

## Case Report

# Pernicious Anaemia Presenting as Bipolar Disorder A Case Report and Review of Literature

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## Abstract

*Objective:* To increase the awareness about the relationship between vitamin B<sub>12</sub> deficiency and affective disorders, especially bipolar affective disorder. *Method:* We present a patient who presented with a clinical picture of bipolar disorder along with cognitive symptoms and on investigation was found to have vitamin B<sub>12</sub> deficiency. *Results:* Vitamin B<sub>12</sub> supplementation led to amelioration of all the symptoms. *Conclusion:* Subjects presenting with recurrent affective symptoms with inter-episodic residual symptoms should be investigated for vitamin B<sub>12</sub> deficiency (German J Psychiatry 2010; 13(4): 181-184).

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## Introduction

Pernicious anaemia is characterised by vitamin B<sub>12</sub> deficiency which arises due to lack of intrinsic factor in the gastric mucosa. B<sub>12</sub> deficiency usually manifests clinically in the form of megaloblastic anaemia, lethargy, weight loss, weakness, leucopenia, thrombocytopenia, accumulation of fat around heart, liver, peripheral nerves and skin lesions in the form of vitiligo, hyperpigmentation and angular stomatitis (Oh & Brown, 2003; Kannan & Ng, 2008; Kasper et al., 2005). The neurological symptoms include myelopathy, neuropathy, dementia and rarely optic nerve atrophy (Kasper et al., 2005).

Since the early descriptions of pernicious anaemia and other causes of vitamin B<sub>12</sub> deficiency, association with many psychiatric disorders like mood disorders (depression, mania, mixed episodes), confusion, slowed mentation, delirium, panic attacks with and without phobia, hallucinations, delusion, psychosis (acute and chronic), catatonia and insomnia have been described (Shulman, 1967; Edwin et al., 1965; Evans et al., 1983; Herr et al., 2002; Hector & Burton, 1988).

However, most of this literature is in the form of case reports/case series and very few case reports in the literature have described manifestations of bipolar disorder to be associated with vitamin B<sub>12</sub> deficiency (Smith, 1967; Lewis et al., 2009; Reid, 2000; Dommissie, 1990, 1992; Jacobs et al., 1990; Goggans, 1984).

In this case report, we describe a subject who presented with a clinical picture of bipolar disorder along with severe cognitive symptoms and on investigation was found to have vitamin B<sub>12</sub> deficiency and review the literature with respect to association of bipolar disorder with vitamin B<sub>12</sub> deficiency.

## Case Report

Mr. X, 55 years old vegetarian from an urban background, with no past and family history of mental illness presented with an illness of 10 years duration. The first episode occurred 10 years back and was characterised by low mood, irritability, anhedonia, anxiety, ideas of hopelessness, worthlessness, decreased sleep and appetite and psychosocial dysfunction. After about 3 months of onset of symptoms he

was treated with fluoxetine 20 mg/day along with benzodiazepines, with which he improved significantly over the period of 2 months, but continued to have residual symptoms in the form of excessive worry, on and off anxiety without any stressor and occasional sadness. Besides this as per family he started remaining serious and wouldn't crack jokes like before, would not show interest in household matters and at times avoid going to work. Fluoxetine was stopped after about 6 months of partial recovery.

About 4 years after the first episode he again had similar episode of moderate to severe intensity with psychosocial dysfunction and was again treated with fluoxetine with which he improved partially, but continued to have residual symptoms as described. Once again fluoxetine was stopped after 6 months of partial recovery. Gradually, the residual symptoms kept on worsening and he would occasionally complain of forgetting day to day things and would misplace things but these symptoms did not lead to marked occupational dysfunction.

