'Glutaric Aciduria Type I- An Easily Diagnosable and Treatable Metabolic Disorder'

Sir,

Diagnosis of Inborn error of Metabolic (IEM needs specialized investigations like gas chromatography/ mass spectrometry (GC/MS) and tandem mass spectrometry (TMS) which are not widely available in developing countries like India. We report two cases of GA-I, where the clinical features and neuroimaging findings gave us the clue for diagnosis.

Case 1

A six-month-old girl presented with sudden onset choreic movements of limbs, tongue thrusting and excessive crying, five days after a respiratory tract infection. There was no history of seizures. The head circumference was above the 97th centile. There was hypotonia in the limbs and trunk. Cerebrospinal fluid (CSF) analysis was within normal limits. In view of the choreiform movements that appeared after infection and normal CSF findings, a possibility of post-infectious demyelinating illness or IEM like organic acidemias precipitated by viral illness was considered.

Arterial blood lactate was 2.4mmol/L. Magnetic resonance imaging (MRI) of the brain revealed wide CSF spaces anterior to the temporal lobes with temporal lobe hypoplasia giving the 'bat-wings' appearance. Diffuse white matter signal abnormality, bilateral high signal in the lentiform nucleus, dilated sylvian fissures and open opercula were seen on the axial T2W MR image (Fig.1A). These findings suggested a diagnosis of GA-I. TMS revealed increased levels of glutaryl-carnitine (0.92µmol/L; upper limit-0.56µmol/L) suggesting GA-I.

Case 2

Two-year old boy presented with breath-holding spells and large head. MRI done by the treating pediatrician revealed bilateral subdural collections. There was no history of head injury, abnormal movements, seizures or episodes of altered sensorium. Child underwent drainage of the subdural collections, but the head size continued to increase and repeat imaging revealed re-accumulation of the subdural collections. Examination showed large head (52 cm), hypotonia and normal reflexes. MRI when carefully reviewed showed bilateral huge subdural effusions, basal ganglia changes and white matter hypomyelination (Fig.1B). This suggested IEM like GA-I. TMS revealed increased glutarylcarnitine (0.98µmol/L) and urine GC/MS showed increased

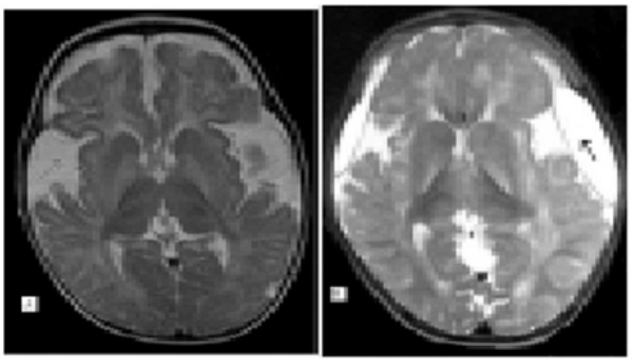

Fig. 1A. Axial T2W MR scan reveals fronto-temporal atrophy, dilated sylvian fissures with open opercula (arrow), diffuse white matter signal abnormality, and bilateral high signal in the lentiform nuclei. Widening of the sylvian fissure gives the 'bat-wing' appearance.

Fig. 1B. Axial T2W MR scan reveals similar features along with huge bilateral subdural collections (arrow).

excretion of glutaric acid and 3-hydroxyglutarate suggesting a diagnosis of GA-I.

Both cases were started on riboflavin & carnitine supplements along with protein restricted diet especially lacking lysine and tryptophan. Care of patients during infections was advised *as per* the recent guidelines.[1] Follow up after 6 months, in the first case, revealed that the abnormal movements had stopped and she was gaining milestones. The second child did not have any further encephalopathic episodes.

