PSYCHIATRIC SYNDROMES IN PERNICIOUS ANAEMIA
- A CASE REPORT

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ABSTRACT
Surveys of psychiatric population had previously shown a high incidence of patients with low serum vitamin B₁₂. A variety of psychiatric syndromes have been described, ranging from mild disturbance in mood state like depression to manic-al excitement; psychotic conditions like paranoid states and schizophrenia; and cognitive dysfunctions such as memory defect, delirium and dementia. A case of a 67-year-old Chinese lady suffering from pernicious anaemia, but presenting with prominent paranoid delusions is reported. Treatment with cyanocobalamin and anti-psychotic medication led to prompt resolution of her psychotic experience. Subsequently she developed a transient depressive syndrome which also responded well to a short course of antidepressant.

Keywords: Vitamin B₁₂, Psychiatric syndromes.

INTRODUCTION
Changes in the nervous system secondary to vitamin B₁₂ deficiency are known to occur in the spinal cord, peripheral nerves and brain. The brain lesions which form part of the neurological syndrome of vitamin B₁₂ deficiency was first described by Preobrazensky in 1902. Thomas Addison, in his original classical description of pernicious anaemia, said "the mind occasionally wanders" (quoted by JM Holmes, 1956)³. Smith in a review of megaloblastic anaemia noted that as early as 1905, Langdon had already drawn attention to a group of patients whose mental symptoms preceded the onset of anaemia³. To maintain that there is a direct relationship between psychiatric illness and vitamin B₁₂ deficiency, ideally there should be no previous history of psychiatric illness. Moreover, it should be possible to demonstrate a relapse of the illness when vitamin B₁₂ is withheld, and resolution of the illness when vitamin B₁₂ therapy is instituted⁴. The following case report demonstrates clearly the emergence of a psychiatric syndrome which was preceded by a history of pernicious anaemia, as well as resolution of symptoms after institution of vitamin B₁₂ and anti-psychotic drug treatment.

CASE REPORT
The patient was a 67-year-old Chinese female who presented with a one-week history of abnormal beliefs characterized by persecutory ideas against certain politicians. For instance, she complained that government officials were following her wherever she went, that her telephone and television set had been tapped into and her food poisoned. She objected to her son signing any contract with the Armed Forces as she believed he would also be persecuted. She would lock herself at home and even disallowed her children leaving home for work because of fear that they would be harmed. Police reports were made by the patient who also requested for protection from her persecutors.

Five years before the present admission, the patient had received treatment for anaemia with blood transfusion and monthly intra-muscular injections. She defaulted after less than a year of treatment. Dietary intake was adequate, and there was no history of previous gastric surgery.

Mental state examinations revealed prominent and fairly elaborate paranoid delusions. Her mood was not depressed and there were no hallucinations. Cognitive functions were unremarkable.

Physical examination showed evidence of an anaemic state: marked conjunctival pallor with a functional ejection systolic murmur at the left sternal edge. Apart from a broad based gait, there were no other physical signs.

Haematological investigations revealed severe anaemia with pancytopaenia (Table I). Blood films showed anisocytosis and macro-ovalocytosis with hypersegmentation of the neutrophils. Reticulocyte count was low (0.7%). Serum iron, total iron binding capacity and ferritin measurements were normal. Other tests for renal, thyroid and liver functions, as well as a direct Coombs' test were normal. Serum folate was raised whilst vitamin B₁₂ was markedly low. Parietal cell antibodies were detected at 1:40 dilution. Other auto-antibodies were not sig-

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Coombs' test were normal. Serum folate was raised whilst vitamin B₁₂ was markedly low. Parietal cell antibodies were detected at 1:40 dilution. Other auto-antibodies were not significantly raised. The patients was diagnosed to have pernicious anaemia with organic delusional syndrome.

Treatment with folic acid, ferrous sulphate and daily intramuscular injection of cyanocobalamin 100 mcgm raised the reticulocyte count to 27% and haemoglobin to 6.6 g/dl within a week. Serum vitamin B₁₂ reached 1770 pmol/l. No blood transfusion was administered. Concomitant treatment with trifluperazine 15 mcgm daily led to fragmentation of her paranoid delusions which disappeared completely within two weeks.

The patient was followed up monthly with cyanocobalamin injection. However, three months after remission of her paranoid symptoms, she developed a depressive syndrome of moderate severity characterized by low mood, sleep disturbance, loss of interest for pleasurable activities and undue worries. There were no delusions or hallucinations. She admitted to having passive death wishes but denied any suicidal intent. No psychosocial factors of aetiological importance to her depressive episode could be elicited. The haemoglobin level then was 11.9 g/dl.

