Dual pathology as a result of spinal stenosis and vitamin B12 deficiency

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Abstract Vitamin B12 deficiency can confound the clinical assessment of patients presenting with features of spinal disorders. Speciality practice within spinal surgery may lead the clinician to a focus upon spinal explanations for symptoms and that belief may be reinforced by supporting imaging. In the presence of mainly sensory symptoms consideration and exclusion of non surgical causes needs to occur. This study aimed at identifying the prevalence of vitamin B12 deficiency; the presence of dual pathology on imaging performed; the implementation of replacement therapy and their subsequent clinical response as perceived by patients. This was performed through a retrospective review of patients presenting to specialist spine out-patient clinics over a 4-year period via access to pathology reports followed by a telephone survey. 457 patients were investigated of which 8.5% were vitamin B12 deficient. 70% of patients had repeat levels and 31% continued to be deficient. 26% of these patients were not placed on any supplemental therapy. 72% of patients on treatment had self perceived improved outcomes as compared with 55% not on treatment. 73% of patients underwent MRI/CT imaging. 59% of which had evidence of spinal stenosis. In older patients with sensory symptoms, the coexistence of B12 deficiency should be considered. Detection of deficiency with consequent treatment results in better global outcomes than no treatment. Unless the correct blood test is done, the pathology will remain undetected, and patients may continue with their primary symptoms despite high-risk spinal surgical procedures.

Keywords Spinal stenosis · Vitamin B12 · Peripheral neuropathy · Dysaesthesia · Coexisting pathologies

Introduction

Spinal stenosis is common and has few physical findings [1, 2]. The diagnosis is primarily based on self-reported symptoms and may be further supported by imaging. The symptoms of vitamin B12 deficiency are non specific and may overlap with those of spinal stenosis. They include numbness and tingling of extremities, ataxia, and other neurological disturbance. If left untreated the neurological changes may become irreversible. Diabetic patients have specific risk factors with prolonged use of metformin being related to vitamin B12 deficiency [3].

Radiographic features of spinal disorders have been extensively described in the literature with high levels of sensitivity and specificity in symptomatic individuals. However, radiographic features of degenerative spinal disorders are common amongst the general population [1, 2] with previous studies having identified a high prevalence (20–76%) of lumbar disc abnormalities [4] and radiographic features of cervical spinal cord compression on MRI scans in healthy asymptomatic individuals [5].

Interpretation of imaging for spinal disorders requires careful assessment and close corroboration with patient history and examination as radiographic features of spinal stenosis may not necessarily correlate with patient symptoms. Similarly, neurological symptoms and signs may not be associated with spinal disorders despite radiographic features of spinal pathology.

Patients referred for spinal assessment may not have been thoroughly investigated in the primary care setting and therefore reversible causes of peripheral neuropathy may

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not have been excluded or established. Identifying these patients is vital in order to ensure patients are not exposed to unnecessary investigations or surgical procedures and more importantly that correct diagnosis and treatments are established. Attention should be paid to features in the clinical assessment. Walking distance is an important distinguishing feature. Although patients with peripheral neuropathy may have difficulty in walking due to the loss of distal sensory awareness, spinal claudication with a claudication distance is rather specific to spinal stenosis.

Establishing a diagnosis may include tests of exclusion. Speciality practice within spinal surgery may lead to a focus upon spinal explanations for symptoms and that belief may be reinforced by supporting imaging. In the presence of mainly sensory symptoms consideration and exclusion of non surgical causes needs to occur.

Diabetes mellitus, hypothyroidism, vitamin B12 and other nutritional deficiencies are some of the many causes of peripheral neuropathy [6, 7] (Table 1). These may present with symmetrical peripheral neuropathy or mononeuropathy with varying combinations of dysaesthetic symptoms and weakness along with abnormal reflexes, mimicking features of spinal stenosis. Simple blood tests can be used to investigate these, the treatment of which may alleviate patient symptoms.

Vitamin B12 is one of eight water-soluble vitamins which are involved in the metabolism of every cell in the body, affecting DNA and fatty acid synthesis and regulation. It has a vital role in the normal functioning of the nervous system and production of blood cells. The deficiency of this vitamin has been shown to create an imbalance between CSF levels of myelinotoxic and myelinotrophic cytokines and growth factors, being a key factor in the pathogenesis of vitamin B12 deficient neuropathy [8]. On the other extreme, recent studies identify vitamin B12 assisting to alleviate indices of neuropathic pain in diabetic rats [9]. It has also been shown to be superior to nortriptyline in the treatment of diabetic peripheral neuropathy even in cases of normal vitamin B12 levels [10].

This study aims to raise the awareness of clinicians to the possible co-existence of vitamin B12 deficiency in spinal surgical outpatients. Treatment of this co-existing pathology may improve clinical outcomes. We aimed to establish the prevalence of vitamin B12 deficiency in patients presenting for spinal surgical assessment and secondly to audit their subsequent management.

Methodology

This was a retrospective cohort study in a University Hospital outpatient setting. The audit was registered locally within the trust.

Table 1 Causes of peripheral neuropathy

	Investigations
Trauma	EMG, NCS
Systemic disease	
Diabetes	Blood sugar
Kidney failure	Renal function
Liver disease	Liver function
Alcoholism	Liver function/USS liver
Hypothyroidism	Thyroid function tests
Vitamin deficiencies	Biochemical analysis
Autoimmune disorders (SLE, RA)	Autoimmune screen
Drugs (vincristine, metronidazole, amiodarone, phenytoin)	Plasma levels
Neoplasia	
Infections	
HIV/AIDS	FBC, HIV screening
Syphilis	STD screening, T pallidum assays
Guillain–Barre syndrome	Serology for mycoplasma, EBV, CMV, borrelia, VZV, coxsackie, campylobacter
Inherited	
Charcot–Marie–Tooth syndrome	EMG, NCS, genetic testing
Friedreich’s ataxia	ECG, EMG, NCS, muscle biopsy

The majority of the disorders listed here would be apparent from the history if diagnoses have been established. The investigations listed are not exhaustive. Simple haematological and biochemical tests should be ordered alongside these

EMG Electromyography studies, *NCS* nerve conduction studies, *FBC* full blood count, *EBV* Epstein–Barr virus, *CMV* cytomegalovirus, *VZV* Varicella Zoster virus

All patients screened for vitamin B12 levels over a 4-year period (2005–2008) were identified. Those patients with an abnormal result were further scrutinised for this study. Repeat testing was assessed and imaging reports reviewed to identify dual pathology. A structured telephone survey and outcomes study was conducted. The primary care clinicians were contacted and current clinical records were obtained.

Results

An average of 1800 new outpatients were seen each year. The study population was 457 patients (229 males; 228 females) which were investigated for vitamin B12 levels. 39 (8.5%) of these patients were vitamin B12 deficient (26 males; average age 63; range 23–83). Two deceased were excluded from the study. In three, contact details were

unobtainable and were excluded from the structured telephone survey.

26 of the remaining 37 patients had repeat vitamin B12 levels, 8 of which continued to have persistently low levels. There were 11 patients that had no evidence of repeat testing. 19 patients with B12 deficiency had not received adequate replacement therapy for a variety of reasons (Fig. 1).

27 of these 37 patients with vitamin B12 deficiency also had spine MRI or CT imaging performed (5 cervical; 22 lumbar). Although all of these patients had elements of coexisting degenerative changes, the majority (59%) had documented spinal stenosis (Fig. 2).

Results of phone survey

Of the 39 patients, 5 were excluded (2 deceased; 3 not contactable), leaving a total of 34 patients (87% follow up). 25 patients were on vitamin B12 supplemental therapy and 9 not; this was confirmed with their individual GPs. Patients were then asked to grade their perceived response to treatment according to the global outcome score (Fig. 3).

Fig. 1 Vitamin B12 deficient patients and subsequent follow up

Fig. 2 Imaging findings of patients with vitamin B12 deficiencies

Fig. 3 Global outcome scores of patients with vitamin B12 deficiency

72% of patients on treatment felt they had improved outcomes (much better/better) as compared with 55% of patients not on supplemental therapy. Furthermore, 7 of the 16 patients on supplements and 2 patients not on supplements all of which who rated their symptoms as 'better' did not have any further vitamin B12 levels reported and therefore the adequacy of treatment of their deficiency is not known ($P > 0.05$, Fisher's test).

Discussion

Vitamin B12 is important for the normal functioning of the neurological system, deficiency of which can result in varied neurological symptoms which may mimic those of spinal stenosis. In the era where imaging modalities are readily available, MR or CT imaging may often constitute the primary investigation, and other reversible causes may remain unrecognised. This can have a significant health impact on surgical patients as failure to identify and treat reversible causes may result in permanent and irreversible neurological damage. A goal of all treatment is to get the patient better quicker. Failure to identify co-morbidity slows recovery and may impair the response to surgery. There are cost implications for persistent symptoms after surgery in terms of investigations and persistent disability. Ideally, patients should be investigated for reversible

causes prior to specialist spinal referral. It is important to practice medicine in a holistic approach, and not simply concentrate on operative spinal disorders in specialised clinics. An index of suspicion such as a ‘burning’ nature to the pain, diabetic patients, particularly those on metformin, and patients with sensory symptoms at rest may warrant further metabolic investigations. Obvious risk factors for B12 deficiency should also alert the clinician (Table 2), as should other factors from the history which may cause peripheral neuropathy (Table 1). These should be investigated and treated accordingly prior to embarking on high risk spinal procedures.

The findings of this retrospective cohort study are fourfold. First, the prevalence of vitamin B12 deficiency as identified by this study is 8% in a subgroup of spinal patients. Only approximately 6% of the total pool of patients presenting to the spine outpatient department were investigated for vitamin B12 levels. No specific protocol exists for the investigation of vitamin B12 levels. As a result of this audit we would recommend that any patients ‘at risk’ with dysaesthetic symptoms should be investigated for potential reversible causes of peripheral neuropathy. It is standard practice within our clinics for such patients to have simple haematological, biochemical and endocrine tests, prior to or alongside specialised imaging.

Second, all of the patients who had imaging of their spine had evidence of spinal pathology, the majority of which was spinal stenosis followed by intervertebral disc disease. Degenerative features were found to coexist with the majority of these scans. Patients who were vitamin B12 deficient also had coexisting spinal pathologies, both of

which may be contributory to patient symptoms either individually or in combination.

Third, 72% of patients felt their symptoms to have improved following vitamin B12 supplementation as compared with 55% of patients without. However, this was not statistically significant. Although the global outcome score is a validated measure of subjective patient perception of symptoms, no objective measures were used. This coupled with the low patient numbers makes it difficult to draw any definitive conclusions. Nevertheless, the identification and treatment of vitamin B12 deficiency is important, not only to treat symptoms of peripheral neuropathy which if left may become irreversible, but also to prevent the haematological and other biochemical disturbances as a result.

Fourth, 26% of patients who were identified as being deficient were not placed on any supplemental therapy. Furthermore, 30% of patients were not investigated for further levels, and finally, 22% continued to be deficient implying inappropriate replacement therapy. Standard practice in our clinics is such that once abnormal results are identified, general practitioners are informed and replacement treatment left to the primary care provider. However, the results appear to identify an important failing of communication or the implementation of treatment which inevitably has great medicolegal implications and more importantly consequences on patient wellbeing.

Vitamin B12 deficiency, in addition to other biochemical and endocrinal abnormalities can confound the clinical assessment of patients presenting with features of spinal disorders, particularly in the presence of radiographic confirmed spinal stenosis.

Cross-sectional studies identify the prevalence of vitamin B12 to be from 12% [11] to as high as 44% [12] in patients greater than 65 years of age, with the prevalence predominantly affecting the male sex and increasing with age [11]. This parallels that of spinal stenosis which also tends to affect the elderly population and similarly that of imaging findings which convey increasing frequency of degenerative features with advancing age [1, 2]. With such parallel prevalence in these three diagnostic entities coupled with the similar/identical nature of clinical symptoms, vitamin B12 levels should be assessed in all patients presenting with features of spinal stenosis even in the presence of positive imaging findings.

We acknowledge the limitations of this retrospective study and in particular the selection bias that may be implied from only 6% of patients having been investigated for vitamin B12 levels. The reason for this is unclear. However, prior to the acknowledgement of the results of this study no consensus existed on biochemical investigations for potentially reversible causes of peripheral neuropathy. Patients with dysaesthetic symptoms or a

Table 2 Causes of vitamin B12 deficiency [13]

Pernicious anaemia
Dietary deficiency
Malabsorption
Crohn’s disease
Chronic pancreatitis
Whipple’s disease
Parasitic infections
Post surgical malabsorption
Gastrectomy
Terminal ileal resection
Food B12 malabsorption (inability to release B12 from food or intestinal transport proteins)
Atrophic gastritis
Chronic <i>H. Pylori</i> infection
Long terms antacid use
Chronic alcoholism
Idiopathic

description of ‘burning’ pain and any non-specific neurological symptoms would have been preferentially investigated and so that is where the selection bias occurs. It is impossible to quantify this on the data we have. Now our practice involves assessment of vitamin B12, folate, glucose and other biochemical abnormalities in all patients with dysaesthetic symptoms even if they have pathological symptom-related findings on MR imaging. Such abnormalities are initially corrected prior to embarking on more invasive procedures.

Conclusion

In older patients with sensory symptoms the coexistence of B12 deficiency should be considered. Detection of deficiency with consequent treatment results in better global outcomes than no treatment.

Despite blood abnormalities some patients did not receive therapy due to administrative failures of communication. Unless the correct blood test is done the pathology will remain undetected, and patients may continue with their primary symptoms despite high-risk spinal surgical procedures.

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Conflict of interest None.

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