Glucagon Stimulation C-peptide testing

HOSP #		WARD	Endocrinology ward
CONSULTANT	Dr. Heleen Vreede	DOB/AGE	22 y Male

Abnormal Result

Patient presented with Diabetic Ketoacidosis and a glucose value of 27.4 mmol/L.

Presenting Complaint

Signs and symptoms typical of Diabetic Ketoacidosis

History

Patient was diagnosed with diabetes 7 years ago after presenting with diabetic ketoacidosis. Upon diagnosis he was given insulin in the hospital. Upon discharge he was given Metformin and Glimeperide (oral hypoglycemic medication – reason for oral agents unknown – likely because of his young age?). Defaulted Rx completely. Presented with DKA again. Restarted about 2 y ago on insulin.

The differential diagnosis at the current presentation is thus one of:

1. Ketosis prone diabetes
2. LADA (Latent auto-immune diabetes of the adult)
3. Type1 – went into honeymoon phase after diagnosis and now relapsed

To differentiate – the clinicians prompted to do antibodies, insulin levels and a glucagon stimulation c-peptide dynamic

test.

Examination

N/A

Laboratory Investigations

Date	05/02/2021	02/02/2021	28/08/2018	25/01/2018	05/06/2017	03/03/2017	03/03/2017	24/02/2017	16/09/2016	14/04/2015
Na		134 L					137.000			133 L
K		4,6					4.890		4,5	UOLD2
Cl		93 L								
Urea		13,4 H					5.000			1,9 L
Creat		91					69.000		66	34 L
Glu Random				27,4				21.860		
HbA1c (NGSP)		12,7	>14	13,7	>14			12,8	13,7	
Total chol	5,04						ô- 4,98			
Triglyceride	1,74						1,25			
HDL chol	1,35						1,16			
LDL chol (calc)	2,89						3,25			
Total chol									8,99	
U creat	4,1						1,9			
U albumin	32.70						<3			
U alb : creat	8.0 H						UTC			
Test referred						Anti-IA2 Antibody Positive; Anti-GAD antibody Positive				

Other Investigations

A glucagon-stimulated C-peptide level was drawn.

0 min	1.5 ug/L	0.5 nmol/L
1 min	2.0 ug/L	0.67 nmol/L
2 min	1.9 ug/L	0.63 nmol/L
3 min	1.9 ug/L	0.63 nmol/L

Final Diagnosis

LADA – latent autoimmune diabetes of the adult

Take Home Message

Serum c-peptide has traditionally been thought to be an inconvenient method as immediate lab analysis is required before degradation (when collected in serum gel or plain sample tubes). This is because c-peptide is a small linear peptide, which is susceptible to enzyme proteolytic cleavage. Gel tubes are therefore traditionally required to be transported to the lab on ice, promptly centrifuged and separated, then stored in frozen conditions unless lab analysis is possible at that center.

However, c-peptide sample collection for c-peptide determination in whole blood in EDTA prepared tubes is stable at room temperature for up to 24 h. Venous blood c-peptide levels can be measured in the random, fasting, or stimulated scenarios. Random samples are taken at any time during the day without consideration of recent food intake, whereas fasting samples are taken after an 8- to 10-h fast.

Stimulation methods include using

- glucagon
- intravenous/oral glucose
- tolbutamide
- sulfonylurea
- glucose-like peptide 1
- amino acids
- a mixedmeal

In this case a glucagon stimulation yielded sufficient results to assist the clinicians in making the diagnosis, indeed a case of atypical diabetes presentation.

An uncommon cause of unconjugated hyperbilirubinemia

HOSP #		WARD	Red Cross Endocrinology
CONSULTANT	Dr Jody Rusch	DOB/AGE	27 day female

Abnormal Result

TSH > 100

Free T4: 0.5 pmol/L

Presenting Complaint

Patient was brought to the ER being lethargic.

History

Term Neonate; Had a history of profound jaundice after birth, with unconjugated hyperbilirubinemia.

The patient’s mother lives in Athlone, gave birth at Carl Bremer hospital where a cord blood TSH was done, but results not available at the time.