The patient was treated with antidepressant dothiepin (Prothiadan) 75 mgm nocte, while trifluperazine was stopped. She showed excellent response; her sleep pattern was normalized, the appetite improved and depressed mood elevated - all these by the end of the second week of antidepressant treatment. Within a month the depressive episode had completely resolved. She remained symptom free with another two months of treatment. Since then, she has stopped dothiepin on her own, but continued to receive cyanocobalamin injections. The haemoglobin level was maintained at 12.6 g/dl. She has remained well over the subsequent eighteen months.

DISCUSSION

Surveys of psychiatric population had previously shown a high incidence of patients with low serum B₁₂ levels. Edwin et al reported that 15% of a large group of patients had values below 150 ng/l and 6% below 100 ng/l.(11) In a survey of 117 new admissions to a psychogeriatric unit, Shulman found that 12% had serum vitamin B₁₂ levels below 150 ng/l compared with 5% of elderly non-psychiatric patients assessed by the same laboratory.(12) The above patient had a very low serum vitamin B₁₂ of only 41 pmol/l on admission.

A variety and variability of psychiatric symptoms have been described since their association with vitamin B₁₂ deficiency was known. They vary from a mild mood disorder to grossly psychotic behaviour.(13) Thus disorders of mood state such as depression and violent maniacal excitement, psychotic conditions like paranoid states and schizophrenia, and cognitive dysfunctions notably memory defect, delirium and dementia may be encountered. Other manifestations include visual and auditory hallucinations, severe agitation, paranoid behaviour and epilepsy. In a prospective controlled study of 27 patients with pernicious anaemia, Shulman found that a third of them had psychiatric symptoms rated as moderate or severe, the commonest being depression and memory impairment.(14) Smith's collection of five female and one male patients also had depression as the presenting condition. One of them had psychotic features as well.(15)

The above patient presented with prominent and elaborate paranoid delusions. Her past history of treatment for anaemia as well as clinical evidence of anaemia led to further investigations for an organic cause. She responded well to anti-psychotic drug treatment and cyanocobalamin injection. Indeed it is well known that patients with pernicious anaemia look and feel much better the day after the initial injection of vitamin B₁₂. Interestingly, her mental state subsequently devel-

oped into that of a depressive syndrome inexplicable by exogenous factors such as psychosocial stressors. Her serum B₁₂ was normal and her haemoglobin level was 11.8 g/dl. Smith's case reports of six patients with megaloblastic anaemia all had depressive features, with psychotic symptoms in one.(16) Shulman's prospective controlled study of the psychiatric status of 27 patients with pernicious anaemia and 21 anaemic patient controls who did not have pernicious anaemia showed that one third of both groups had psychiatric symptoms rated as moderate or severe. Before treatment, the most frequent symptoms were depression and memory impairment. However, only the latter appeared to be related to vitamin B₁₂ deficiency. Indeed, three-quarters of the patients with pernicious anaemia showed objective impairment of memory on a simple learning test. On re-testing after treatment the majority had returned to normal, sometimes within twenty hours of the first injection.(17)

Although there is definite clinical evidence of psychiatric syndromes associated with low vitamin B₁₂, the latter may sometimes be the consequence rather than the cause of the abnormal mental state since vitamin B₁₂ deficiency can result from inadequate nutrition.(18) Hence the latter may be a sequel of a mixed nutritional deficiency in depressed or demented patients who have neglected their diet.(19) This is unlikely to be the case in the above patient; her extremely low haemoglobin of 4g/dl on admission and the past history of anaemia indicated that the medical condition had indeed preceded the psychiatric syndrome. Before accepting a causal link between vitamin B₁₂ deficiency and psychiatric disturbance, Zucker et al suggested four criteria (1) the absence of other organic causes for the mental symptoms, (2) a non-relapsing course, (3) poor response to other treatments, and (4) a positive and well maintained response to vitamin B₁₂ administration.(20)

The exact pathophysiology of cerebral metabolism produced by vitamin B₁₂ deficiency is not completely understood. Studies of cerebral blood flow and oxygen consumption show that cerebral syndromes are due to the deficiency state, and are not related to the degree of anaemia. Metabolic studies reveal impaired uptake of oxygen and glucose, especially in the presence of mental symptoms such as forgetfulness, confusion and disorientation.(19) Electroencephalographic studies in pernicious anaemia show that abnormalities are common (over 60%). Mild abnormalities show as excessive theta activity, and severe abnormalities as delta activity which is sometimes paroxysmal or focal.(21) Such abnormalities bear no simple relationship to the severity of anaemia but appear to reflect a specific defect in cerebral metabolism.(20) Tracings improve seven to ten days after commencement of treatment.(20)

