

Methylmalonic Acidemia

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History of the Disease

- First described in 1967 as neonatal catastrophe with elevated urine methylmalonic acid, severe ketoacidosis unresponsive to Vitamin B12 (Cobalamin)
- Described in 1969-70 with Adenosylcobalamin deficiency with homocystinuria, cystathioninuria, & hypomethioninuria

Incidence

- mut-, mut 0, cblA, & cblB;
1:48 – 61,000 live infants
- cblC, cblD & cblF;
Unknown
cblD may be X-linked

Current MMA Classifications

- Mutase Apoenzyme defects;
mut- partial defect
mut 0 complete deficiency
- AdoCbl Synthesis defects;
cblA & cblB
- Defects of AdoCbl & MeCbl;
cblC, cblD & cblF

Range of Metabolic Abnormalities

- Methylmalonic Acidemia ONLY;
mut-, mut 0, cblA, & cblB
- Methylmalonic Acidemia PLUS;
Homocystinuria
cblC, cblD & cblF

Complications

- Metabolic Stroke
- Megaloblastic Anemia
(cb1C most common)
- Hemorrhagic Pancreatitis
- Chronic Renal Failure
(B12 non-responders most common)
- Osteoporosis

Chronic Renal Failure

- 20-60% of Adolescents with non B12 responsive defects;

mut0 0-8% B12 responsive

mut- 0-10% B12 responsive

cbIA ~90% B12 responsive

cbIB ~40% B12 responsive

Chronic Renal Failure

- May not show any symptoms
- Potential Symptoms;
 - High Blood Pressure
 - Poor Growth
 - Electrolyte Imbalances
 - Hard to control Acidosis

Chronic Renal Failure

- Most common kidney biopsy finding – Interstitial Nephritis
- Decreased Renal function appears to correlate with elevated MMA levels
- MMA potentially the cause of tubular damage

Monitoring for CRF in MMA

- B12 Non-Responders for sure
- Monitor Growth & Blood Pressure
- Potential Lab studies;

BUN/Cr

24 hour Creatinine Clearance

MMA levels ???

Potential Treatments for CRF

- Low Protein Diet
- Oral Antibiotics to clear Gut Bacteria
- +/- Carnitine supplements
- +/- Treat elevated Uric acid levels
- +/- Treat Acidemia
- Kidney Transplant ????????



QUESTIONS ??????