Examination

No overt abnormalities on examination was found, except the single sign of jaundice.

No defects at the base of the tongue was observed.

No abnormalities in the neck was observed.

Laboratory Investigations

TSH > 100

Free T4: 0.5 pmol/L

Other Investigations

The patient had an ultrasound of the abdomen done (since it was the first occurence of hyperbilirubinemia, and in fact is termed pathological jaundice).

Cord blood TSH was retrospectively reviewed as being 178 uIU/ml.

Final Diagnosis

Congenital hypothyroidism

Take Home Message

Congenital hypothyroidism (**CH**) is thyroid hormone deficiency present at birth. If untreated for several months after birth, severe congenital hypothyroidism can lead to growth failure and permanent intellectual disability. Infants born with congenital hypothyroidism may show no symptoms, or may display mild symptoms that often go unrecognized as a problem. Significant deficiency may cause lethargy, hypotonia, hoarse cry, infrequent bowel movements, significant jaundice, and hypothermia.

Causes of congenital hypothyroidism include

- iodine deficiency (most common cause)
- developmental defect in the thyroid gland, either due to a genetic defect or a biochemical defect in thyroxine production
- pituitary defects – congenital hypopituitarism (present

at birth) may be the result of complications around delivery, or may be the result of insufficient development (hypoplasia) of the gland, sometimes in the context of specific genetic abnormalities.

Hypoglycemic seizures

HOSP #	MRN90378429	**WARD**	Endocrinology Ward
CONSULTANT	Jody Rusch	**DOB/AGE**	14 y girl

Abnormal Result

Fingerprick glucose 2.9 mmol/L

Presenting Complaint

Hypoglycemic seizure

History

The patient is a known type 1 diabetic patient who presented to the Internal Medicine Paediatric specialist OPD during two occasions of hypoglycemic seizures before.

The pateint had, according to the mothed, no post-ictal state.

She was admitted to the Endocrinology ward for a fast provocation test. At two hours, the glucose measured 2.9mM on point-of-care glucometer – glucose and other parameters on laboratory values however is illustrated below.

2 weeks after this presentation patient presented again with hypoglycemic seizures – mother is a nurse – puts in drip after

which the patient’s condition normalizes.

IGF-1 normal, Ketones raised (quantitative beta-hydroxybutyrate, Insulin: 6 nmol/L, glucose: 3.5mM, hGH: 1.9 ug/L.

Examination

On examination the patient had no signs and symptoms of hypoglycemia (during the provocative test). And after the hypoglycemic seizure there were no “post-ictal” symptoms identified.

