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LETTER TO THE EDITOR

Chemotherapy-induced peripheral neuropathy (CIPN) and vitamin B12 deficiency

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Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) continues to be a major concern for oncological practise considering the increasing number of cancer survivors and the lack of standardised prevention or treatment [1]. The incidence of CIPN depends on the chemotherapy agent administered but is estimated to occur in one third of all patients undergoing chemotherapy [2, 3]. The prevalence of CIPN has been estimated to be 68.1 % the first month after the administration of neurotoxic chemotherapy agents and 60 % 3 months post chemotherapy treatment. Patients were found to still have 30 % prevalence 6 months or more after chemotherapy according to the results published in a systematic review conducted in 2014 [4]. Patients experiencing moderate to severe CIPN report a reduced quality of life [5], chronic discomfort [6] and disruption of physical abilities for general life activities which can be temporary or permanent [5].

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Currently in clinical practise, CIPN is assessed using the common toxicity scales; however, these rely heavily on the patient's subjective reports rather than quantitative testing [7]. CIPN is a potentially rescindable side effect although reversibility may be dependent on early detection or identification and modification of chemotherapy treatment [7]. Permanent CIPN has still been reported, especially sensory symptoms in the lower extremities among patients treated with oxaliplatin up to 11 years after treatment [8]. Early differential diagnosis and prevention of permanent CIPN need to be a priority for extending the quality of life of cancer patients.

Patients with a previous history of a vitamin B12 deficiency have been identified as a predisposing condition that may increase the risk of developing CIPN [5]. However, patients who have had no previous history of a vitamin B12 deficiency may not be tested before chemotherapy commences for vitamin B12 status. Moreover, a potential vitamin B12 deficiency may develop during chemotherapy administration [9] that can therefore potentially predispose the patient to developing and/or delaying the development of CIPN.

We present a clinical case of a cancer patient who developed CIPN and was found to be vitamin B12 deficient after completing a chemotherapy regimen. Upon vitamin B12 administration, the severity of CIPN decreased that allowed the patient increased functional ability in daily activities including the ability to walk.

Case study

A 53-year-old female was enrolled in a randomised clinical trial and was randomised to the placebo arm. Initial B group vitamin status pathology blood, a neurological exam involving the total neurology score (TNS) and electro-neurological examination in addition to other history and questionnaires,

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was conducted prior to the commencement of chemotherapy. The same independent neurologist following chemotherapy administration conducted the neurological examination and TNS. Blood vitamin B group pathology and questionnaires were assessed at post chemotherapy and at a 3-month follow-up visit. This patient's case report details and results are documented in Table 1.

The patient was overweight and generally healthy. The patient had been diagnosed with osteoarthritis with increased difficulty in walking, adding to this patient's weight issue. The patient worked in an office and had a generally sedentary lifestyle.

Blood pathology results

The blood pathology tests for this patient before chemotherapy was in the reference range, 107 pmol/L (ref range >35 pmol/L) presented in Table 2. After chemotherapy administration (Table 3 documents the chemotherapy regime), the vitamin B12 status decreased and was deemed as deficient as presented in Table 2 and Fig. 1. After supplementation with a B group vitamin complex (equivalent to 1000 μg/day of vitamin B12) and receiving one intramuscular vitamin B12 injection (dose 1000 μg), the blood vitamin B12 level reverted back to baseline (106 pmol/L). Other blood pathology conducted for B vitamin status including vitamin B1, B2, B6 and folate were found to be equivalent to baseline blood levels. The exception was vitamin B6, which had increased after supplementation with the oral B vitamin complex (95 nmol/L at baseline to 250 nmol/L reference range 35–110 nmol/L). Therefore, as vitamin B12 was the only B vitamin found deficient after chemotherapy administration, changes in the patient's neuropathy symptoms were correlated by administration of vitamin B12.

