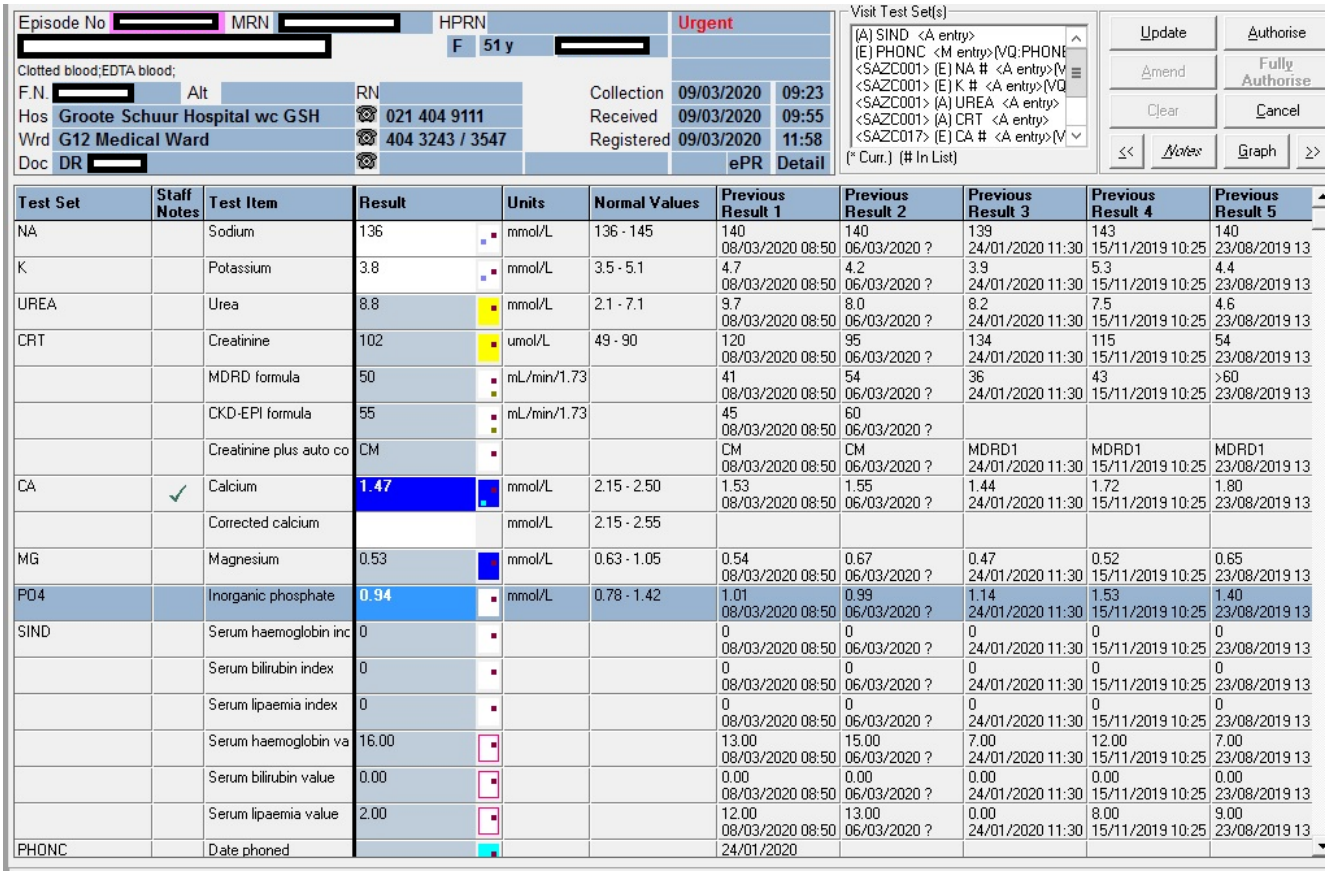
A case of persistent hypocalcemia

HOSP #	MRN63985901	WARD	Medical Ward
CONSULTANT	Dr. Heleen Vreede	DOB/AGE	51 year Female

Abnormal Result



Episode No [redacted] MRN [redacted] HPRN Urgent

[redacted] F 51 y [redacted]

Clotted blood;EDTA blood;

F.N. [redacted] Alt RN

Hos Groote Schuur Hospital wc GSH ☎ 021 404 9111 Collection 09/03/2020 09:23

Wrd G12 Medical Ward ☎ 404 3243 / 3547 Received 09/03/2020 09:55

Doc DR [redacted] ☎ Registered 09/03/2020 11:58

ePR Detail

Visit Test Set(s)