Laboratory Investigations

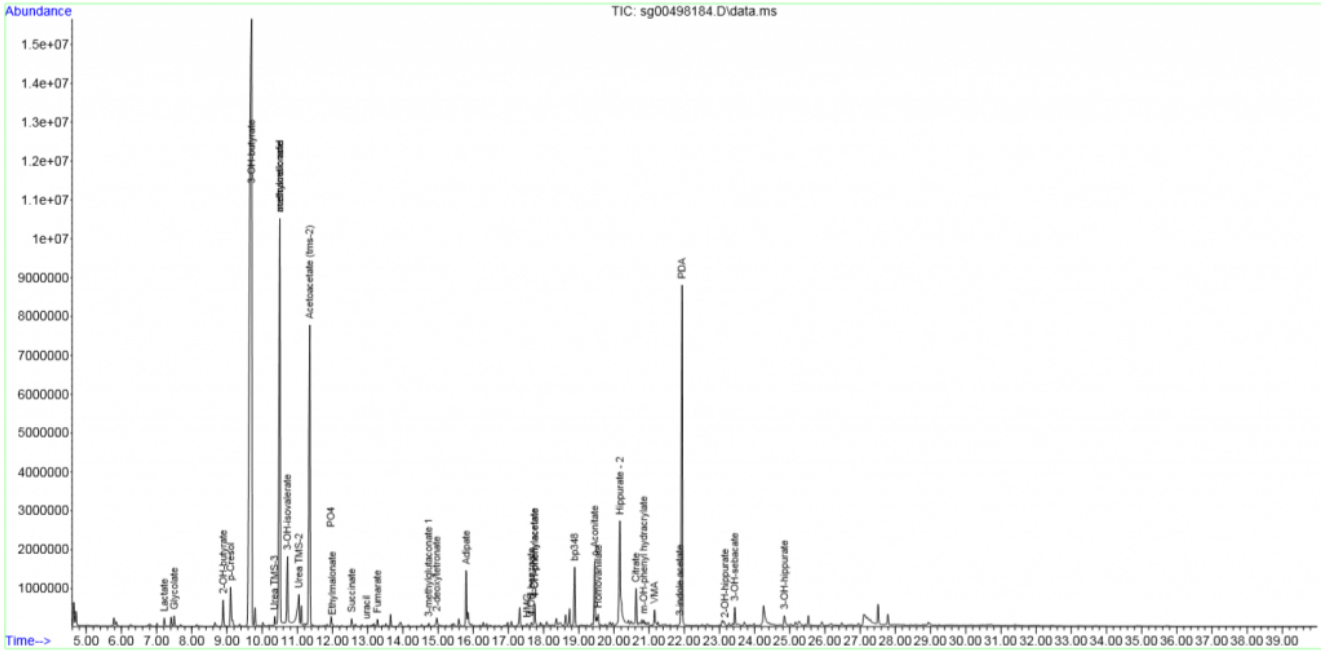
Glucose 3.5 mmol/L /L
Insulin: **6** nmol/L
Lactate 1.5 mmol/L (0.5 – 2.2)
Beta-hydroxybutyrate 1855 umol/L (20 – 270)
Ammonia 56 umol/L (11 – 35)
Cortisol 367 nmol/L
Cortisol reference intervals (when performed on a Roche Cobas analyzer):
Levels in adults: Morning (06:00-10:00) 133 – 537 nmol/L ; Afternoon (16:00-20:00) 68 – 327 nmol/L
Human growth hormone 1.9 ug/L

IGF-1 (Insulin-like growth factor I) @ 22/02/2021 09:30 : **366.0** ug/L (170.0 – 527.0)
Tanner stages Boys vs Girls:
Stage I 63 – 271 ug/L ; 71 – 394 ug/L
Stage II 114 – 411 ug/L ; 122 – 508 ug/L
Stage III 166 – 510 ug/L ; 164 – 545 ug/L
Stage IV 170 – 456 ug/L ; 174 – 480 ug/L
Stage V 161 – 384 ug/L ; 169 – 400 ug/L

Synacthen stimulation test:

Time on 22/02/2021	Cortisol (nmol/L)
14h00 (Baseline)	316
14h30	597
15h00	436

Other Investigations



Urine organic acid analysis profile: The 3 prominent peaks on the left are from left to right: B-hydroxybutyrate, Acetoacetate (with TMS derivative 1), Acetoacetate 2nd peak (with TMS derivative 2). TMS = trimethylsilyl derivative reagent, PDA = pentadecanoic acid (internal standard).

Final Diagnosis

Type 1 Diabetes with ketoacidosis and occasional episodes of hypoglycemia

Possible reasons for the hypoglycemia may be:

1. Ketogenic diet (fairly easily excludable I think).
2. Ketone utilisation disorder:
   - SCOT (succinyl-CoA:3-ketoacid CoA transferase) deficiency

- Mitochondrial acetoacetyl-CoA thiolase (beta-ketothiolase) deficiency

Take Home Message

There are two predominant ketone utilisation disorders: SCOT deficiency and beta-ketothiolase deficiency. These disorders produce fairly continuous ketones, as they cannot be metabolised in the muscle and brain upon these deficiencies, which are autosomal recessive (as is most inherited metabolic diseases).

Giving the mother a urine dipstick home to measure urine at home mane before meals, midday just before meals and late afternoon or so before meals may be advised to assist with the diagnosis of one of the above disorders.