Results of the neurological testing

Total neuropathy score used in the clinical trial

The neurological test results presented in Table 4 showed that the patient's peripheral sensory and motor nerve function had decreased after chemotherapy administration compared to baseline. The neurologist's examination of the patient found no numbness, tingling or pain in the hands or feet at baseline. There was however noted interference to the electrical testing for the patient at baseline that occurred due to the application of copious amounts of a moisturiser just prior to testing. This interference with the electronic testing showed a mild impairment in motor function and interference with the baseline assessment of the sural nerve. The neurologist noted through

Table 1 Medical details of participant PMP

PA 032 PMP	Details
DOB	17/06/59
Diagnosed	Breast cancer in March, 2012
Surgery	PA Hospital 27 March 2012—right breast lumpectomy and axillary clearance
	Previous surgery: appendectomy, cholecystectomy, basal cell carcinoma on nose (flap repair)
Results	Grade II IDC and DCIS—oestrogen and progesterone positive, HER2 negative
Nodes positive/removed	0/9
Recruited for study	2 June 2012
Race	Caucasian
Marital Status	Married
Other medical considerations	Psoriasis, hypothyroidism, osteoarthritis, reactive arthritis, asthma (late onset), osteopenia, obesity
Medications	Thyroxin 100 mcg daily
Allergies	Codeine, pethidine
Diet history	No history of being a vegan or vegetarian. Normally consumes red meat (beef, lamb, kangaroo) three to four times a week, chicken or pork two to three times a week and fish or seafood approximately three to four times a week. She does drink caffeine, approximately four to five cups a day (tea), rarely drinks alcohol, does not smoke or take recreational drugs
Height	162 cm
Weight	129 kg
BMI	49.2
Chemotherapy regime	Carboplatin and docetaxel (TC) four times every 3 weeks

Table 2 Blood pathology results

Blood pathology	Baseline, 5 Jun. 2012	After chemo, 25 Sept. 2012	Last follow-up, 8 Dec. 2012	Ref range
Vitamin B1 (TDP)	140	140	180	66–200 nmol/L
Vitamin B2 (FAD)	280	310	230	180–470 nmol/L
Vitamin B6 (P5P)	95	90	250 H	35–110 nmol/L
Red cell folate	2249	2163	2170	>900 nmol/L
Holo TC (vitamin B12)	107	29 L	106	>35 pmol/L
Results from the PA Hospital		13 Jul. 2012	22 Jun. 2013	Ref range
Serum vitamin B12		H >1476	411	162–811 pmol/L
Red cell folate		1265	1290	545–3370 nmol/L
Serum ferritin		H 743	H 395	15–290 ug/L

assessment that despite the application of the moisturiser and impairment to ambulatory walking due to osteoarthritis, the motor nerves examined for the patient's hands and feet were all functioning within the normal reference ranges.

Following chemotherapy administration, the neurologist's examination and electronic testing of sensory and motor peripheral nerves reported a notable reduction in function. The patient was identified as exhibiting level 2 CIPN that confirmed numbness, tingling and neuropathic pain up to the ankle and the wrist of her lower and upper extremities, respectively. The pin sensibility is the test from the TNS that examines small nerve damage, and the patient's score after chemotherapy administration indicated that nerve damage was evident proximal to the wrist and ankle. Furthermore, there was loss of tendon reflexes, a hallmark representative of nerve damage. The sural nerve was not detectable by electronic testing at baseline or after chemotherapy administration.

Following the administration of an intramuscular injection of vitamin B12 (dose 1000 μg) with a concomitant oral administration of a vitamin B group complex (equivalent to 1000 μg per day of vitamin B12), sensory nerve function was restored to the fingers and toes (level 1 CIPN) after 60 days. Motor function remained unchanged, and pin sensibility still indicated nerve damage in the wrists and ankles. The sural nerve was positively detected. The patient's menopause-triggered severe hot flushes complicated the clinical neurological picture; this being indicative of autonomic nerve function involvement.

