Emergencies in adults with Inherited Metabolic Diseases(IMD)

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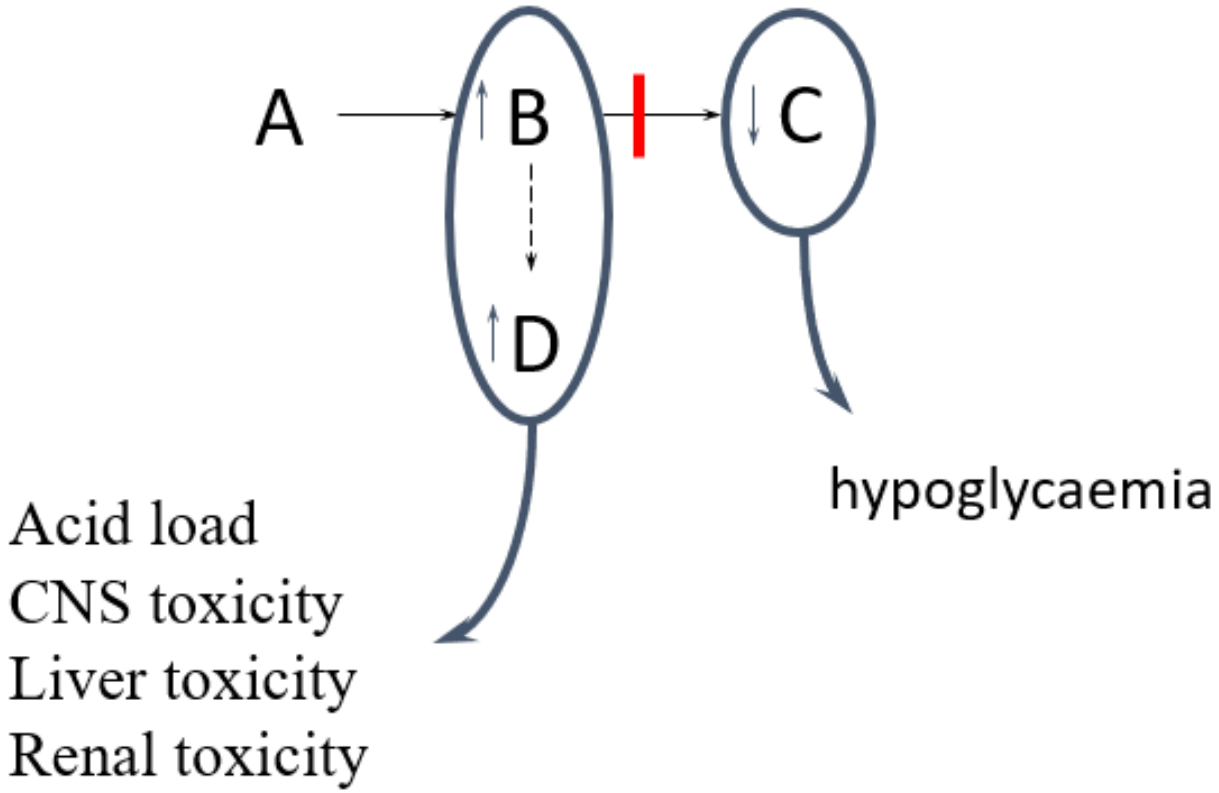
Declaration for Reena Sharma

I have the following financial interest or relationship/s to disclose with regard to the subject matter of this presentation:

- Consulting fees and grant to attend academic conferecnes: Sanofi, Amicus, Travere
- Chief investigator and principal investigator for various clinic trials and some of the conditions may be part of this presentation

Adult IMD – Relevance

- They are collectively not that rare
- Adult presentations increasingly recognised
- Missing the diagnosis can be catastrophic
- Treatment improves prognosis
- There are implications for relatives



It could be deficiency of an enzyme or transporter

Two main ways this could present in ER

- Already have a diagnosis of IMD: Urea cycle defect, organic acidaemia, Maple Syrup Urine Disease (MSUD) tyrosinaemia etc
- Orange triage in AE
- If there is an emergency regime that has been provided, then they please follow that urgently: Mostly IV dextrose, saline and protein restriction where appropriate
- Any delay in this makes metabolic decompensation worse
- Treat the intercurrent illness

  https://bimdg.org.uk/site/guidelines.asp

Adult IMD – Flags

Patients who do not have a confirmed diagnoses, but the presentation could make you suspect IMD:

- Previous similar unexplained episodes
- PMH – social +physical development
- FH – consanguinity, symptoms, deaths
- Affected siblings
- Remains a mystery after standard evaluation
- Triggers - catabolic states, diet, drugs
- History of Dietary aversion(s)

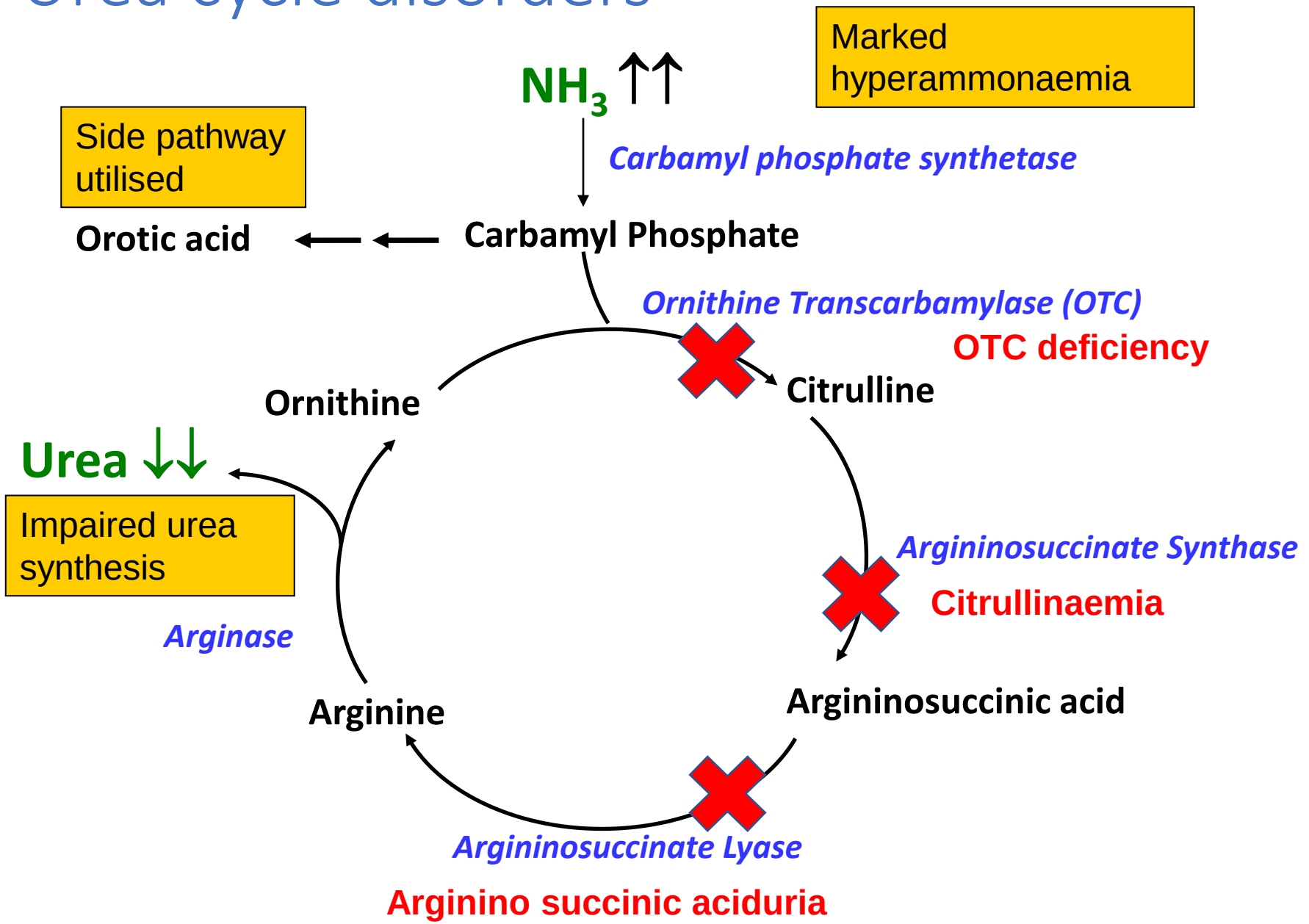
Case 1

- 57 y female
- Mild Learning difficulties and epilepsy
- Had planned GI surgery
- Post op reduced consciousness
- 3rd day ammonia was checked, and it was ammonia >300
- Blood organic and amino acid
- Arginosuccinic aciduria

