and relatively well-tolerated option for the treatment of acute mania. The combination was associated with a low risk of prolactin elevation, corrected QT interval prolongation, metabolic disturbances, and side-effects did not differ significantly from that in placebo recipients.[10] The European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study was a two-year prospective, observational study that enrolled 3,684 adult patients with bipolar disorder, and initiated or changed oral treatment for an acute manic/mixed episode. Symptom severity was assessed using the Clinical Global Impression-Bipolar Disorder (CGI-BP) and Young Mania Rating Scale (YMRS). One finding from this landmark study was that the rating scales were useful in randomized, controlled, medication trials but regular clinical evaluation was more helpful in assessing psychosocial and functional progress of manic patients.[11]

Conclusion

Patients with bipolar disorder can rarely be managed with a single agent as was illustrated by this case. Severe, unremitting mania is a psychiatric emergency and complex psychopharmacological strategies may be needed to control the symptoms. The treating physician should make informed decisions and use psychotropic medications with proven safety and efficacy. In this case, the judicious use of pharmacotherapy was successful, and physical interventions like ECT were not needed.

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