Neurological conduction studies

The neurologist conducted extra nerve conduction tests in addition to the tests required for the TNS. These electrical tests assessed large nerve activity. The nerve conduction study (NCS) normal values used were ascertained from the University of Michigan Medical School [10]. The NCS conducted on this patient indicated that nerve damage occurred after chemotherapy administration, of which the data is presented in Table 5. The main areas affected post chemotherapy administration were the hands (palms), wrists, sural nerve and in part the peroneal nerve. The sural nerve at baseline as discussed was unable to be found due to a large amount of

Table 3 Chemotherapy regime and administration

Date	5 Jun. 2012	26 Jun. 2012	17 Jul. 2012	7 Aug. 2012
Sodium chloride	100 mL IV	100 mLIV	100 mL IV	100 mL IV
Granisetron (3 mg)	3 mg IV	3 mg IV	3 mg IV	3 mg IV
Dexamethasone (8 mg)	8 mg IV	8 mg IV	8 mg IV	8 mg IV
Docetaxel (75 mg/m^2)	184 mg IV	184 mg IV	184 mg IV	184 mg IV
Cyclophosphamide (600 mg/m^2)	1480 mg IV	1480 mg IV	1480 mg IV	1480 mg IV
Discharge medication				
Ondansetron (oral)	8 mg BD×2 days	8 mg BD×2 days	8 mg BD×2 days	8 mg BD×2 days
Dexamethasone (oral)	8 mg BD×2 days	8 mg BD×2 days	8 mg BD×2 days	8 mg BD×2 days
Metolopramide (oral)	10–20 mg 4–6 HRLY PRN×5 days	10–20 mg 4–6 HRLY PRN×5 days	10–20 mg 4–6 HRLY PRN×5 days	10–20 mg 4–6 HRLY PRN×5 days
Dexamethasone (oral) to be taken the day before next chemotherapy	8 mg BD×1 day	8 mg BD×1 day	8 mg BD×1 day	
Pegfilgrastim INJ (6 mg) subcutaneous		6 mg ONCE×1 day	6 mg ONCE×1 day	6 mg ONCE×1 day

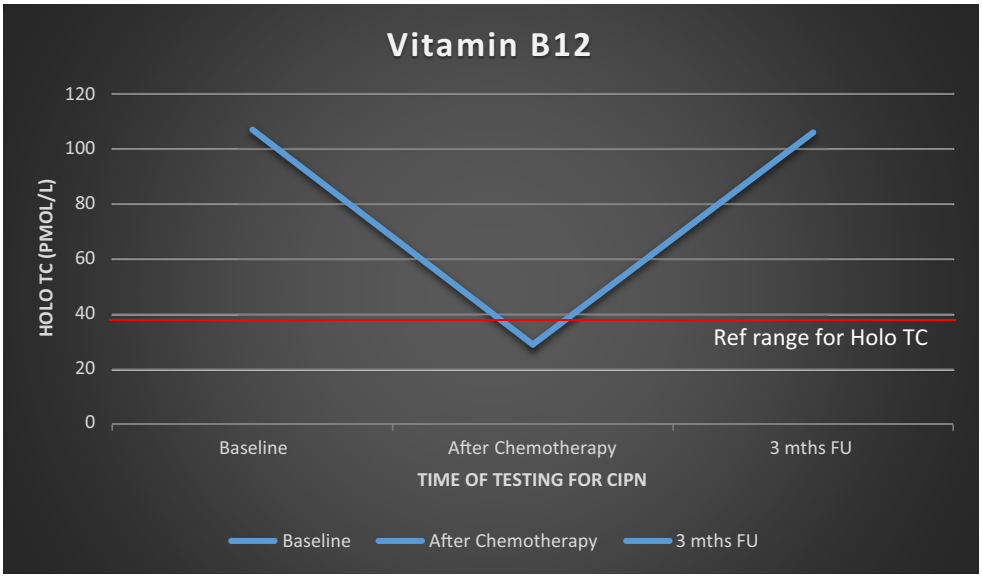

Fig. 1 Vitamin B12 results (Holo TC) for case study before and after chemotherapy

moisturiser applied by the patient prior to testing. This made it difficult to ascertain if damage had occurred or if the sural activity was low before chemotherapy administration. Considering the fact that the activity of the sural nerve had improved by the last neurological test, it can be postulated that there may have been some activity prior to chemotherapy.