Urine organic acid analysis can sometimes pick up a marker to diagnose beta-ketothiolase deficiency:

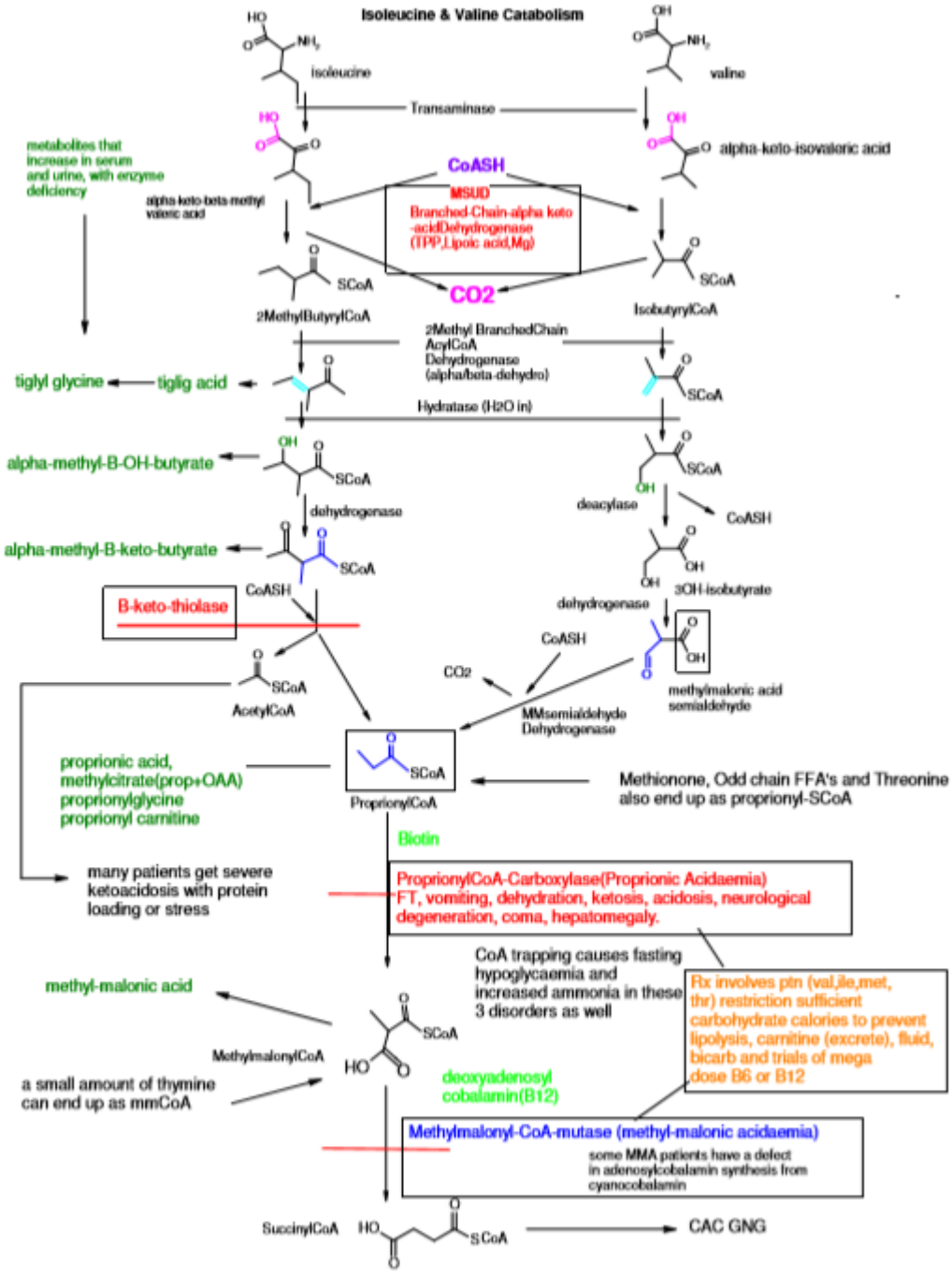


Figure 2 – The metabolism of Isoleucine and valine (credits to George van der Watt). In beta-ketothiolase deficiency, alpha-methyl-beta-keto-butyrate will accumulate, and can be detected on urine organic acid analysis by GC-MS.