OTC deficiency

- 30y female
- Post partum reduced level of consciousness
- Ammonia 250
- OTC deficiency
- X linked condition

Urea cycle disorders



Hyperammonaemia Encephalopathy

- Trigger factors are infections
- Body building shakes
- Post partum phase
- Post operative phase
- Secondary causes:

Significant referral for post bariatric surgery patient: few years post op, intercurrent illness, encephalopathic, raised ammonia due to Zinc deficiency leading to secondary CPS 1 defect

High ammonia secondary to organic aciduria

Medications i.e. Na Valproate

Liver disease

IEM - First-line Investigations

- FBC (EDTA)
- U+E's, calcium, HCO3, Cl, LFT's, CK (Clotted)
- Glucose, Lactate (Fluoride)
- ABG
- NH3 (EDTA or Li Hep on ice, to Lab ASAP)
- Ketones
- Acylcarnitines
- Plasma AA (Li Hep)
- Urine AA + OA and orotic acid (plain container)
- Abdominal scan for portal hypertension

IEM – Treatment principles

- Prevent catabolism
- Limit intake of offending substance
- Increase excretion of toxic metabolites
- Ammonia scavenger therapy
- Electrolyte and ph and fluid correction
- IV 10% dextrose

Rhabdomyolysis, raised CK

- Patients of any age
- Muscle aches raised CK with or without myoglobinuria
- could be due to unaccustomed exercise and without any previous history
- Intercurrent infection

Common diagnosis

- FAOD (Fatty acid oxidation defect): VLCAD (Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD), CPT 2 (Carnitine palmitoyltransferase II defect)
- GSD (Glycogen Storage Diseases): McArdle (GSD 5), GSD 9, 10, 11, 7
- RYR1 mutation
- Mitochondrial defect

Case 1

- 70 y old retired GP. Had multiple episodes of rhabdomyolysis since childhood precipitated by flu, D and V 2-3 a year)
- Diagnosed with CPT 2 age 40
- Chronic renal failure
- Renal transplant

17 Y male

- 3 admission over a course of 2 years with dark urine colour
- Dipstick urine blood ++++
- Raised ALT
- Had Liver tests
- Saw urologist for cystoscopy and renal scan
- It was the 4th admission that CK was measured, and it was 50,000
- Found to have point mutation for Mcardle's (GSD V)

Case 1

- 21 year old female presented with acute myositis-- Creatine Kinase (CK) elevated at 6,588 U/l.
- Muscle aches and cramps following physical activities or missed meals and been present since the age of 16.
- Her parents were from Pakistan but it was not a consanguineous marriage.
- Further investigations ruled out glycogen storage diseases. Skin fibroblast studies confirmed Very Long Chain Acyl-CoA Dehydrogenase Deficiency (VLCAD) .
- Her sister aged 25y, had been under rheumatologist for over 6 years with muscular symptoms and slightly raised CK of ~300 U/l. She has also confirmed VLCAD.

Raised CK

- Carnitine profile
- Lactate
- Ammonia
- Urinary Organic acid
- Genetics
- Skin biopsy for fibroblast fatty acid flux studies
- Muscle biopsy for storage, glycogen enzymes and mitochondrial studies
- Non ischaemic forearm test

Stroke and IMD

- CVA under 60y i.e. young stroke; should consider following conditions
- Homocystinuria (Plasma total homocysteine)
- Fabry (white cell enzyme)
- Mitochondrial disease: MELAS

Case study:

Seizures aged 9y

Pulmonary embolism 2013 on CT pulmonary angiogram

Extensive DVT 2018 including thrombosis and IVC and has been on Rivaroxaban since then

Osteoporosis 2019

Presented with seizure in 2020

MRI brain and CT angiogram 2020 showed occlusion of both internal carotid arteries and left

vertebral artery and minor ischaemic changes in the brain

Homocystinuria diagnosed 2021 (Age ~28Y)