Ten years after the initial episode, the residual symptoms suddenly started worsening. He started having episodes of anxiety more frequently and the other symptoms suggestive of depressive episode emerged over the period of 6-8 weeks and the forgetfulness also increased. Four months after the worsening of symptoms he was started on antidepressants (bupropion 150mg/day, paroxetine 20-40 mg/day) along with benzodiazepines. Over the period of 6 months the symptoms did not improve and in addition, he started complaining of excessive fatigability and had weight loss of 8 to 10 kgs. He was investigated at that time and was found to have haemoglobin of 6.5g%, MCV 101 fl, bilirubin 2.1mg%, MCH 36.8pg, normal G6PD levels and a negative Coomb's test for IgG and C3. He was seen by the neurologist and the possibility of megaloblastic anaemia (in view of the increase in mean corpuscular volume) was considered. He was started on oral B<sub>12</sub> supplementation. While on oral B<sub>12</sub> supplementation and about 4 weeks after stoppage of antidepressants, all of sudden he became more active, started talking excessively, stopped complaining of fatigability, had increased self confidence, started socializing excessively with known and unknown people, did spend money excessively and had decreased need for sleep. These symptoms lasted for 8 to 10 days and then abated. During this period he also became non-complaint with B<sub>12</sub> and stopped the same.

Following this, he began to exhibit mood fluctuations, increasing forgetfulness, difficulty in naming objects and people. He seemed to have no distress or concern over his memory lapses and there were no diurnal fluctuations or any effect of sleep on these lapses. While driving, he started losing way enroute and met many road traffic accidents, would have difficulties in new learning, calculations and in activities requiring motor co-ordination. He began to sway while walking. He would behave in a socially inappropriate manner, and would be easily distractible. His appetite decreased, self care deteriorated and he began to have daytime drowsiness. During this period he was seen by another psychiatrist and diagnosed as having bipolar affective disorder and was started on valproate with which his condition further worsened. There was no history of psychotic symptoms, grandiosity, head injury, fits and skin lesions.

Following this, he was brought to our centre for the first time after about 10.5 years of onset of symptoms and on physical examination was found to be pale with pitting oedema upto shin, impaired fine touch and vibration, impaired asterognosis, sluggish ankle reflex, positive Romberg's test, dysdiadochokinesia and swayed while walking. On mental status examination, he was distractible, disoriented to time and place, with impaired memory (immediate and recent memory impairment with preserved remote memory), comprehension, calculation, abstraction, judgment and insight. His mini mental status examination score was 16 with impairment in all the domains of cognitive functions. There were minor diurnal fluctuations in the cognitive symptoms. He was admitted to the inpatient unit and on investigation his haemoglobin was 7.2 g%, with megaloblastic blood picture; serum B<sub>12</sub> levels were 98.5 pg/ml (211-911pg/ml is normal) and his MRI showed diffuse cerebral atrophy. Neuropsychological testing showed deficits in visuo-motor coordination, memory and intelligence (intelligence quotient 67). Other investigations in the form of liver function test, renal function test, thyroid function test, electrocardiogram, ultrasound abdomen and electroencephalogram were within normal limits.

With the available information and investigation findings a diagnosis of dementia due to other specified diseases classified elsewhere (with B<sub>12</sub> deficiency), subacute combined degeneration of spinal cord due to B<sub>12</sub> deficiency, megaloblastic anaemia and delirium were considered. An independent diagnosis of bipolar affective disorder was considered initially but in view of the residual affective symptoms and cognitive symptoms since the first episode a possibility of affective disorder due to B<sub>12</sub> deficiency was also considered. In view of the diurnal fluctuation in symptoms (especially cognitive symptoms) he was initially started on olanzapine 2.5 mg/day and valproate was stopped. Along with this he was started on injectable vitamin B<sub>12</sub> supplementation along with folate. He was given hydroxycobalamin 500 microgram/day i.m. for 7 days along with folic acid, followed by 500 microgram/day i.m. every alternate day for the next two weeks. Over the period of 3 weeks on inpatient stay, he had significant improvement in cognitive functioning (MMSE improved from 16 to 30), started walking without support and without swaying. With improvement of cognitive functioning, no affective symptoms were observed. Olanzapine was stopped after 4 weeks.

Further investigations revealed anti-parietal cell antibodies and he was diagnosed as a case of pernicious anaemia. His olanzapine was stopped and he was continued on injectable B<sub>12</sub> and folate supplementation.

