

# A complex case of bipolar disorder responding to combined drug therapy

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**The aetiology of bipolar affective disorder is complex and can involve genetic, environmental, biochemical and organic factors. Here, Dr Kamlana describes a puzzling case of bipolar disorder in a patient with brain scan abnormalities, who responded well to combined treatment with mood stabilisers, an atypical antipsychotic and an SSRI together with a programme of rehabilitation.**



**B**ipolar affective disorder is a common condition which, among mental illnesses, ranks second only to unipolar depression as a cause of worldwide disability.<sup>1</sup> Many patients have a poor outcome, a third suffer chronic symptoms and between 13 and 24 per cent develop rapid cycling disorder, in which four or more episodes occur within a year.<sup>2</sup>

Several organic factors have been linked with bipolar disorder, particularly in patients whose illness begins in older age (over 65 years). For example, non-dominant hemisphere cerebrovascular accidents can predispose to the development of mania, especially if there is either a previous history of depression or family history of affective disorder. Other brain disorders (or systemic disease with cerebral involvement) can also present with mania or severe (often psychotic) depression. Accompanying the affective syndrome, there is usually evidence of disorientation and other features of confusion along with visual hallucinations, all of which are less common in primary bipolar illness.

Here, I present a complex case of bipolar affective disorder, with a possible organic component, which responded well to combined

drug therapy and a programme of gradual rehabilitation.

## Presentation

A 47-year-old married woman was admitted to a specialist neuropsychiatric unit under Section 3 of the Mental Health Act. She presented with irritability, impulsivity, disinhibition, distractibility, poor concentration and worsening of social functioning, and had been found wandering the streets in her nightclothes and flagging vehicles. She had approached strangers for cigarettes and had no sense of road safety.

She showed pressure of speech and increased energy and overactivity. Her sleep was disturbed and she lacked insight. Her mood would quickly change to feeling very depressed with suicidal thoughts, and these changes could occur several times a day. She was given a diagnosis of bipolar disorder.

There was no family history of psychiatric illness. Her past psychiatric history included detoxification from lorazepam 17 years earlier. About 10 years after this, she consulted a GP for anxiety and depression and another two years later (five years prior to the latest admission), she took an overdose and was admitted to the Affective Disorder Unit under Section 3 and was diagnosed with psychotic depression. At that time, she was severely

depressed and expressed persecutory delusions. She was also convinced that she had cancer of the bowel. She was treated with ECT and her medications included mirtazapine, olanzapine and diazepam.

She had two further admissions over the next three years, the most recent being two years prior to her latest admission. At this time, she showed marked behavioural disturbance and mood fluctuations for which she was prescribed gabapentin. She repeatedly managed to abscond from the psychiatric unit, was physically aggressive towards staff and considered a risk to herself and others. She remained unmanageable despite being on maximum dosages of amisulpride 500mg twice daily and olanzapine 20mg daily as well as gabapentin 600mg three times daily. Investigations at the time included CT and MRI brain scans and an EEG, which were all reported to be normal.

The only other medical illness of note in our patient was type 2 diabetes, which was stabilised on metformin 500mg three times daily and simvastatin 40mg at night.

At her latest admission, a neuropsychiatric assessment showed significant deterioration from her estimated good average premorbid level of cognitive function across all areas, which was particularly marked in relation to working memory with significant impairment being pres-

ent in relation to new verbal learning. An MRI brain scan was also performed, which showed global atrophy. There was no marked atrophy of the caudate nuclei and no positive features to suggest a fronto-temporal predominance to the atrophy. These signs were considered to be possibly indicative of early Alzheimer's disease. The neuropsychiatric and scan results raised the suspicion of an underlying organic component to the bipolar disorder but this could not be verified due to her initial symptoms predating the scan abnormalities.