The main nerves affected as demonstrated by the NCS tests were sensory nerves. The amplitude of the peroneal nerve was the only motor nerve identified as demonstrating decreased nerve function after chemotherapy administration. This is congruent with the symptoms displayed by the patient.

Results of patient neurotoxicity questionnaire

Throughout the clinical trial, patients were asked to complete a patient neurotoxicity questionnaire (PNQ). This is a linear scale and indicates the level of CIPN that the patient has experienced in the past week. The results of this patient's PNQ were 0 out of 4 at baseline for any numbness, pain, burning or tingling as well as difficulties with daily activities. At the 3-month follow-up visit, the patient registered 3 out of 4 for numbness, pain, burning or tingling in the arms and legs. Weakness in the arms and legs was 1 out of 4 at baseline and 3 out of 4 at the 3-month follow-up visit.

Two months after the intervention with an intramuscular (IM) injection of B12 and B vitamin supplement, the numbness, pain, burning, tingling and weakness of the arms and legs was ranked 1 out of 4 by the patient. The inference with daily activities was ranked 0 out of 4.

The results that documented post chemotherapy administration (25 August 2012) indicated that the patient had difficulties with buttoning clothes, zippers, typing on a keyboard,

Table 4 TNS results

Total neuropathy score (TNS)			
Item	Baseline score, 02 Jun. 2012	After chemotherapy, 25 Aug. 2012	3 Months later, 17 Jul. 2012, (2 months after beginning of B12 supplementation)
Sensory symptoms	0	2	1
Motor symptoms	1 (right hand sweating reduced testing)	2	2
Autonomic symptoms	1 (sweating)	1	2 (menopause post chemo)
Pin sensibility	0	2	2
Vibration sensibility	0	0	0
Strength	0	0	0
Tendon reflexes	0	4	2
Sural amplitude score	4	4	2
Peroneal amplitude score	0	0	0
Total	7	15	11

Table 5 NCS study results

Sensory NCS							
Nerve/sites	Rec site	Latency, Ms 2 Jun. 2012	Peak ampl, μV	Latency, Ms 25 Aug. 2012	Peak ampl, μV	Latency, Ms 17 Nov. 2012	Peak ampl, μV
R median Palm	III	1.30	4.3	2.8	10.2	2.85	4.9
L median Palm	III			2.70	12.0	3.30	5.0
L ulnar Wrist	Digit V	1.95	19.5				
R ulnar Wrist	Dorsum of hand	1.30	26.1	1.65	1.5	1.85	3.1
L ulnar Wrist	Dorsum of hand	1.65	13.2	1.70	3.6	1.65	3.9
R sural Calf	Lat malleolus			2.65	6.7	2.35	5.1
NB: First baseline tests were difficult due to moisturiser used by patient							
Motor NCS							
Nerve/sites rec site		Latency, Ms 2 Jun. 2012	Peak ampl, μV	Latency, Ms 25 Aug. 2012	Peak ampl, μV	Latency, Ms 17 Nov. 2012	Peak ampl, μV
L median—APB							
Wrist		5.10	7.7	4.45	8.0	3.80	7.7
Elbow		9.45	7.8	9.05	7.3	9.35	7.8
R comm peroneal—EDB							
Ankle		4.05	2.9	3.15	3.3	4.05	2.2
Fib Head		9.65	4.8	10.55	0.7	10.15	2.3
R tibial (knee)—AH							
Ankle		5.05	10.4	3.55	8.3	4.65	3.7

writing, walking, putting on jewellery, knitting, sewing, working and dialling or using a telephone. At the 6-month follow-up (17 November 2012) which is 3 months post administration of B12 and B group vitamins, all of the identified daily issues were resolved and no further difficulties were reported aside from some shortness of breath.

On 2 October 2012, the patient presented at the Princess Alexandra Hospital Breast Cancer Clinic following receipt of blood results. The patient's Holo TC (vitamin B12) result was reported as 29 (ref >35 results reported on 25 November 2012) indicating a deficiency in blood vitamin B12. The patient's oncologist was informed and requested administration of vitamin B12 intramuscularly (dose 1000 μg). The patient was also provided with three bottles of a vitamin B complex from the manufactures that supplied the active supplement for the clinical trial that the patient had been enrolled in. The patient was advised to take one capsule twice daily with food, morning and night. At the oncology appointment on 2 October 2012, the patient reported that numbness was present up to the hips in both legs and from the wrists to the elbows (grades 3 to 4 CIPN on the NCI-CTC scales as assessed by the oncologist). The patient was referred to a physiotherapist for the numbness (CIPN) and lymphoedema.

The patient reported 1 week later on 9 October 2012 significant improvement in CIPN symptoms which had reduced dramatically to the feet and hands. On 17 November 2012 which was the patient's 6-month follow-up, the patient described numbness in the toes and on the tips of the fingers to be approximately 50 %.

Other medical notes

The patient presented to the breast cancer oncology and radiation public clinic at the Princess Alexandra Hospital in Brisbane, Australia on 29 May 2012. After the first administration of the chemotherapy regime on 6 June 2012, the cancer care coordinator reported that the patient had experienced terrible joint and bone pain, severe diarrhoea and nausea. In addition, the patient had a rash and possible fistulas and mouth ulcers. Throughout the chemotherapy administration regimen, the patient reported severe joint and muscle pain; nausea and vomiting; fluid retention; CIPN; diarrhoea and a rash.

The patient had a history of hypothyroidism, which was medicated with 100 mcg of thyroxin daily as documented in Table 1. The patient's thyroid function was monitored throughout the chemotherapy administration regimen (TSH=5 and 4.5 mU/L). The full blood count and serum chemistry was representative of a patient undergoing chemotherapy with a low white cell count (WCC) and was neutrophilic, which recovered after chemotherapy cessation (WCC=1.5 to 5.4 ref range 4–11×10ˆ9/L, neutrophils 0.1 to 3 ref range 2–7.5×10ˆ9/L). The patient throughout chemotherapy regimen was borderline type 2 diabetic (blood glucose=6), experienced gout (uric acid 0.39 mmol/L ref range 0.14–0.35 mmol/L),

had raised liver enzymes (GGT=75 U/L, ALT=60 U/L, AST=56 U/L) and borderline calcium (2.24 ref range 2.24–2.65 mmol/L).

Discussion

The serum vitamin B12 as seen in Table 2 assists this case report in assessing the participant's vitamin B12 status pre and post chemotherapy administration. The patient was found deficient in vitamin B12 on 2 October 2012 (Holo TC 29 pmol/L) which is 3 months after the serum vitamin B12 test conducted on 13 July 2012 (>1476). This serum vitamin B12 blood test was taken the day before the patient's third administration of chemotherapy (17 July 2012). The raised serum vitamin B12 level found could be representative of liver damage. It has been found that when the liver is damaged, vitamin B12 is released giving a reading of high serum vitamin B12; [11, 12] however, tissue reserves are being depleted and the patient can result in a deficiency of vitamin B12 [11].

The blood pathology tests for this patient showed raised liver enzymes and a raised serum vitamin B12 level which could represent the liver releasing stored vitamin B12. The Holo TC is the active vitamin B12 blood pathology assay for blood levels of vitamin B12 being released from the liver and transported to body tissues [9]. Holo TC blood results have also been found to be raised from liver damage [11]; however, it has been reported that it can detect an early deficiency in vitamin B12 compared to serum vitamin B12 levels [9].

