A rare cause of Cholestasis

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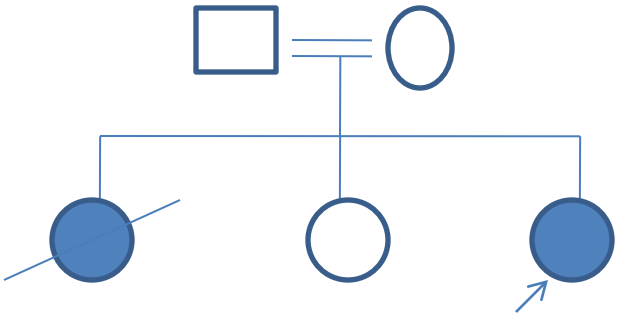
History.....

- 3 month old child
- Born to 3 ^{0} consanguineous marriage, Normal birth weight



- First female sibling-expired at 40 days of life
- 2 nd sib-well-4 years old
- H/o jaundice, pale stools, high coloured urine since day 20 of life
- Skin lesions since 25 days of life

On examination….

- Sick looking, FTT,
- Icthyosis
- Icterus
- Redundant skin folds, muscle wasting
- Flexion contractures of both knees, flexion deformity of thumbs

Diagnosis: PCSI + icthyosis + contractures

?syndromic

Multiple brains at work……

- Geneticist, Gastro enterologist opinion sought

Investigated…

- CBC -20,900 cells/cu.mm, Hb-7.2 gm%, platalet-9.7 lakhs
- PT- 13/14
- RFT-mild metabolic acidosis (Hco_3-14 mmol/l)
- LFT- bili-8.7 mg/dl, DB-5mg

- SAP-861 (100-644)IU/l
- SGOT-59 (0-45) , SGPT-27 (0-45)IU/L
- **GGTP- 34 IU/L** (7-98)
- Total protein-6 gm%, S.Albumin-2.9 gm%
- Thyroid profile-N
- Urine specific gravity-1.010, 2+ protein
- Urine for reducing substance, amino aciduria --ve

- CRP –ve, blood culture –no growth
- USG abdomen- increased renal echogenesity with poor corticomedullary differentiation with microliths, GB not visualized (fed baby), minimal free fluid
- Child was treated with iv albumin and other vitamin supplements

- ARC Syndrome was diagnosed
- Parents counselled
- Genetic analysis was planned- VIPAR6, VPS338 gene analysis
- At Great Ormond street hospital for children. U.K.

ARC SYNDROME

- *Arch Dis Child 2001;**85:415–420***
- Eleven pedigrees have been reported since the association was first described in 1973.
- An association between

  -**A**rthrogryposis,

  -**R**enal tubular dysfunction, and

  -**C**holestasis.
- **Autosomal recessive** inheritance is suggested by the frequency of parental consanguinity and recurrence in siblings.

- Notable **clinical variability**, even within the same family.
- Affected siblings with and without arthrogryposis have been reported.
- **Renal tubular dysfunction** ranges from isolated renal tubular acidosis to complete Fanconi syndrome.
- **Hepatic histology** shows variable combinations of cholestasis, intrahepatic biliary hypoplasia, giant cell hepatitis, lipofuscin deposition, and fibrosis, ultimately progressing to cirrhosis.

Additional features…

- Failure to thrive,
- Nephrogenic diabetes insipidus,
- Neurogenic muscular atrophy (which appears to be responsible for the arthrogryposis),
- Cerebral malformations, and nerve deafness.
- Most patients die by the age of 7 months, but those surviving longer have shown severe developmental delay.
- Dysmorphism- lax skin, low set ears, high arched palate, proximally placed thumbs, and cryptorchidism
- Ichthyosis
- Diarrhoea, recurrent febrile illnesses, and
- Abnormal giant platelets
- Bleeding tendencies inspite of normal coagulation profile.