Chylous blood in an infant with febrile encephalopathy: Clues to metabolic etiology (Very Long Chain Acyl CoA Dehydrogenase Deficiency)

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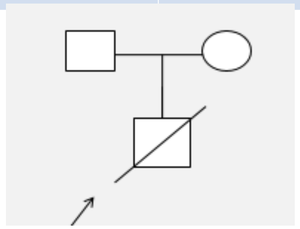
ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7 2022

INTRODUCTION

- ✓ Acute febrile encephalopathy usually has infective etiology
- ✓ We present a 5-month-old infant with acute onset febrile encephalopathy with seizures.
- ✓ Examination revealed poor sensorium, hepatosplenomegaly, and anasarca.
- ✓ Blood sample was lipemic on multiple occasions
- ✓ Lipemic sample can be a clue to metabolic etiology
- ✓ A high suspicion of a metabolic disorder most likely Fatty Acid Oxidation defect was further proven on Genetic testing.

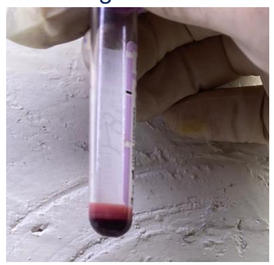
LIPEMIC BLOOD

Primary causes	Secondary causes
• Lipoprotein lipase deficiency • Apolipoprotein C2 deficiency • Apolipoprotein A2 deficiency • GP1HBP1 deficiency • Familial combined hyperlipidaemia • Familial hypertriglyceridaemia	• Diabetes mellitus • Metabolic syndrome • Nephrotic syndrome • SLE • Paraproteinaemia • CKD • Hypothyroidism • Hypopituitarism • Drugs :steroids, acitretin

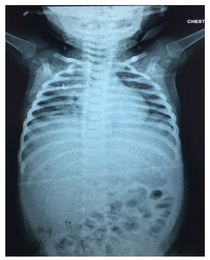


MATERIALS & METHODS

- ✓ A 5-month-old infant
- ✓ Born to non-consanguineous parents with uneventful birth history and normal development
- ✓ Presented with fever 5 days duration
- ✓ followed by seizures and poor feeding from 3rd day of illness.
- ✓ Admitted on 5th day of illness with worsening encephalopathy and multiple subtle multifocal seizures /atypical absences.
- ✓ At arrival he had poor sensorium with no spontaneous eye opening, poor perfusion, moderate hepatosplenomegaly and anasarca.
- ✓ Inv : mildly increased inflammatory markers
- ✓ CSF: Cellular and raised proteins.
- ✓ Albumin : 3.5, SGOT/SGPT :580/230
- ✓ ALP: 318, GGT : 544 Bld sugar low X2 times
- ✓ Coagulation & Lipd profile could not be processed by lab owing to Lipemic nature of blood specimen.
- ✓ Managed with IV broad spectrum antibiotics, Antiseizure medications and Nil per orally for the substrate reduction and was evaluated further.
- ✓ Keeping a possibility of fatty acid oxidation defect blood sample for exome sequencing was sent as metabolic screen also could not be processed including serum ammonia.



LIPAEMIC BLOOD SAMPLE



HEPATOSPLENOMEGALY

RESULTS

- ✓ Whole exome sequencing : likely pathogenic homozygous missense variation c.637G>A (p. Ala213Thr) in exon 8 of ACADVL gene confirming VLCADD.
- ✓ Parents were carrier for the variant in heterozygous state.
- ✓ Clues to the metabolic aetiology in the index case was lipemic blood

FOLLLOW UP

- ✓ Infant within 24 hours of admission developed clinical worsening and succumbed to pulmonary haemorrhage during CSF procedure.
- ✓ The genetic confirmation in first born index case resulted in genetic counselling for subsequent pregnancy even though with a poor outcome of the index case.

DISCUSSION

- ✓ Differentials of hepatosplenomegaly with seizures are vast .
- Infective:
  - Cerebral malaria
  - Septicemia with meningitis
  - Brucellosis
  - Leptospirosis
  - Typhus
- Storage disorders: Infantile Gaucher . NPC –A
- Metabolic disorders:
  - Galactosemia
  - Hereditary fructose intolerance
- Mitochondrial cytopathies : Alpers
- Hepatic encephalopathy
- ✓ The index case had febrile encephalopathy and hepatosplenomegaly triggered
- ✓ Lipemic sample with no obvious secondary causes led to suspicion of metabolic etiology of FAOD.
- ✓ Despite infective CSF parameters and fever triggered encephalopathy and hepatosplenomegaly Lipemia was big clinical handle to plan further investigations..
- ✓ Fatty acid oxidation disorders (FAOD) are rare, metabolic disorder caused by defects in enzymes and proteins involved in the transport and metabolism of fatty acids in the mitochondria

FINAL DIAGNOSIS

1. Acute febrile encephalopathy
2. Very Long Chain Acyl CoA Dehydrogenase Deficiency

CONCLUSIONS

- ✓ Encephalopathy triggered by fever is not always infective, a metabolic etiology in such cases need high suspicion & urgent addressal.
- ✓ Lipaemia in absence of any secondary cause should alert physician for a metabolic etiology of the symptoms.
- ✓ It is critical to identify quickly and accurately the key signs and symptoms of patients with FAOD so as to manage metabolic decompensations and prevent mortality.

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