# A case of Miliary Pulmonary Tuberculosis complicated by refractory hypercalcaemia following vitamin D replacement

Poster EP28
Bone and Calcium

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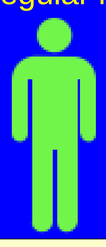
## CASE HISTORY

A 54-year-old man was admitted to hospital with a new diagnosis of Miliary Pulmonary Tuberculosis (TB). Early in admission he developed septic shock with multiorgan failure requiring organ support and anti-TB medications. Recovery was complicated by persistently low Glasgow coma score (GCS), noradrenaline dependency and limb threatening microvascular injury. At day-25 he was apyrexial but remained hypotensive and drowsy with no evidence of sepsis or hypoadrenalism. Over the next 48 hours, he showed signs of rapid recovery as alertness normalised and blood pressure improved; noradrenaline was withdrawn, allowing him to leave bed and engage in active rehabilitation. He was found to be mildly hypocalcaemic and severely vitamin D deficient. Vitamin D replacement was commenced with a weekly Colecaliferol (40,000 units) regime. Unexpectedly, recovery was severely setback during Vitamin D replacement which unmasked refractory symptomatic hypercalcaemia.

## EARLY HOSPITAL ADMISSION

54M
- Homelessness
- Alcohol dependence
- Current Smoker
- No kown PMHx
- No regular meds

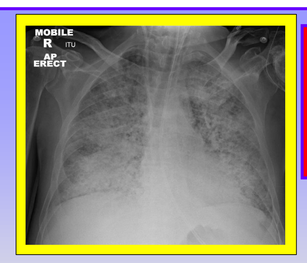


Emergency Department
- Chronic Cough
- Fever
- Triggers for sepsis
- Septic six

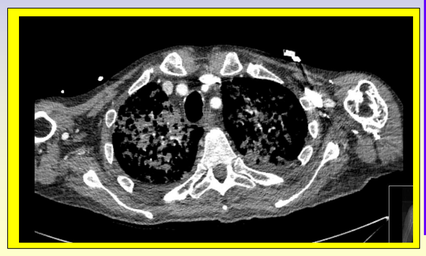
Investigations:
Selected Blood Tests
- Ca (adj) 2.14 mmol/L
- Vitamin D 7.0 nmol/L
- FT3 < 1.5 pmol/L

Imaging
- CXR & CT-chest
- Echo

Other
-Bronchial washings (AFFB) Mycobaterium TB



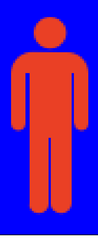

**CXR**
**Extensive confluent infiltrates throughout**



**CT-Chest**
**Widespread infiltrates and cystic airsapces predominantely in upper lobe**

## PROLONGED HOSPITAL ADMISSION (15 months)

ITU Admission
- Septic shock
- Assisted Ventilatory support
- Inotropes
- Haemofiltation
- Blood products



**Treatment and factors improving ITU recovery**

1. Intravenous Levofloxacin/Amikacin/Isoniazid/Rifampicin >>> Nasogastric regime Moxifloxacin/Pyrazinamide/Isoniazid/Rifampicin
2. Levothyroxine for acquired hypothyroidism following euthyroid sick syndome (non-thyroidal illness)
3. Addition of Prednisolone for recurrent Miliary TB; unintentionally effect of treating hypercalcaemia
4. Weaning respiratory support and physiotherapy

**Treatment and factors delaying ITU recovery**

1.Colecaliferol (40,000 units) regime >>> refractory hypercalcaemia [Ca peak 4.69 mmol/L; Vitamin D 7.0 >> 105 nmol/L (few weeks), PTH < 0.7 pmol/L {fully suppressed}, Myeloma screen –ve, ACE 83 U/L]
2. Preripheral vascular disease, Ischaemic left leg wityh necrotic toes; intravascular injury
3. Recurrence of chest sepsis
4. Persistent hypotension – short course of Fludrocortisone; Short Synachen test - normal

## DISCUSSION

The Institute of Medicine (IOM) and National Osteoporosis Society recommend a target Vitamin D of 50 nmol/L or greater. The National Osteoporosis Society guideline further advocates Vitamin D replacement treatment when total vitamin D is less than 30 nmol/l or is between 30–50 nmol/L for individuals with additional clinical risk factors such as chronic kidney disease. In recent years numerous regimes for high dose Vitamin D replacement have been published for patients with Vitamin D deficiency. The Endocrine Society advocate initial Vitamin D dose 50,000 units once weekly for 8 weeks with aim to reach a threshold target of greater than 75 nmol/L and maintenance Vitamin D [1,500-2,000 units/day] therapy thereafter. The Osteoporosis society suggests a total replacement of 300,000 IU as split weekly doses (50,000 IU for six weeks; or 40,000 IU for seven weeks) or as split daily doses (800 IU, five a day for 10 weeks). Similarly, the Australian and New Zealand Bone and Mineral Society (ANZBMS), Endocrine Society of Australia (ESA) and Osteoporosis Australia guidelines recommend a replacement strategy 50,000 units of Vitamin D2 or D3 once monthly for 3-6 months with maintenance Vitamin D 1,000 units/day therapy thereafter. It is important to remember that the Vitamin D DRI's and Vitamin D replacement regimes were not intended to cover persons with disease states such as Miliary Pulmonary Tuberculosis. In cases of symptomatic Vitamin D deficiency or severe hypocalcaemia due to vitamin D deficiency (calcium <1.9 mmol/L is a medical emergency) rapid Vitamin D replacement may be desirable. However, such vitamin D loading regimes may not be applicable to the critical ill patient where there are multiple acute physiologically adaptive processes taking place.

## CONCLUSIONS

In this case report, this critically ill patient had severe Vitamin D deficiency but only mild hypocalcaemia. He developed life threatening hypercalcaemia due to Vitamin D replacement. In this case we hypothesis that there was an upregulation of CYP27B1 1-alpha hydroxylase in TB granulomas similar to that seen in the macrophages in sarcoidosis. It is apparent from this case report that rapid super-physiological correction off Vitamin D using current Vitamin D replacement guidance; led to problematic symptomatic hypercalcaemia and prolonged recovery time. Caution should be exercised when using high dose Vitamin D in critically ill patients with vitamin D deficiency, particularly those with granulomatous disease. When Vitamin D replacement is needed we suggest both 25-hydroxyvitamin D3 and calcium levels are closely monitored. It would therefore seem prudent to stratify critically ill patients with granulomatous disease into a closely monitored group with calcium, phosphate, parathyroid hormone and 25-hydroxyvitamin D3 monitoring to optimise recovery times.

## REFERENCES

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