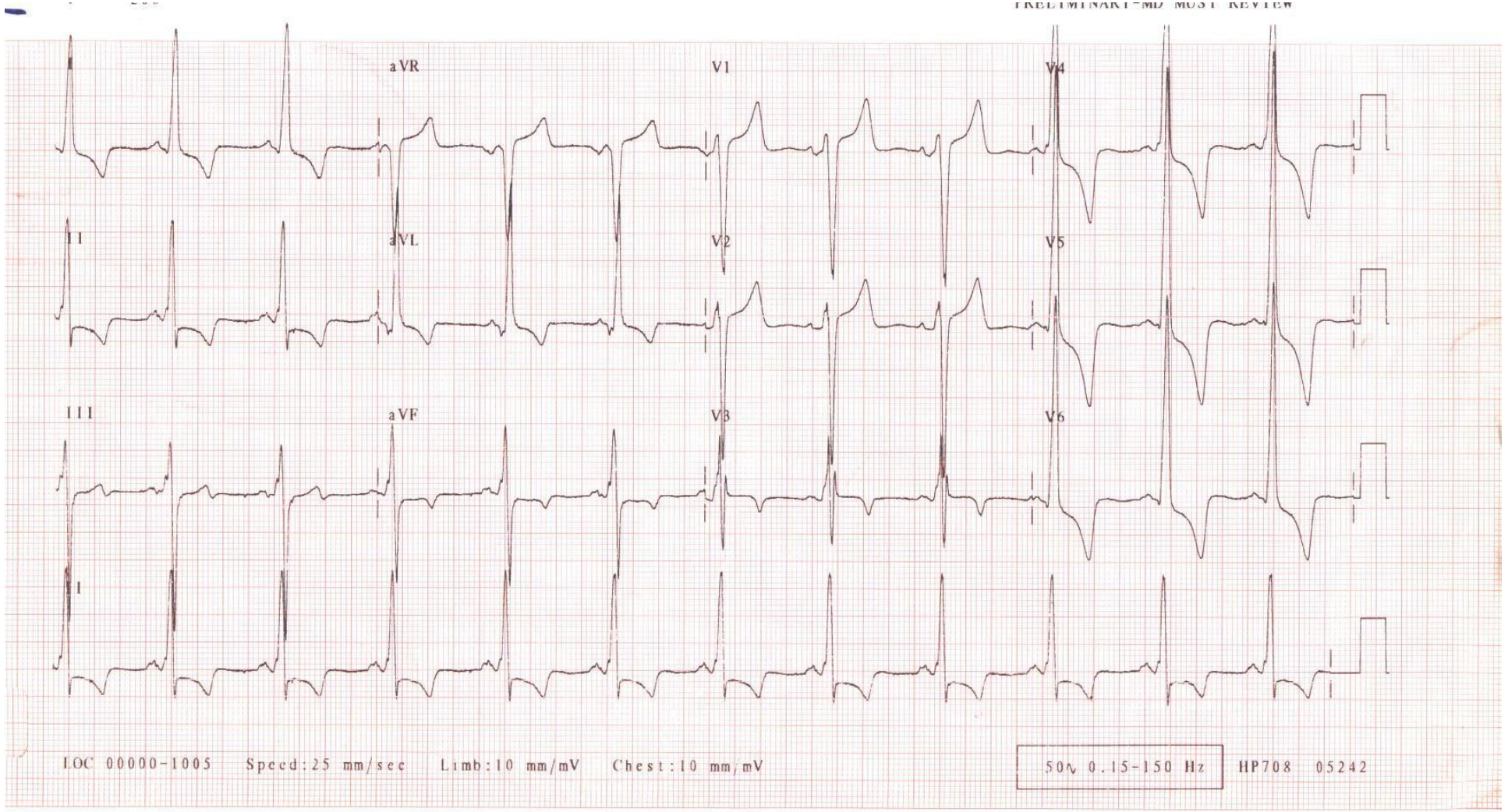
Heart block, arrhythmias, LVH

- Can happen in a few metabolic conditions but in some it could be the presenting feature
- Carnitine transport defect, Fabry cardiomyopathy, Danon disease
- Dilated cardiomyopathy in Mitochondrial disease

LVH NGS gene panel: fabry gene is part of that panel, acid alfa galactosidase/ White cell enzyme

CPT defect: carnitine profile

Danon: gene mutaion



41 year old . Main involvement was cerebral with multiple strokes. No cardiac symptoms or signs. ECHO showed typical hypertrophy.

Thank you for listening

We are only a phone call away!

On call Metabolic Consultant

Salford Royal Hospital