Shulman suggested a preliminary screening of all psychiatric patients for haemoglobin level and blood film before further vitamin B₁₂ estimation.(22) However, this will exclude cases which present with mental symptoms in the pre-anaemic phase.(23) In practice, the routine screening of psychiatric population remains of doubtful value. It would seem preferable to confine attention to those at greatest risk, such as (1) patients with organic psychiatric illness of uncertain cause, (2) patients with unexplained fatigue, (3) anaemic patients, and (4) those with a history of gastric surgery.(22) Still it is important to consider vitamin B₁₂ deficiency in the differential diagnosis of all patients with unexplained acute organic states or dementing syndrome, and to pursue treatment vigorously at the earliest opportunity.

REFERENCES


ANSWER TO ELECTROCARDIOGRAPHIC CASE
Diagnosis: Ventricular tachycardia.

DISCUSSION

Broad complex tachycardia may be due to ventricular tachycardia (VT), supraventricular tachycardia with aberrancy or preexcited tachycardias due to an accessory pathway. The commonest cause is VT, comprising of more than 80% of all broad complex tachycardia. Another 15% is due to supraventricular tachycardia with aberrancy, and only about 5% is due to preexcited tachycardia due to an accessory pathway (i.e., atrioventricular septal defect, aortic arch anomalies, or others). Hemodynamic status and age should not be used in the differential diagnosis of a broad QRS tachycardia as there is too much overlap. The electrocardiographic features distinguishing VT from supraventricular tachycardia with aberrancy include atrioventricular dissociation, presence of capture or fusion beats, QRS duration > 140 ms for right bundle branch block and > 160 ms for left bundle branch morphology, positive or negative QRS concordance in the precordial leads, frontal plane axis showing left axis deviation. In patients with right bundle branch morphology VT, a monophasic R or biphasic QRS in V1 and a QS pattern or r/S ratio < 1 in V6 are more suggestive of VT whereas a triphasic QRS with a downward notch that touches the baseline in V1 with a small initial Q and r/S ratio > 1 in V6 are suggestive of supraventricular tachycardia with aberrancy. In patients with left bundle branch morphology VT, a broad R (≥0.04 sec) in V1 or V2, a notched or slurred downstroke on the S or QRS wave in V1/V2 and a distance of ≥70 ms from onset of ventricular complex to the nadir of the QRS or S in V1 or V2 were found to be highly predictive of VT. A diagnosis of supraventricular tachycardia with aberrancy will be favoured by a triphasic QRS complex in V1, ventricular rates > 170/min and presence of preexcitation syndrome.

In this patient, the ECG during tachycardia (Fig 1) showed no evidence of atrioventricular dissociation, capture or fusion beats. The QRS duration was 120 ms. The RBBB morphology is however biphasic and the axis is in the fourth quadrant which makes it very unlikely to be due to a supraventricular tachycardia with aberrancy. An electrophysiological test done, confirmed that the broad complex tachycardia was VT which was inducible by ventricular extrasystoles during isoproterenol infusion. The tachycardia had retrograde conduction over the His bundle and 1:1 ventriculoatrial conduction and thus atrioventricular dissociation could not be seen on the ECG. Atrioventricular dissociation, capture and fusion beats were demonstrable only by rapid atrial pacing. Verapamil was able to slow down and terminate the tachycardia. Post verapamil, tachycardia was no longer inducible. The ECG during sinus rhythm (Fig 2) illustrates T wave inversion in the lateral precordial leads. This is not seen in patients with supraventricular tachycardia unless associated with preexcitation. This form of tachycardia with RBBB and left axis deviation morphology is a relatively uncommon form of VT which is often misdiagnosed as supraventricular tachycardia with aberrancy. It is characterised by: (i) occurs in young asymptomatic patients without obvious organic heart disease (ii) ECG during sinus rhythm shows a repolarization abnormality (ST depression and T wave inversion) over the inferior and lateral precordial leads (iii) VT complex during the episodes of VT showed a RBBB and left axis deviation with a QRS duration of <140 ms and (iv) responds to verapamil. The suspected mechanism is triggered activity originating in the Purkinje system near the left posterior fascicle, although localized reentry within the His Purkinje system has been advocated by others. The treatment of such patients include drugs such as verapamil or beta blockers. Curative therapy may be achieved by catheter ablation.

REFERENCES: