A case report on the use of oral thiamine in a palliative care patient in the management of peripheral edema in a community setting in New South Wales, Australia

Vicki May Ling Tai

SUMMARY

Thiamine deficiency is common in malnourished states presenting with nonspecific symptoms including anorexia but may progress to irreversible neurological and cardiovascular sequelae if left unrecognised and untreated. A 42-year-old male with advanced lung cancer had visceral and neuropathic pain related to malignancy. Progressive oedema had been noted in hospital. Factors including heart failure, lymphatic obstruction, protein loss or deficiency were considered but multiple investigations including blood tests such as serum albumin, echocardiography and radiology failed to determine an underlying cause. An analgesic review prompted a switch of opioid and a change in delivery route from oral to subcutaneous. In terminally unwell patients medications given subcutaneously is not unusual. After stabilising, the patient elected discharge home. The community nurse subsequently reported difficulty accessing subcutaneous sites due to oedema.

Review of records revealed thiamine deficiency had not been considered. Shortly after oral supplementation an improvement in oedema was noted by the patient, his wife and the community and palliative care nurses. The patient reported increased diuresis without increase in fluid intake within days. Contours of his face became more defined with swelling of ankles, calves and arms with “woody” induration of his skin from chronic distension improving. The patient reported improved comfort of his skin. Diuretic doses needed reduction in the month following.

Mechanisms for thiamine deficiency include inadequate intake, increased utilization or increased loss. Cancer patients are known to be prone. There is a spectrum of disorders associated with thiamine deficiency; the underlying cause attributed to inhibition of a series of enzyme- catalysed reactions. Organ systems affected may include the nervous system, eye, gastrointestinal tract, heart and blood vessels. Body storage of thiamine is minimal and may be depleted within two weeks. A major limitation to this report is lack of evidence of thiamine deficiency. Thiamine status can be determined by erythrocyte transketolase activity or whole blood thiamine levels but technical and practical issues meant that it was not done in this patient. Guidelines suggest supplementation prior to verification of deficiency is valid as thiamine is nontoxic.

Thiamine supplementation is inexpensive and safe; deficiency states are insidious in presentation. Micronutrient deficiency states in frail patients may be mistaken for expected decline. Peripheral oedema is common towards the end of life and may lead to loss of skin integrity, infection and skin discomfort. Thiamine supplementation was commenced as an “outside chance” but had surprisingly good results. There were no other variables in this case. Several questions are now raised and hopefully more research will be done in this area.

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CASE REPORT

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ABSTRACT

Introduction: Thiamine deficiency may present insidiously and has a spectrum of symptoms. Whilst outbreaks occur in developing countries, select communities in developed countries are also susceptible. Body stores of thiamine are low and depleted easily. Initially, deficiency may present with anorexia, malaise, generalized weakness and paresthesias with edema and palpitations. Over time it may progress to frank peripheral neuropathy and cardiac involvement [1]. Palliative care patients are frail, often malnourished with weight loss with catabolic states contributing to deficiency of micronutrients. Symptoms as described are often attributed to underlying disease or treatment received. A previous study found high rates of thiamine deficiency in terminally ill patients admitted to a palliative care unit [2]. **Case Report:** A 42-year-old Aboriginal Australian male community based palliative care patient with peripheral edema affecting quality of life and access of subcutaneous sites for medications received thiamine supplementation. This resulted in improvement of edema, access of subcutaneous

sites for medications and most importantly patient satisfaction and comfort. **Conclusion:** Thiamine deficiency should be considered in the frail, malnourished. Presentation may be insidious and symptoms may be overlooked in those who are palliative. Supplementation is inexpensive. Biochemical verification is not always feasible and for practical reasons often supplementation precedes detection. More research needs to be done in this area.

Keywords: Edema, Malnourished, Micronutrient, Palliative, Thiamine deficiency

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Tai Vicki¹

Affiliations: ¹MB, ChB, BAO (NUI), LRCPI&SI, FRACP, FACHPM, FRCP(Glasg), Staff Specialist, Central Coast Palliative Care Services, New South Wales, Australia; Conjoint Fellow, School of Medicine and Public Health, The University of Newcastle, New South Wales, Australia.

Corresponding Author: Vicki May Ling Tai, Central Coast Palliative Care Service, Killarney Vale, NSW, Australia, NSW 2261; Ph: +61 2 43367777; Fax: +61 2 43367773; Email: Vicki.Tai@health.nsw.gov.au

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INTRODUCTION

Thiamine (vitamin B1) is an important coenzyme in carbohydrate metabolism and a deficiency syndrome is well described in literature [1]. Once deficiency is recognized, replacement therapy is relatively inexpensive and safe. Severe deficiency may lead to death.

Insidious presentation may occur after prolonged dietary deficiency and susceptible individuals include those who are malnourished with poor protein-calorie balance. It has been noted that it is surprising that thiamine deficiency as a cause of cognitive impairment in the palliative care setting has not been more recognized [2] and reports have focused on neurological and

neuropsychiatric sequelae [2, 3]. Palliative care patients commonly have anorexia, malaise and generalized weakness. Nausea and vomiting is not uncommon, also affecting nutritional intake. Peripheral edema has been used in prognostic prediction models in palliative care settings [4]. All of the aforementioned signs and symptoms are also known to occur in thiamine deficiency.

CASE REPORT

A 42-year-old Aboriginal male with advanced metastatic non-small cell lung cancer was reviewed as a palliative care patient in the community. During an inpatient stay one month prior with pneumonia, an increase in his peripheral edema had been noted. Investigations including an echocardiogram, ventilation perfusion scan and left upper limb venous Doppler did not reveal any contributors. His serum albumin and renal function were normal (Table 1). He was commenced on diuretics and completed his antibiotic treatment.

Table 1: Blood tests done as inpatient one month prior to commencement of thiamine

Test	Result	Reference range	Units
Sodium (Na)	138	134–145	mmol/L
Potassium (K)	3.6	3.5–5.0	mmol/L
Chloride	95	98–107	mmol/L
Bicarbonate	31	22–29	mmol/L
Urea	7.8	3.1–8.1	mmol/L
Creatinine	75	64–104	umol/L
Anion Gap	16	7–17	mmol/L
Estimated GFR (CKDEPI)	106	Regarded as normal high	mL/min/1.73 m ²
Bilirubin	5	3–20	umol/L
Protein	70	60–83	g/L
Albumin	38	35–52	g/L
Alkaline Phosphatase	102	41–119	U/L
Gamma GTP	119	12–64	U/L
ALT	36	<55	U/L
AST	29	12–36	U/L
Calcium	2.36	2.10–2.55	mmol/L
Corrected Calcium	2.40	2.10–2.55	mmol/L
PO ₄	1.12	0.74–1.52	mmol/L
Mg	0.86	0.67–1.05	mmol/L
CRP	45	<5	mg/L
WBC	14.9x10 ⁹	4–11x10 ⁹	/L
Hb	126	135–180	g/L
Plts	189x10 ⁹	150–400x10 ⁹	/L
TSH	0.595	0.4–3.5	mIU/L

Prior to discharge, a discussion with his Oncology team included a ceiling of care discussion, the patient declining any escalation of care beyond that for symptomatic management and wished to return home for terminal care. Significant right sided chest wall pain was attributed to metastatic replacement of the lateral right fourth to seventh rib involvement.

His pain control had been complex and at the time of review included both neuropathic and strong opioids. Strong opioids were delivered via a subcutaneous syringe driver over 24 hours and he had required multiple additional “as required” doses to help control pain. Suitable subcutaneous sites were limited due to edema. Interventional pain management had been discussed but the patient refused. A review of his records post discharge revealed that thiamine deficiency had not been considered. A discussion revealed that the patient had particularly poor dietary intake.

CASE MANAGEMENT

Oral thiamine at a dose of 100 mg three times daily was commenced. The dose of the neuropathic agent was maximised but rapidly had to be reduced to baseline due to side effects of myoclonus. There had been no recent changes with regard to his diuretic management. Approximately, one week subsequent to thiamine initiation, Patient’s wife and the community palliative care nurse noted improvement in both facial and lower limb edema. A subsequent review visit by the Author also affirmed this with noted particular resolution of lower limb edema. The patient reported increases in urinary output most marked in the days subsequent to supplementation. Dry mucous membranes and skin prompted the dosages of his diuretic medication to be reduced in the month following. There was some improvement in his pain level requiring fewer “as required” opioid doses. In the weeks following the implementation, there was discussion regarding a staged switch in route from subcutaneous back to oral opioid. Unfortunately, in the weeks following review the patient was admitted with increasing shortness of breath related to a chest infection and died.

DISCUSSION

Thiamine deficiency may produce a spectrum of symptoms ranging from mild and non specific nature to life-threatening. Whilst known to affect those whose diet is poor, and observed in those who have a higher demand of thiamine, such as the pregnant, it is also seen in association with certain diseases including cancer, liver disease, infections and hyperthyroidism. In more affluent societies, deficiency is common in alcoholics and may progress to Wernicke-Korsakoff syndrome. The subject in this case presentation had cancer, a poor dietary intake and edema unexplained by routine investigations.

The supplementation of thiamine resulted in reported diuresis, reduction of peripheral edema, improved skin integrity and comfort and access of subcutaneous sites.

This case report was limited by several factors. It was not practicable to test for thiamine levels in this community setting. We, therefore, do not have direct evidence of either deficiency or replenishment, however, there were no other factors to explain the improvement of his edema other than the temporal relationship between supplementation and resolution of edema.

Several questions are raised. Should we more frequently assess for thiamine or micronutrient deficiency in the palliative care population? What impact will it have if we do so? How do we make those tests more readily available and what would we use as our screening criteria?

CONCLUSION

Consideration of possible thiamine deficiency and supplementation may assist in symptom management in the palliative care setting. With this patient, improvement in peripheral edema particularly in the first few weeks following commencement of thiamine allowed us to continue using subcutaneous medications and improve comfort. There is a limitation to this report. There were no rigorous biochemical and measurement data to confirm initial thiamine deficiency and results of repletion in this patient. Several questions are raised and more work needs to be done in this area.

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Author Contributions

Vicki May Ling Tai – Substantial contributions to conception and design, Acquisition of data, Analysis

and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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