(A) SIND <A entry>
(E) PHONC <M entry>[VQ:PHONE
<SAZC001> (E) NA # <A entry>[V
<SAZC001> (E) K # <A entry>[VQ
<SAZC001> (A) UREA <A entry>
<SAZC001> (A) CRT <A entry>
<SAZC017> (E) CA # <A entry>[V
(* Curr.) (# In List)

Update | Authorise | Amend | Fully Authorise | Clear | Cancel | << | Notes | Graph | >>

Test Set	Staff Notes	Test Item	Result	Units	Normal Values	Previous Result 1	Previous Result 2	Previous Result 3	Previous Result 4	Previous Result 5
NA		Sodium	136	mmol/L	136 - 145	140 08/03/2020 08:50	140 06/03/2020 ?	139 24/01/2020 11:30	143 15/11/2019 10:25	140 23/08/2019 13
K		Potassium	3.8	mmol/L	3.5 - 5.1	4.7 08/03/2020 08:50	4.2 06/03/2020 ?	3.9 24/01/2020 11:30	5.3 15/11/2019 10:25	4.4 23/08/2019 13
UREA		Urea	8.8	mmol/L	2.1 - 7.1	9.7 08/03/2020 08:50	8.0 06/03/2020 ?	8.2 24/01/2020 11:30	7.5 15/11/2019 10:25	4.6 23/08/2019 13
CRT		Creatinine	102	umol/L	49 - 90	120 08/03/2020 08:50	95 06/03/2020 ?	134 24/01/2020 11:30	115 15/11/2019 10:25	54 23/08/2019 13
		MDRD formula	50	mL/min/1.73		41 08/03/2020 08:50	54 06/03/2020 ?	36 24/01/2020 11:30	43 15/11/2019 10:25	>60 23/08/2019 13
		CKD-EPI formula	55	mL/min/1.73		45 08/03/2020 08:50	60 06/03/2020 ?			
		Creatinine plus auto co	CM			CM 08/03/2020 08:50	CM 06/03/2020 ?	MDRD1 24/01/2020 11:30	MDRD1 15/11/2019 10:25	MDRD1 23/08/2019 13
CA	✓	Calcium	1.47	mmol/L	2.15 - 2.50	1.53 08/03/2020 08:50	1.55 06/03/2020 ?	1.44 24/01/2020 11:30	1.72 15/11/2019 10:25	1.80 23/08/2019 13
		Corrected calcium		mmol/L	2.15 - 2.55					
MG		Magnesium	0.53	mmol/L	0.63 - 1.05	0.54 08/03/2020 08:50	0.67 06/03/2020 ?	0.47 24/01/2020 11:30	0.52 15/11/2019 10:25	0.65 23/08/2019 13
PO4		Inorganic phosphate	0.94	mmol/L	0.78 - 1.42	1.01 08/03/2020 08:50	0.99 06/03/2020 ?	1.14 24/01/2020 11:30	1.53 15/11/2019 10:25	1.40 23/08/2019 13
SIND		Serum haemoglobin inc	0			0 08/03/2020 08:50	0 06/03/2020 ?	0 24/01/2020 11:30	0 15/11/2019 10:25	0 23/08/2019 13
		Serum bilirubin index	0			0 08/03/2020 08:50	0 06/03/2020 ?	0 24/01/2020 11:30	0 15/11/2019 10:25	0 23/08/2019 13
		Serum lipaemia index	0			0 08/03/2020 08:50	0 06/03/2020 ?	0 24/01/2020 11:30	0 15/11/2019 10:25	0 23/08/2019 13
		Serum haemoglobin va	16.00			13.00 08/03/2020 08:50	15.00 06/03/2020 ?	7.00 24/01/2020 11:30	12.00 15/11/2019 10:25	7.00 23/08/2019 13
		Serum bilirubin value	0.00			0.00 08/03/2020 08:50	0.00 06/03/2020 ?	0.00 24/01/2020 11:30	0.00 15/11/2019 10:25	0.00 23/08/2019 13
		Serum lipaemia value	2.00			12.00 08/03/2020 08:50	13.00 06/03/2020 ?	0.00 24/01/2020 11:30	8.00 15/11/2019 10:25	9.00 23/08/2019 13
PHONC		Date phoned				24/01/2020				

Total calcium of 1.47 mmol/L (2.15 – 2.50)

Presenting Complaint

The patient has been having persistent hypocalcemia despite supplementation with calcium.