The patient's liver results indicated possible damage as noted by raised liver enzymes, so it may be postulated that it was releasing stored vitamin B12 resulting in a vitamin B12 deficiency 3 months post serum vitamin B12 test. This patient's vitamin B12 deficiency was symptomatic as displayed by the peripheral neuropathy and fatigue. Therefore, the differential diagnosis of the patient's symptoms included chemotherapy and a vitamin B12 deficiency.

According to the blood pathology tests, clinicians would normally not consider this patient's presentation of CIPN as a possible vitamin B12 deficiency in addition to the neuropathy from the chemotherapy due to the serum vitamin B12 results from July, 2012. Had the patient not participated in a clinical trial assessing B vitamin status, the vitamin B12 most likely would not have been re-tested as the previous tests indicated a saturated state. Therefore, this raises the question of whether testing vitamin B12 during chemotherapy is worthwhile. Similarly, it is difficult to ascertain whether it gives an accurate reading of the patient's vitamin B12 state.

Intrinsic factor antibodies play an important role in a vitamin B12 deficiency. If a patient is continually found to be low or deficient in vitamin B12 after chemotherapy, then testing for intrinsic antibodies would be indicated. However, if a patient's vitamin B12 level is in normal range without supplementation 6 to 12 months post chemotherapy, then testing for intrinsic factor or parental cell antibodies would not be indicated. For this patient, the serum vitamin B12 was 411 pmol/L 7 months post chemotherapy administration, which is in the reference range. The patient stated that during the 7 months post last neurological exam, no oral vitamin B12 supplementation was consumed nor had an intramuscular vitamin B12 injection been administered. Therefore, it can be assumed that this participant does not have intrinsic factor antibodies. The patient was given a pathology request form for intrinsic factor antibody test, but it was not performed.

The patient's baseline blood test indicated a normal vitamin B12 level as measured by Holo TC assay 107 pmol/L ref >35 pmol/L). Prior to the third cycle of chemotherapy, the patient's serum vitamin B12 was reported as elevated >1476 pmol/L (162–811 pmol/L). Subsequently, the patient's Holo TC assay after completion of the full chemotherapy regime indicated a deficiency in vitamin B12 (29 pmol/L ref >35). No other B vitamin markers were found to be deficient. After 2 months of vitamin B12 administration (1000 μg intramuscularly and 1000 μg taken orally daily), the vitamin B12 levels from the Holo TC assay had risen to 106 pmol/L (ref >35 pmol/L). Seven months post last blood pathology test, the patient's vitamin B12 levels was 411 pmol/L (162–811 pmol/L) without vitamin B12 administration indicating normal vitamin B12 absorption and metabolism and possibly no intrinsic factor antibodies.

The patient's neurological test showed no neuropathy at baseline, however displayed CIPN (grades 2 to 3 on NCI-CTC scales) after chemotherapy. After 2 months of vitamin B12 administration (1000 μg intramuscularly and 1000 μg taken orally daily), the patient's CIPN was reduced to the tips of the fingers and toes (grade 1 on NCI-CTC scales). Therefore, a patient experiencing a vitamin B12 deficiency while undergoing chemotherapy may display a severe CIPN. This presentation of severe CIPN is normally attributed to the administration of the neurotoxic chemotherapy agent, and vitamin B12 may not be tested. For this patient, the vitamin B12 status was tested and found to be deficient; therefore, the severe CIPN presentation was due to both the administration of the neurotoxic chemotherapy agent and a vitamin B12 deficiency. This diagnosis/presentation would have gone unnoticed without a request for vitamin B12 pathology blood test.

This case report indicates that chemotherapy administration may lower vitamin B12 status in certain patients and that this may predispose them to the development of peripheral neuropathy, possibly of increased severity. The development of peripheral neuropathy would then be causal due to both the neurotoxicity of chemotherapy administration and a concomitant vitamin B12 deficiency. The extent of the peripheral neuropathy from the chemotherapy agent cannot be ascertained until the patient's vitamin B12 status has been recovered towards a normal range.

The clinical relevance of this case study is of significant importance to clinicians as vitamin B12 is not a common pathology test requested in those patients presenting with moderate to severe CIPN due to vitamin B12 deficits following the administration of certain chemotherapeutic agents.

A vitamin B12 deficiency is medically acknowledged as causal for peripheral neuropathy and has been identified as a potential risk factor for differentially diagnosing the development of CIPN [3]. This then questions as to how and when should a request for testing the blood level of vitamin B12 be conducted and when to intervene with treatment for those diagnosed with a deficiency of vitamin B12. One of the confounding factors for cancer patients is the taste and smell of taking an oral B vitamin complex. For some patients, taking a prophylactic oral vitamin B complex is not an option during chemotherapy administration; therefore, intramuscular vitamin B12 injections maybe the only option for certain patients.

One option for clinical application may be to request vitamin B12 blood levels with every pathology test conducted before the administration of neurotoxic chemotherapy agents. Identifying those patients who are at increased risk of a vitamin B12 deficiency may lead to better patient management by reducing the risk of developing CIPN during chemotherapy administration with neurotoxic agents. The blood pathology level of serum vitamin B12 or Holo TC at which vitamin B12 treatment would be implemented would need to be determined. Neurological symptoms can be experienced by patients not undergoing chemotherapy at 200 pmol/L [11]; hence, the intervention range of vitamin B12 may be 250 pmol/L for serum vitamin B12 and 35 pmol/L for Holo TC. Therefore, prevention of neurological side effects from a vitamin B12 deficiency would be avoided, and the development of CIPN would only be from the neurotoxic chemotherapy agent.

The cost analysis of conducting vitamin B12 pathology tests for each patient being administered a neurotoxic chemotherapy agent is prohibitive. Hence, it is proposed that a vitamin B12 pathology test be conducted before chemotherapy administration and when the patient presents with moderate to severe CIPN. Patients may be advised to take an oral B vitamin complex or vitamin B12 supplement prophylactically through chemotherapy administration. Alternatively, a prophylactic IM injection of vitamin B12 may be administered to those patients deemed at risk of a vitamin B12 deficiency through chemotherapy administration.

Conclusion

Vitamin status, in particular vitamin B12, can play a role in the development of CIPN in certain patients. Patients experiencing moderate to severe CIPN should have their vitamin B12 levels pathologically tested, and if serum vitamin B12 levels are found below 200 pmol/L or Holo TC is below 35 pmol/L, then vitamin B12 should be administered intramuscularly and orally for the duration of the chemotherapy administration. Administration post chemotherapy for a period of approximately 3 months should be continued depending on the patient's tolerance for oral supplementation.

A protection from vitamin B12 may be inferred for CIPN development. Oral supplementation with a B vitamin complex or vitamin B12 supplement may reduce the risk of CIPN development in certain patients. However, some patients may not tolerate the smell of the vitamin B capsule or may have difficulty with ingestion of the supplement. Also, the pungent smell of their urine from the B vitamin supplementation can be off putting for some patients and may increase their feeling of nauseousness. As an alternative, intramuscular administration of vitamin B12 may be more appropriate for certain patients.

Monitoring of vitamin B12 levels may also be implemented, so early intervention with B12 administration can occur before the patient is found deficient. This could be through adding serum vitamin B12 to the blood pathology request forms for patients that will undergo chemotherapy with neurotoxic agents before chemotherapy cycles commence and at presentation of moderate to severe CIPN.

This case report outlines the importance vitamin B12 may play in CIPN development and the clinical relevance for medical practitioners.

Further clinical trials looking at vitamin B12 levels in patients with neurotoxic agents will be undertaken. The next study which is being designed is a clinical trial aimed at taxol agents only. One arm will be a control monitoring CIPN and vitamin B12 status with no intervention, and the other arm will be administered intramuscular vitamin B12 monthly during chemotherapy and 3 months post chemotherapy. This clinical trial is aimed at gathering further information pertaining to vitamin B12 levels during chemotherapy administration and possible prevention of CIPN.

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