The patient's medications were titrated to citalopram 20mg in the morning, gabapentin 400mg three times daily, quetiapine 300mg twice daily and valproate semisodium 1000mg twice daily. She remained an inpatient in the neuropsychiatric unit and gradually began to make good symptomatic recovery over the following 9-14 months, as measured using the Health of the Nation Outcome Scale (HoNOS). She was compliant with her medications and Section 17 leave. Her progress was reviewed regularly in the multi-disciplinary ward rounds. She developed a strong therapeutic relationship with staff, and showed no manifest symptoms of psychotic depression or mania. Her insight also improved.

This gradual process of rehabilitation was carefully managed with the co-operation of her husband. She began to resume a meaningful life within and beyond the unit and appeared to be enjoying her family and social life. However, she expressed ambivalent feelings towards her husband, who visited her at weekends in hospital. They had a nine-year-old son and her husband also had a child from another relationship.

A pre-discharge meeting was planned and the following after-care plan was implemented:

- Ensure compliance with present drug therapy using the NOMAD monitored dosage system.
- A support, time and recovery (STR) worker to visit the patient once a week at home
- Follow-up at the outpatient clinic with a psychiatrist to monitor progress and medication review
- Regular home support from a community psychiatric nurse
- Social worker support, including a seven-day follow-up
- Crisis team follow-up, initially once a month post-discharge
- Telephone counselling once a month post-discharge
- Follow-up from her GP regarding physical healthcare.

The patient was discharged successfully and continues to make good symptomatic recovery three years later. Her cognitive function has remained static. She has managed to gain employment in a primary school as a lunchtime assistant and she also does voluntary work at the local cattery. She continues to remain well and comply with her medications.

### Discussion

This report describes a complex case of bipolar disorder, which appeared to have an organic component. According to ICD-10, the criterion for inclusion in the category of organic mood (affective) disorders is the presumed direct causation by a cerebral or other physical disorder whose presence must either be demonstrated independently, *eg* by means of appropriate physical and laboratory investigations, or assumed on the basis of an adequate history.<sup>3</sup> The mood disorder must follow on from the presumed organic factor and be judged not to represent an emotional response to the patient's knowledge of having, or having the symptoms of, a concurrent brain disorder. In this case, however, the

patient's mood disturbances predated the abnormal scan findings, and therefore organic bipolar disorder could not be verified.

This case emphasises the difficulty distinguishing between organic and non-organic psychiatric illness. Organic disorders often present with hallucinations and disorientation; however, others have symptomatology more typical of non-organic psychiatric illness. In our case, in addition to structural brain changes, there were probably also genetic, functional and biochemical factors involved in the aetiology of the bipolar disorder. Other examples of diagnostic difficulty arising between organic and non-organic psychiatric disorders have been described by Lishman.<sup>4</sup>

In our case, despite the patient showing a history of resistance to treatment, combined treatment with mood stabilisers (gabapentin and valproate semisodium), an atypical antipsychotic (quetiapine) and an SSRI (citalopram), together with a programme of gradual rehabilitation following her most recent admission was surprisingly effective.

According to the 2006 NICE guideline,<sup>5</sup> key maintenance treatment of bipolar disorder is either a mood stabiliser or an atypical antipsychotic, which is started as monotherapy in order to achieve complete symptom control of the index episode as well as sustained remission and to prevent relapse. If monotherapy fails, there is evidence to support combination therapy with an atypical antipsychotic plus a mood stabiliser.<sup>6</sup> The Consensus Group of the British Association for Psychopharmacology (BAP)<sup>7</sup> emphasised that in difficult to treat cases, combination therapy is usually necessary. There is also evidence to suggest that gabapentin is effective in refractory mood disorders.<sup>8</sup>

Regular monitoring of patients on combination therapy for bipo-

lar disorder is important, including weight, waist, glucose, lipid, prolactin and blood pressure measurements, in accordance with the NICE guidelines, and this was the case with our patient. It is also important to remember that the management of bipolar disorder is a long-term commitment between the patient, the GP, the psychiatrist and the patient's family. Such collaborative working was of paramount importance in the recovery of this refractory patient.

## Declaration of interests

None declared.

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