History

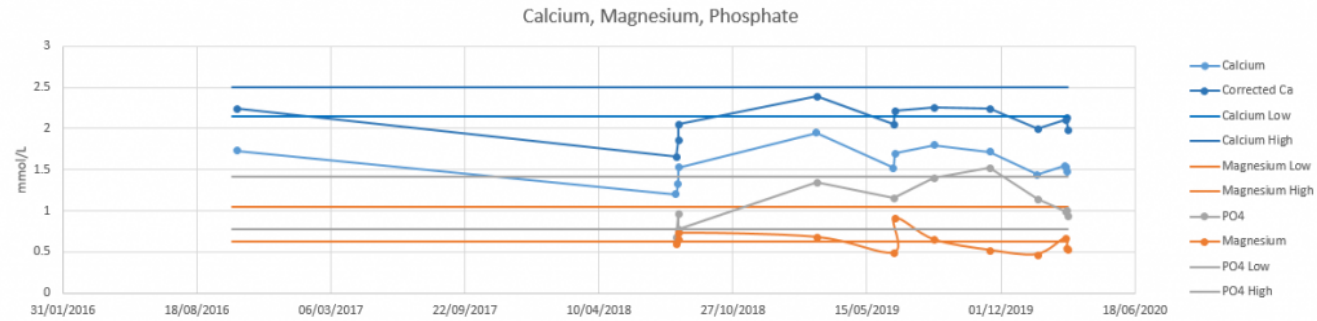


Figure 1 – Illustration of the patient's CMP over time: Calcium: blue; Magnesium: orange; Phosphate: grey
Reference ranges are the horizontal lines without dotted markers

Examination

Not available.

The typical findings in a patient with true hypocalcemia (low ionised calcium) are

Trouseau's sign

Chvostek's sign

Laboratory Investigations

Arguably, the first important consideration in patients with low calcium is the albumin. The patient had a mean albumin of 12 g/L, significantly lower than normal (40-50g/L). Arguably, the calcium can be corrected with the well known Payne's formula to then be 1.47 + (0.02 x (40-12) = 2.03 mmol/L:

> *Albumin-adjusted calcium (mmol/L) = total calcium (mmol/L) + 0.02 [40 – albumin (g/L)])*

> *Payne RB, Little AJ, Williams RB, Milner JP. Interpretation of serum calcium in patient with abnormal serum proteins. Br Med J. 1973;4:643-646. DOI: 10.1136/bmj.4.5893.643. (View)*

Measurement of serum intact parathyroid hormone (PTH) should be performed in all patients with hypocalcemia; it is the most valuable laboratory test for determining the etiology of hypocalcemia:

	2019/11/15	2019/06/28	2018/08/03
PTH (pmol/L)	21,8 H	15,5 H	25,8 H

Reference interval: (1.6-6.9 pmol/L)
Vitamin D

	09/09/2020	15/11/2019	03/08/2018
Total Vitamin D (25-OH VitD)	20.5 nmol/L	45.4 nmol/L	23.2 nmol/L

Guidelines for assessment of Vitamin D status:
<30 nmol/L <12 ng/mL Deficient
30-50 nmol/L 12-20 ng/mL Insufficient
>50 nmol/L >20 ng/mL Sufficient
125-150 nmol/L 50-60 ng/mL Safe upper limit
Reference: Revised South African Clinical Guideline for the diagnosis and management of osteoporosis (NOFSA 2017), endorsing the institute of Medicine Dietary Reference intakes for calcium and vitamin D (2010). Note regarding conversion of units:
Divide result in nmol/L by 2.496 to convert to ng/mL
Multiply result in ng/mL by 2.496 to convert to nmol/L

Other Investigations

Anti-Tissue Transglutaminase antibodies: **Negative**: repeated 3 months apart, with sufficient IgA levels in the serum): 0.9 & 0.8 U/mL (EliA c/o: 6.9)

Anti-Gliadin antibodies: **Equivocal**: 7.8 & 9.6 U/mL (EliA c/o: 6.9)

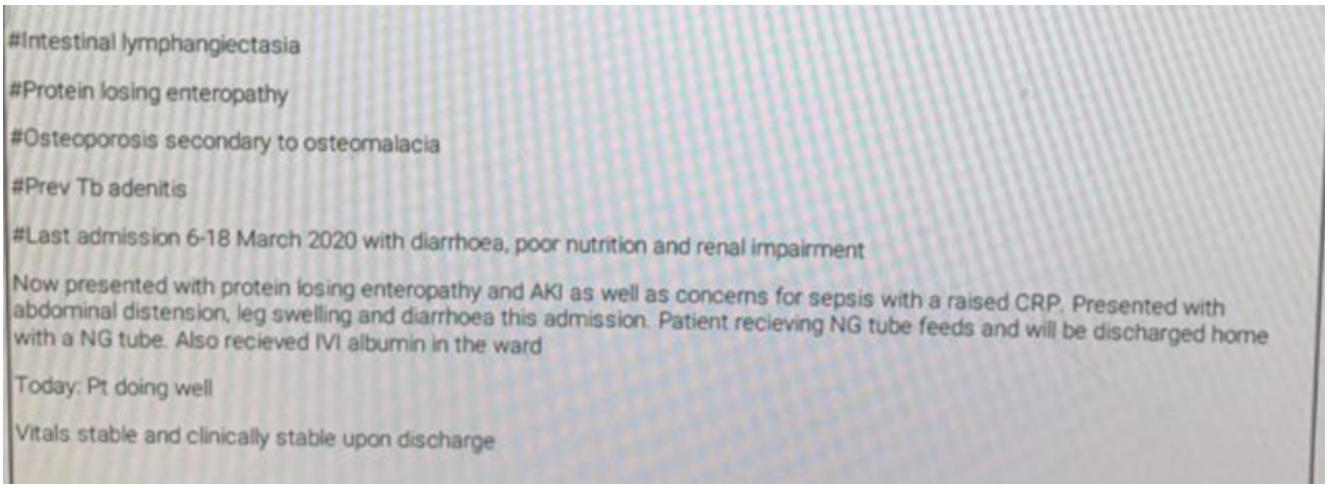
Anti-endomysial antibodies: **Negative**

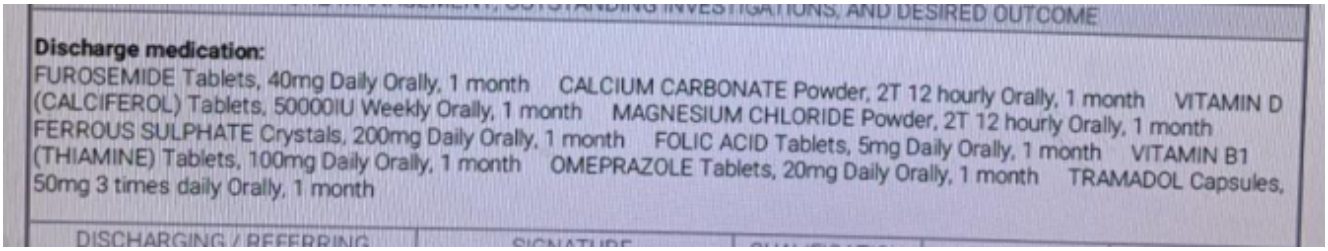
HLA-DQ2: **Positive**

HLA-DQ8: **Negative**

Final Diagnosis

Hypocalcemia likely due to malabsorbtion (telangiectasia stated by the clinicians).





Take Home Message

According to International guidelines the following association is expected for patients with Coeliac Disease:
Positive for HLA-DQ2 (HLA-DQA1*05, DQB1*02)
Positive for HLA-DQ8 (HLA-DQA1*03, DQB1*03:02)

Considering the fact that the albumin was high with an increased PTH, the calcium very likely was physiologically also low (bioactive Ca). The Payne’s formula also failed to correct the calcium to the normal reference range.

Cumulative History:Download

The Vitamin D conundrum

HOSP #		WARD	F22 Orthopaedics Ward
CONSULTANT	Dr. Jody Rusch	DOB/AGE	42 Y Female

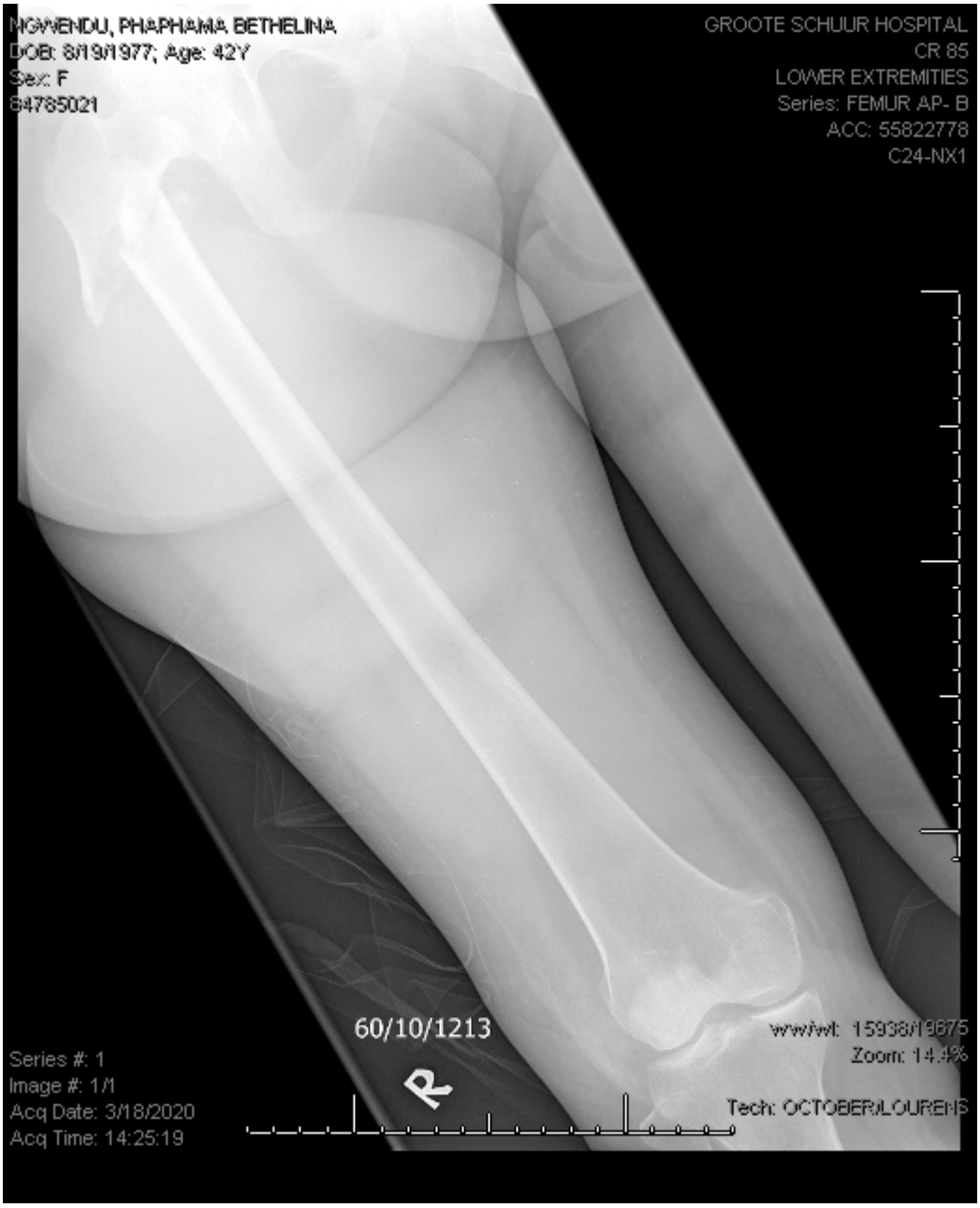
Abnormal Result

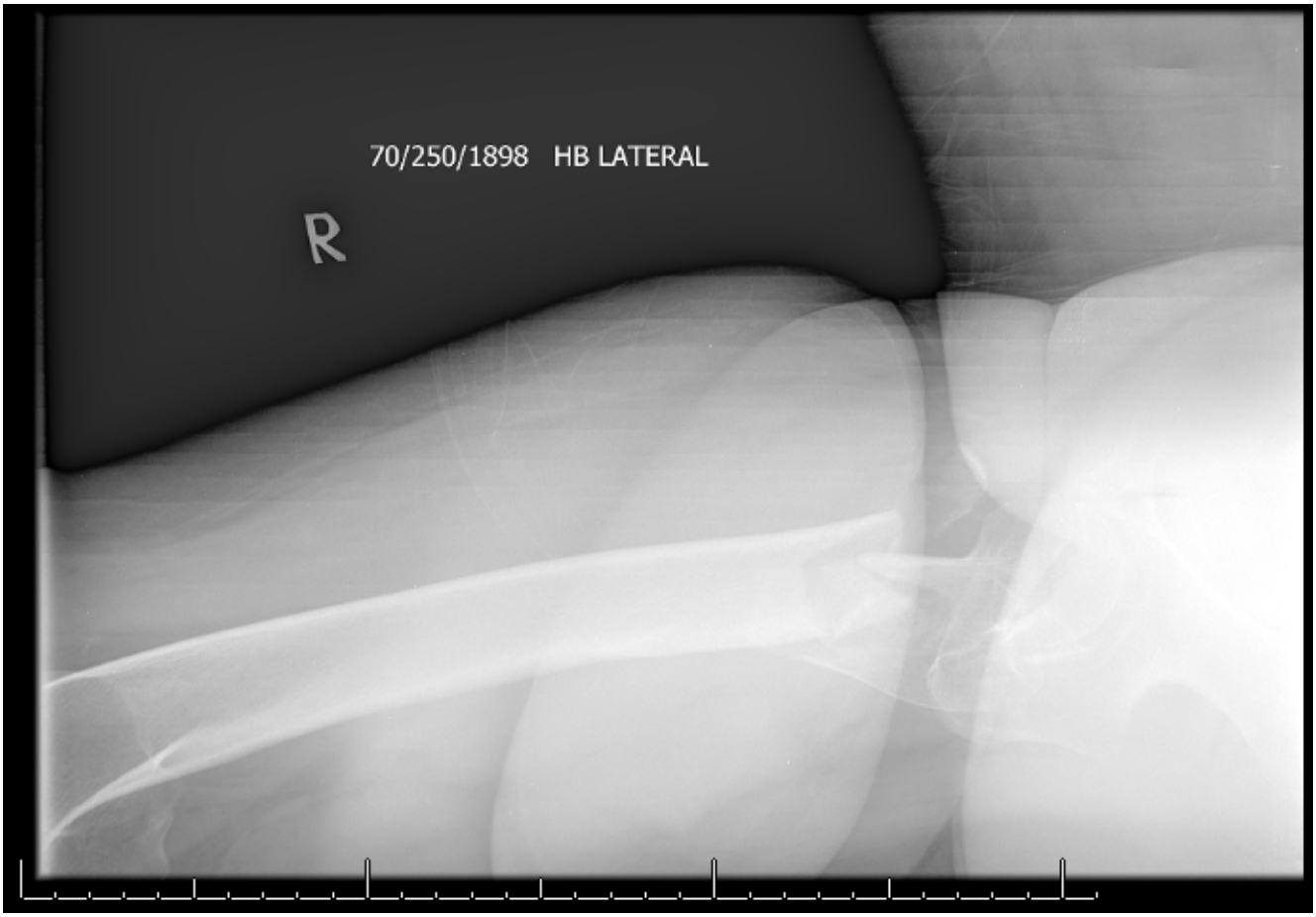
Total Vitamin D of 27.1 nmol/L on 18 March 2020.

Total Vitamin D of 65.4 nmol/L on 01 April 2020.

Presenting Complaint

Patient had a low impact femur fracture on 18 March 2020 :


NGWENDU, PHAPHAMA BETHELINA
DOB: 8/19/1977; Age: 42Y
Sex: F
84785021
GROOTE SCHUUR HOSPITAL
CR 85
LOWER EXTREMITIES
Series: FEMUR AP- B
ACC: 55822778
C24-NX1
60/10/1213
R
Series #: 1
Image #: 1/1
Acq Date: 3/18/2020
Acq Time: 14:25:19
ww/wl: 15938/19875
Zoom: 14.4%
Tech: OCTOBER/LOUREN



