## Introduction :

Urea cycle is the final pathway for nitrogen metabolism. Urea cycle disorders are inherited deficiencies of the enzymes involved in the cellular excretion of excess ammonia produced during protein metabolism. Although the majority of recognized patients are children, a delayed presentation is seen in patients with partial enzyme deficiency, including heterozygotes. The diagnosis onlybecomes apparent during times of increasedmetabolic stress, such as with acute or chronic illness.The primary manifestations of elevated blood ammonium affect central nervous system.

## Case Report :

A 42 years old gentleman, previously well, presented with history of right facial weakness for 7 days for which he was taking Tab Wysolone 60 mg/day, followed by malaise for 2 days with sleep disturbances and altered sensorium for 1day. At presentation,he was irritable in a stuporous state. Initial possibilities considered ? Viral encephalitis. He was intubated and connected to ventilator. Initial routine investigations were normal. He was started on acyclovir , Ceftriaxone and antiepileptics. MRI brain showed small T2/FLAIR subcortical hyperintensities. Next day he developed generalized tonic clonic seizures for which antiepileptics were further added. However, seizures persisted and became violent in nature. In view of status epilepticus, he was started on Thiopentone infusion which controlled seizures. CSF study routine was normal.He was evaluated for other causes of encephalopathy and Serum ammonia was found to be high (1200µmol/L).Decided for dialysis and SLED was done. Ammonia detoxification were started. In view of persisting comatose state ,CT brain was done which showed diffuse cerebral edema which was managed conservatively. He became haemodynamicallyunstable, requiring ionotropic support. Urea cycle disorder panel was sent. The patient expired on 7$^{th}$ day since admission.

OROTIC ACID, URINE @
(GC-MS)

| COMPOUND | RESULT | REF. RANGE IN % | ELEVATION FACTOR |
|---|---|---|---|
| Uracil | 9.23 | 2.8 | 3.30 |
| Orotic Acid | 1:20 | 0.3 | 4.00 |

| Test Name | Results | Units | Bio. Ref. Interval |
|---|---|---|---|
| **UREA CYCLE DISORDER PANEL** | | | |
| **UREA CYCLE DISORDER PANEL @** (LC-MS/MS, GC/MS) | | | |
| Glutamine | 305.51 | umol/L | |
| Ornithine | 72.24 | umol/L | |
| Citrulline | 87.71 | umol/L | |
| Arginine | 18.84 | umol/L | |
| Arginosuccinic acid | 0.00 | umol/L | |

**Impression-**
Citrullininemia .
Correlate clinically
**Interpretation**

| | REFERENCE RANGES IN umol/L | | | | |
|---|---|---|---|---|---|
| AMINO ACID | PREMATURE | 1-31 DAYS | 32 DAYS -23 MONTHS | 2-18 YEARS | >=19 YEARS |
| Glutamine | 248-850 | 376-709 | 246-1182 | 254-823 | 205-756 |
| Ornithine | 77-212 | 48-211 | 22-103 | 10-163 | 48-195 |
| Citrulline | 20-87 | 10-45 | 3-35 | 1-46 | 12-55 |
| Arginine | 34-96 | 6-140 | 12-133 | 10-140 | 15-128 |
| Arginosuccinic acid | 0-1 | 0-1 | 0-1 | 0-1 | 0-1 |

## Discussion:

Most likely cause for hyperammonemia of our patient was thought to be urea cycle defect, ornithine transcarbamylasedefect aggravated by steroid exposure for Bell's paralysis. Reports followed,Urinary orotic acid was detected and urea cycle disorder panel showed Citrullininemia.

N-acetylglutamate is required for the urea cycle to take place. Glutamic acid is first combined with Acetyl CoA by Nacetylglutamatesynthetase (NAGS) to create N-acetylglutamate. N-acetylglutamateactivates carbamoyl phosphate synthetase I.

Ammonia is then coverted to carbamoyl phosphateby carbamoyl phosphate synthetase I (CPS I) Ornithine transcarbamylase (OTC) then catalyzes a reaction between carbamoyl phosphate and ornithine to generate citrulline in the urea cycle. Finally urea is formed and excreted. Deficiency in any five of the enzymes in the urea cycle results in theaccumulation of ammonia which could be potentially fatal if untreated.The most common deficiencies are Nacetylglutamatesynthetase (NAGS) deficiency, carbamoyl phosphate synthetase I (CPS I) deficiency, and ornithine transcarbamylase (OTC) deficiency. OTC and CPS deficiency patients may display a`low citrulline and arginine level in the metabolic panel. Urine studies in an OTC

patient typically show a high level of orotic acid, which is a by-product of the cycle and is made from carbamoyl phosphate when OTC is not available. OTC is an X-linked disorder and can have a late presentation from carrier states in which there are varying amounts of residual enzyme activity.

## Conclusion:

Although urea cycle defect is very rare in adult , there should be a strong suspicion and consider in patient with unexplained altered sensorium because delay in initiating treatment may cause devastating outcome.

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