GA-I is a disorder of lysine, hydroxylysine, and tryptophan catabolism caused by deficiency of mitochondrial glutaryl-CoA dehydrogenase.[2] Macrocephaly is found in approximately 75% of patients during infancy and may be an early sign before other neurologic alterations.[1] Rarely, large head can be the only manifestation and children can be otherwise neurologically normal like our second case. They do have neuroradiographic evidence of frontotemporal atrophy.[3]

The most striking finding on neuroimaging is the presence of very wide CSF spaces and open sylvian fissures. This gives the characteristic 'bat-wings' appearance and is a very characteristic finding in GA-I.[4]

GA-I is biochemically characterized by elevated urinary excretion of glutaric acid, 3-hydroxyglutaric acid and increased blood glutarylcarnitine, reduced

plasma carnitine, and reduced or absent glutaryl-CoA dehydrogenase (GCDH) activity in fibroblasts and leukocytes.[3] 3-hydroxyglutarate in urine is the diagnostic marker compound of GA-I.[1] Mutation analysis of the GCDH gene has a sensitivity of 98–99%.[1] Treatment consists of high doses of riboflavin and carnitine along with low protein diet, especially deficient in lysine and tryptophan.[1] Guidelines have been provided for care of these children during stressful episodes.[1]

Our two case reports show how clinical features and neuro-imaging findings can give clue to IEM like GA-I. This is very important in developing countries where facilities for TMS, GC/MS and enzyme analysis are not widely available. Diagnosis of condition like GA-I is important as it is an autosomal recessive disorder and there is 25% chance of recurrence in future pregnancies. The condition can worsen with infections in future, if proper precautions are not taken. It is also important for counseling parents regarding the prognosis and prevent unnecessary interventions like in our second case.

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REFERENCES

1. Kolker S, Christensen E, Leonard J V *et al*. Guideline for the diagnosis and management of glutaryl-CoA dehydrogenase deficiency (glutaric aciduria type I). *J Inherit Metab Dis* 2007; 30:5–22.
2. Goodman SI, Markey SP, Moe PG, Miles BS, Teng CC. Glutaric aciduria: a 'new' disorder of amino acid metabolism. *Biochem Med* 1975;12: 12–21.
3. Nyhan WL, Ozand PT. Glutaric aciduria (Type I). In Nyhan WL, Ozand PT eds. *Atlas of metabolic diseases*. London; Chapman and Hall 1998; 46-52.
4. Amir N, El-Peleg O, Shalev RS, Christensen E. Glutaric aciduria type I: Clinical heterogeneity and neuroradiological features. *Neurology* 1987; 37: 1654-1657.

A Neonate with Complete Thrombosis of the Aorta

Sir,

Complete thrombosis of the aorta in early neonatal period is very rare and often proves fatal. We would like to share with the readers an interesting case of complete thrombosis of the aorta.

A 7-day-old male was referred from a peripheral hospital with history of recurrent convulsions, lethargy and poor feeding since day 2 after birth. A product of a non-consanguineous marriage, born to a 23-year old healthy primigravida mother with a birth weight of 2.6 Kg. He was delivered by emergency lower segment caesarean section (indication: 18 days postdated and thick meconium stained liquor). Initial examination revealed a lethargic, afebrile baby with staring look and absent cry. Admission weight was 2.5 Kg, capillary refill time - 4 secs, both femoral pulses were less palpable compared to upper extremity pulses, heart rate – 146/min, respiratory rate – 56/min. Blood pressure in upper extremity was 65/42 (mean 50) mm Hg; blood pressure in lower extremity was unrecordable. Liver was palpable 1 cm below costal margin in right mid clavicular line and spleen was not palpable. The baby was started on I.V. fluid, injections cefotaxime and amikacin and all the anticonvulsants he was receiving previously at proper doses along with other supportive measures. As initial blood glucose was 33 mg%, the baby had to be maintained on peripheral glucose infusion rate @ 8.5 mg/Kg/min. Seizures did not recur after admission. Appropriate sodium bicarbonate therapy was instituted, as there was metabolic acidosis in arterial blood gas (ABG) analysis.

Six hours after admission, vascular supply of left foot was noted to be grossly compromised. An urgent USG abdomen with Doppler study revealed a thrombus in distal abdominal aorta involving lower end just proximal to bifurcation and thrombus seen extending into both common iliac arteries. Thrombolytic therapy was started with injection Heparin with a loading dose of 100 units/Kg followed by continuous infusion of 25 units/Kg/hr. The infant's condition deteriorated progressively and he succumbed on day 9. 3 days after death of the baby, blood culture report became available revealing growth of *Klebsiella pneumoniae* which were only sensitive to Imipenem and Meropenem. 15 days later report of coagulation studies became available which showed: Prothrombin time – 18 sec (normal 11-15 sec),