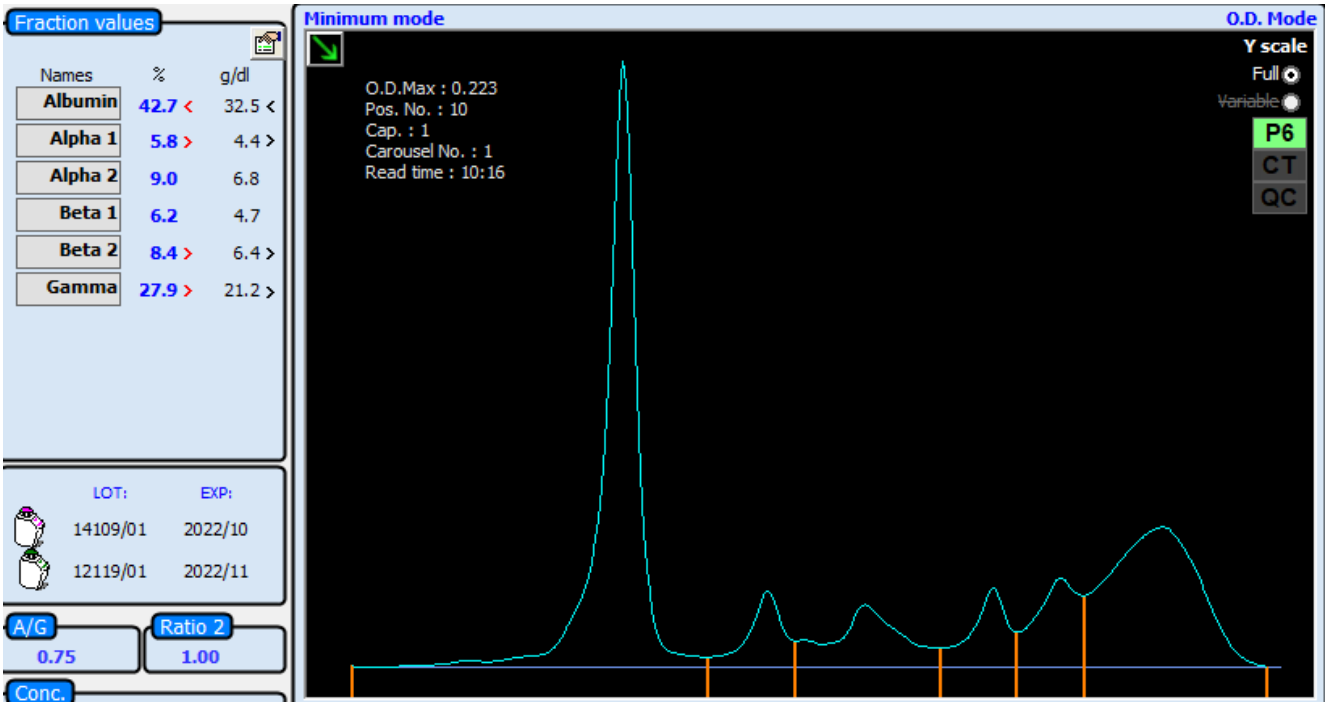
History

Patient is known with:

- previous deep venous thrombosis in 2018, on Warfarin therapy
- ?Epilepsy, patient is on carbamazepine, for which the Endocrinology specialists were of opinion that it may have been the cause of the low Vitamin D level.

