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 B12 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 B12 deficiency. Results: Vitamin B12 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 B12 deficiency (German J Psychiatry 2010; 13(4): 181-184).

Keywords: B12 deficiency, bipolar disorder

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Introduction

Pernicious anaemia is characterised by vitamin B12 deficiency which arises due to lack of intrinsic factor in the gastric mucosa. B12 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 B12 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 B12 deficiency (Smith, 1967; Lewis et al., 2009; Reid, 2000; Domnisses, 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 B12 deficiency and review the literature with respect to association of bipolar disorder with vitamin B12 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 benzodia-
zepines, with which he improved significantly over the pe-
riod 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 fam-
ily 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
complaint of forgetting day to day things and would mis-
place 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
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 com-
plaining 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 B12 supplementation. While on oral B12 supplemen-
tation and about 4 weeks after stopping of antidepressants, all
of sudden he became more active, started talking excessively,
complaining of excessive worry, on and off anxiety without
any stressor and occasional sadness. Besides this as per fam-
ily 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.

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 oed-
dema upto shin, impaired fine touch and vibration, impaired
astrogonosis, 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), com-
prehension, calculation, abstraction, judgment and insight.
His mini mental status examination score was 16 with im-
pairment 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 pic-
ture; serum B12 levels were 98.5 pg/ml (211-911pg/ml is
normal) and his MRI showed diffuse cerebral atrophy. Neu-
ropsychological testing showed deficits in visuo-motor coor-
dination, memory and intelligence (intelligence quotient 67).
Other investigations in the form of liver function test, renal
function test, thyroid function test, electrocardiogram, ultra-
sound abdomen and electroencephalogram were within
normal limits.

With the available information and investigation findings a
diagnosis of dementia due to other specified diseases classi-
ified elsewhere (with B12 deficiency), subacute combined
degeneration of spinal cord due to B12 deficiency, megalob-
lastic anaemia and delirium were considered. An indepen-
dent 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 B12 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 B12 supplementation along
with folate. He was given hydroxycobalamin 500 micro-
gram/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 func-
tioning, 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
B12 and folate supplementation.

On follow-up of 15 months, without any psychotropic me-
dications, 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 B12 showed average func-
tioning in the domains of visuomotor 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 B12 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 anti-depressants and later recognition or development of vitamin B12 deficiency (Smith, 1960; Fraser, 1960; Strachan & Henderson, 1965). There is no consensus with respect to remission of depression without treatment with B12 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 B12 supplementation only. Jacobs et al. (1990) described the case mania and gait disorder due to B12 deficiency.

Only 3 case reports have described association of bipolar disorder with vitamin B12 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 B12 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 B12 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 being diagnosed as having B12 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 B12 deficiency. Further, in our case patient had hypomanic symptoms while receiving low doses of B12 supplementation. This clinical finding also commensurate with the literature where in 2 out of the 3 cases of association of bipolar disorder with B12 deficiency, hypomanic/manic symptoms were seen when the patient was receiving B12 supplementation. Additionally our patient also had cognitive and neurological symptoms which fit into the description of B12 deficiency. The whole clinical picture over the years can be attributed to B12 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 B12 supplementation and family and patient perceiving the improvement in overall behaviour of the patient. Our case highlights the fact that B12 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 B12 deficiency and the B12 levels must be estimated. Our case also highlights the fact that at times patients may develop hypomania like picture while receiving B12 supplement for depressive symptoms, which is usually short lasting.

References


