Clinical Communication to the Editor:

Glucocorticoid induced hypocalcaemia in a patient with established hypoparathyroidism

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ABSTRACT

We report the case of a 61 year old woman with a background of hypoparathyroidism following thyroidectomy who developed clinically significant hypocalcaemia and tetany following the administration of high dose glucocorticoid therapy for giant cell arteritis (GCA). After repeated hospital admissions her calcium concentrations were eventually stabilised after intravenous calcium infusion,oral calcium carbonate and alfacalcidol with ongoing follow up under Rheumatology and Endocrinology departments. Glucocorticoids are known to affect calcium balance via reduced intestinal absorption and increased urinary excretion but are not thought to cause clinically significant hypocalcaemia. This case adds to the list of isolated reports noting significant hypocalcaemia developing post administration of glucocorticoids in a patient with known hypoparathyroidism, postulating PTH deficiency as a risk factor of decompensated calcium homeostasis in such scenarios.

CASE REPORT

A 61 year old female was referred to local endocrinology team with symptomatic hypocalcaemia. She had a history of iatrogenic hypoparathyroidism following total thyroidectomy in 2006 for multinodular goitre. She was stable on combined calcium and vitamin D supplementation

She initially admitted in January 2020 with night sweats, weight loss, headaches and diplopia. She was started on prednisolone 40mg OD for presumed GCA. She went on to have a PET-CT scan which demonstrated large vessel vasculitis.Prednisolone was subsequently increased to 60mg by Rheumatology with a weaning regimen.

In March 2020, she presented with severe paraesthesia and cramping of the extremities. Subsequent investigations confirmed these to be secondary to significant hypocalcemia (corrected calcium: 1.78mmol/L) and hypophosphatemia (phosphate 0.45mmol/L). Electrocardiography revealed normal QTC intervaland remaining biochemistry included: –normal parathyroid hormone (PTH) 32ng/L, replete 25OH-VitD120nmol/L, and low Magnesium 0.76mmol/L. She received IV calcium gluconate in addition to phosphate and magnesium infusions and her corrected calcium was 2.19mmol/L prior to discharge.

Unfortunately she was readmitted again the following day with recurrent, symptomatic hypocalcemia (corrected calcium 1.95mmol/L, phosphate 0.93mmol/L, magnesium 0.65mmol/L). She had further calcium gluconate and magnesiuminfusions. After endocrine review, vitamin D3 supplementation was discontinued and she was commenced on active vitamin D3 metabolite Alfacalcidol and oral calcium carbonate. During a 6 day admission calcium concentrations stabilised at 2.19mmol/L until discharge.

In the 4 month follow-up period post discharge she remained asymptomatic with normocalcemia . Prednisolone therapy was weaned to 30mg and Methotrexate was added for GCA.

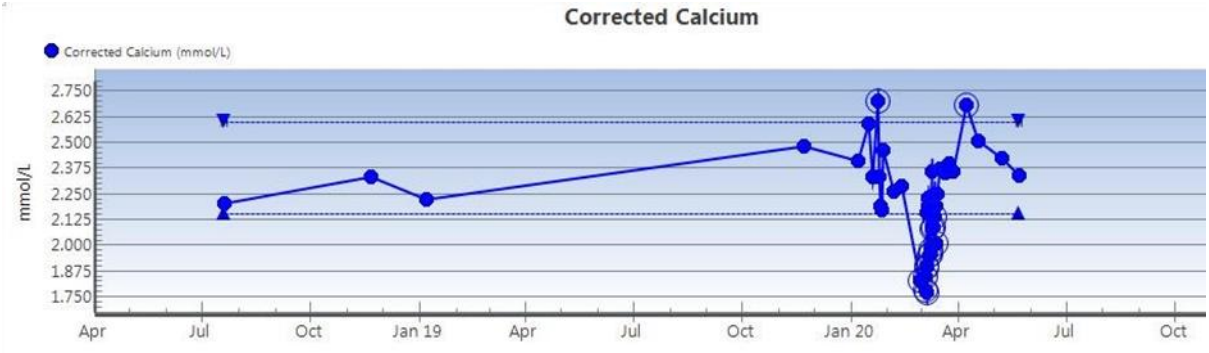

Figure 1 – Serum calcium concentrations plotted before and after commencement of glucocorticoid therapy with high dose prednisolone for GCA. I would propose you plotted this on excel instead using American units (you could do plots for both American and UK if you want but add in one figure. I mean to plot graphs put next to each other in the same figure). The reference two horizontal lines are better if with a different colour

DISCUSSION

In this case on the background of previously stable calcium levels we hypothesize a disruption of calcium homeostasis triggered by high dose glucocorticoid therapy leading to eventual profound hypocalcaemia. The notion of glucocorticoid linked hypocalcaemia is evidenced from literature and experimental studies. The likely pathways underlying this are decreased intestinal absorption of calcium and an increase of urinary calcium excretion [1]. In mouse studies dexamethasone led to a significant reduction of expression of the cytosolic calcium binding protein - calbindin-D9k (CaBP-9k) in the duodenum which could have a notable role to play [2].

A compensatory PTH rise has been noted from human studies. This includes a study by Suzuki Y et al. in which 44 participants on glucocorticoid therapy against controls were found to have elevated PTH, nephrogenous cAMP and fasting urinary calcium levels [3]. It is postulated that steroids may have a direct effect on the glandular secretion of PTH via increased gene transcription and enhanced efficiency of post receptor signalling [4]. This is in addition to a PTH rise indicative of secondary hyperparathyroidism mediated through negative feedback to the calcium sensing chief cells on the parathyroid gland. It likely that in our case in the presence established hypoparathyroidism and the absence of these PTH related protective measures, there was a predisposition to hypocalcaemia after her high dose steroid therapy had been commenced.

Studies reveal glucocorticoid induced hypocalcemia is independent of vitamin D status and its biochemically active metabolites, although there is some evidence to the contrary [5].

This case follows four other cases describing glucocorticoid related hypocalcaemia on the background of hypoparathyroidism [6,7]. The first published in 1964 relates to a 38 year old woman with latent hypoparathyroidism commenced on prednisolone for arthritic pains [8]. More recently Oikonomou D *et al.* describe a 29-year-old woman with hypoparathyroidism complicating subtotal parathyroidectomy presenting to the emergency department with tetany and hypocalcaemia after recent IV glucocorticoid administration for an allergic skin reaction [9].

CONCLUSION

On the background of established hypoparathyroidism, glucocorticoid therapy may lead to clinically significant hypocalcaemia and tetany. This may necessitate admission and intravenous calcium replacement. Routine calcium monitoring of patients commenced on glucocorticoids in this higher risk group should be considered.

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