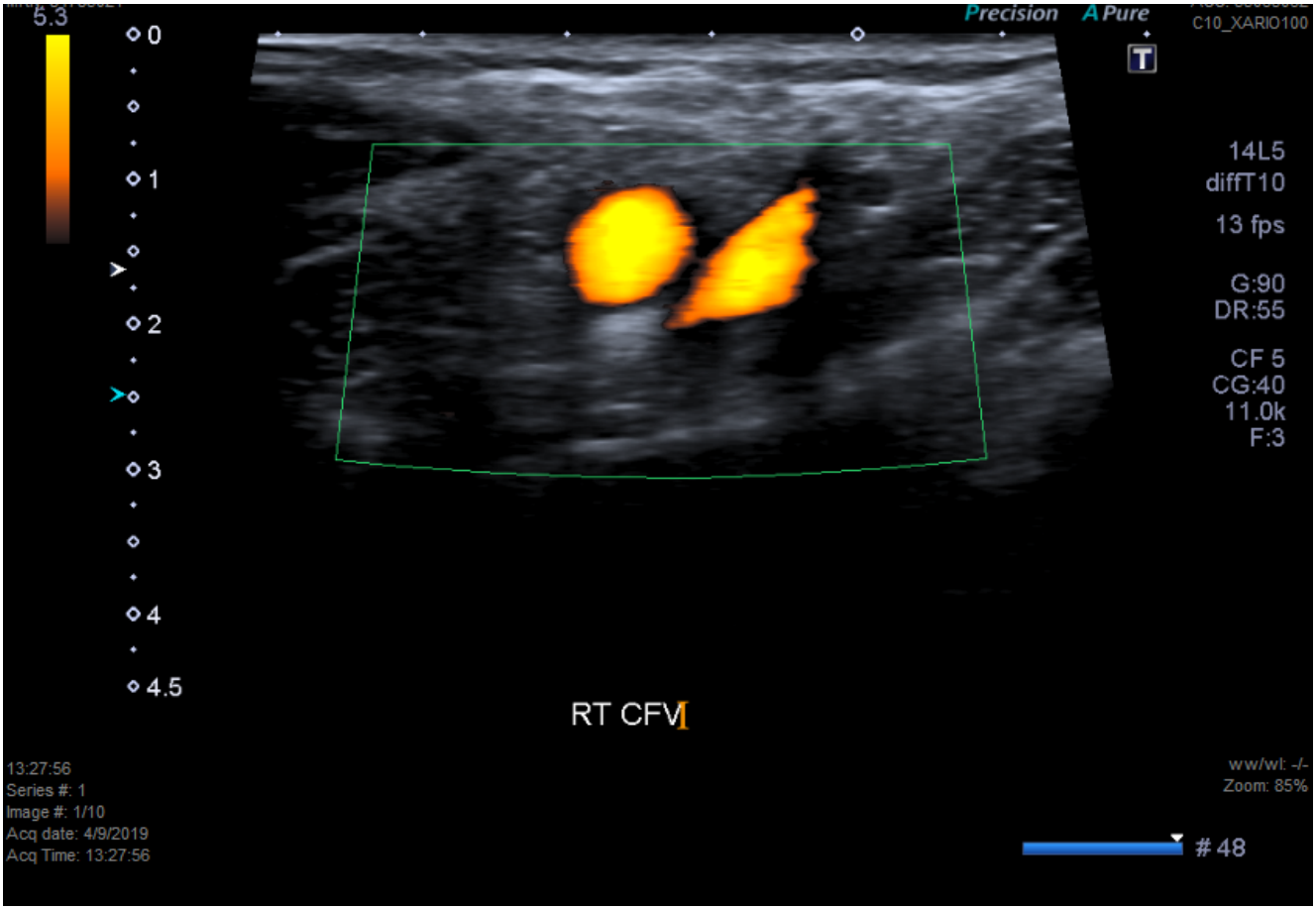
Examination

Laboratory Investigations



Serum protein electrophoresis pattern in keeping with an inflammatory process

Other Investigations



DVT in 2018

Final Diagnosis

Vitamin D deficiency likely due to carbamazepine therapy.

Take Home Message

I was not aware that patients on carbamazepine (or other enzyme inducing agents) have lower Vitamin D levels, and it became evident after a quick literature search that it was in fact the case, see the abstract of the article below, also see another article written by a colleague of mine, Jusine Cole, on the Vitamin D controversies.

> *The Vitamin D cutoff conundrum*

Also, I have learned that although “total Vitamin D”, as the assay is named in our immunoassay package insert and on TrakCare LIS, has to do with the total portion with regards to protein binding (to Vitamin D binding protein) and not so much to the fact that calcitriol and calcidiol is measured.

It is however evident that, since the cross-reaction in the immuno-assay is quite pronounced with the various forms of Vitamin D, that total indeed, might be an accurate description. In reality, the assay is however called the Total 25-hydroxy Vitamin D.

Analytical specificity

The specificity was assessed at 50 % B_0 and the results are summarized in the following table:

Cross-reactant	Cross-reactivity (%)
25-hydroxyvitamin D_3	100
25-hydroxyvitamin D_2	92
24,25-dihydroxyvitamin D_3	149
C3-epimer of 25-hydroxyvitamin D_3	91
1,25-dihydroxyvitamin D_3	not detectable
1,25-dihydroxyvitamin D_2	not detectable
Vitamin D_3	not detectable
Vitamin D_2	not detectable

The Roche Package insert values for specificity for the Total 25-OH Vitamin D assay.

Vitamin D levels and bone turnover in epilepsy patients taking carbamazepine or oxcarbazepine.

Abstract

PURPOSE:

Evidence suggests that enzyme-inducing antiepileptic drugs (AEDs) may decrease serum 25-hydroxyvitamin D (25-OHD) levels and increase bone turnover. We sought to determine whether these are affected by treatment with carbamazepine (CBZ) or oxcarbazepine (OXC).

METHODS:

We measured serum levels of 25-OHD, parathyroid hormone (PTH), osteocalcin (OCLN), bone alkaline phosphatase (BAP), and urinary N-telopeptides of type I collagen cross-links (NTX) in normal controls (n=24) and in epilepsy patients taking CBZ (n=21) or OXC (n=24) in monotherapy. CBZ patients were

subsequently switched overnight to OXC monotherapy, and after 6 weeks, the tests were repeated.

RESULTS:

25-OHD levels were lower in each drug-treated group (OXC, 19.4+/-2.3 pg/ml; CBZ, 20.4+/-2.4) than in the controls (27.5+/-2.8) (ANOVA, $p=0.052$). This difference was significant for the OXC group ($p<0.05$). PTH, BAP, and NTX did not differ significantly among groups. OCLN levels were somewhat elevated in the OXC group (2.79+/-0.47 ng/ml) and more clearly and significantly elevated in the CBZ group (3.63+/-0.36) compared with controls (2.38+/- 0.41) ($p=0.053$). Because the data were very similar between OXC and CBZ groups, they were combined to increase statistical power. The combined drug-treatment group had significantly higher BAP ($p=0.02$) and lower 25-OHD ($p=0.015$) than did controls. The latter remained significant even after accounting for the confounding effects of age on 25-OHD levels ($p<0.05$). No significant differences were found after CBZ patients were switched to OXC.

CONCLUSIONS:

Epilepsy patients taking OXC or CBZ have significantly lower 25-OHD than do normal controls, with a pattern of changes in other bone biomarkers suggestive of secondary hyperparathyroidism. It may be prudent for patients taking CBZ or OXC to be prescribed 25-OHD replacement.