On follow-up of 15 months, without any psychotropic medications, he showed further significant improvement in his behaviour. He had no cognitive or affective symptoms and as per family he would now socialize with family members, show interest in family matters and crack jokes like he used to do 11-12 years back. The neuropsychological examination after 6 months of starting vitamin B<sub>12</sub> showed average functioning in the domains of visuo-motor function and memory and his IQ was 106.

## Discussion

There are case reports in literature which have described association of depression, mania and mixed episodes with B<sub>12</sub> deficiency. Depression is the most common psychiatric disorder seen in subjects with pernicious anaemia and the symptoms are similar to a functional disorder. Patients with depression may present with history of past episodes with spontaneous remission or response to treatment with antidepressants and later recognition or development of vitamin B<sub>12</sub> deficiency (Smith, 1960; Fraser, 1960; Strachan & Henderson, 1965). There is no consensus with respect to remission of depression without treatment with B<sub>12</sub> replacement and some authors have tried to explain this remission on the basis of spontaneous remission of pernicious anaemia. However, some argue that if at all there is improvement in the symptoms of depression, it is usually not complete.

Mania and hypomania has been described in few case reports and case series (Shulman, 1967; Jacob et al., 1990; Goggans, 1984). In the case series of 10 cases, Shulman (1967) described the case of a 72 year old lady who had pernicious anaemia and developed hypomania which responded to chlorpromazine. Goggans (1984) described the case of 81 year old man who was admitted with manic symptoms who initially required psychotropic medications but later maintained euthymia while receiving B<sub>12</sub> supplementation only. Jacobs et al. (1990) described the case mania and gait disorder due to B<sub>12</sub> deficiency.

Only 3 case reports have described association of bipolar disorder with vitamin B<sub>12</sub> deficiency (Durand et al., 2003; Lewis, 2009; Smith, 1960). In their case series of 6 cases, Smith (1967) described a case who initially presented with atypical depression and developed manic symptoms while on B<sub>12</sub> supplement. Durand et al. (2003) described the case of elderly lady who was admitted to the hospital in a state of confusion and further evaluation suggested the presence of depressed mood, guilt complex and that her illness can't be cured. She developed hypomanic features while receiving B<sub>12</sub> supplementation which lasted for 3 days only. Lewis et al. (2009) described the case of a 23 year old lady who initially had symptoms of insomnia, increased goal directed activity in the form of 5 days of non-stop studying, pressured speech, extreme tangentiality, and grandiose delusions followed by catatonia symptoms.

Our patient had history of 3 depressive episodes prior to be diagnosed as having B<sub>12</sub> deficiency. However during the interepisodic period patient continued to have subsyndromal symptoms and was never asymptomatic. This clinical picture fits into typical picture of recurrent depression described with B<sub>12</sub> deficiency. Further, in our case patient had hypomanic symptoms while receiving low doses of B<sub>12</sub> supplementation. This clinical finding also commensurate with the literature where in 2 out of the 3 cases of association of bipolar disorder with B<sub>12</sub> deficiency, hypomanic/manic symptoms were seen when the patient was receiving B<sub>12</sub> supplementation. Additionally our patient also had cognitive and neurological symptoms which fit into the description of B<sub>12</sub> deficiency. The whole clinical picture over the years can

be attributed to B<sub>12</sub> deficiency on the basis of recurrent episodes, residual anxiety, depressive and cognitive symptoms during the interepisodic period, complete recovery from all the symptoms (affective, anxiety, cognitive and neurological) only with B<sub>12</sub> supplementation and family and patient perceiving the improvement in overall behaviour of the patient. Our case highlights the fact that B<sub>12</sub> deficiency should be considered as a possibility in subjects presenting with recurrent depression or bipolar disorder with residual interepisodic symptoms. In such cases detailed clinical examination should be done to evaluate for signs and symptoms of B<sub>12</sub> deficiency and the B<sub>12</sub> levels must be estimated. Our case also highlights the fact that at times patients may develop hypomania like picture while receiving B<sub>12</sub> supplement for depressive symptoms, which is usually short lasting.

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