# PSEUDO-TORCH- A RARE MUTATION CAUSING GLOBAL DEVELOPMENT DELAY, MICROCEPHALY AND EXTENSIVE BAND LIKE BRAIN CALCIFICATION

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## Introduction

- Pseudo-TORCH syndrome (PTS) is an inherited autosomal recessive disorder with homozygous or compound heterozygous mutation in the gene encoding occludin (OCLN) on chromosome 5q13 (OMIM # 251290).
- PTS is characterized by the presence of early onset infantile seizures, developmental delay, spasticity, microcephaly and intracranial calcifications which can be seen at birth even in almost all cases.

## Case Report

3.5 years old boy, product of consanguineous marriage, 6th in order of 6 siblings with three sibling deaths in early neonatal period, delivered full term at 38 weeks with uneventful birth.

His anthropometric measurement at birth showed OFC-30 cm (<3rd centile), length-49cm (25th centile) and weight-2.6kg (10th centile). He required neonatal admission owing to respiratory difficulty and considering small head size and previous siblings' deaths, his neonatal metabolic screening was done that came negative for aminoacidopathies, organic acidemia and fatty acid oxidation defects.

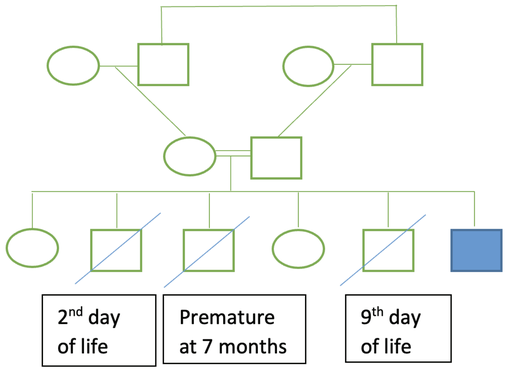
He had first seizure at the age of 3 months, starting as subtle seizures and apneic episodes followed by tonic seizures and later evolved into myoclonic jerks. Seizures were refractory to treatment with only partial control with polytherapy. (Levetiracetam, carbamazepine, valproic acid, clonazepam, steroids, vigabatrin and ketogenic diet).

There was global developmental arrest with partial neck holding only, speech confined to cooing and vision was limited to fixation only.

At 1 year examination, he had marked microcephaly with OFC of 33.5 cm (3rd centile), prominent sutures with tower shaped skull, high-arched palate, low-set ears, and sloping forehead and signs of spasticity.

CT brain done at 6 months of age showed mild hydrocephalus with symmetrical bilateral calcification involving thalami as well as pons. Considering microcephaly, brain calcification, previous neonatal deaths, extensive workup for TORCH done.

Systemic examination and investigation showed no visceromegaly, heart defect, cataract or thrombocytopenia. MRI Brain showed malformation in terms of pachygyria,lissencephaly and agenesis of corpus callosum. Child had intractable seizures despite being on multiple anti-epileptic drugs with frequent episodes of status epilepticus. Unfortunately, child expired at 3.5 years of age. Genetic counselling of family has been done.



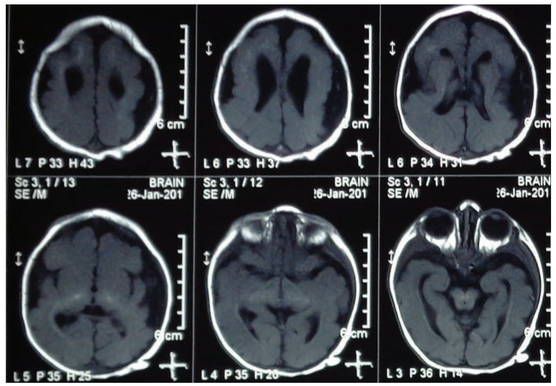



**Figure 1:** MRI Brain T1W images showing pachygyria,lissencephaly and agenesis of corpus callosum with calcification involving periventricular areas, bilateral thalami and midbrain.

| INVESTIGATION | FINDINGS |
|---|---|
| **TORCH Serology** | Negative |
| **Neonatal Metaboli Screening** | Negative for aminoacidopathies/ organic acidema/ fatty acid oxidation defect, hypothyroidism |
| **Ammonia, Lactate, Anion gap** | Normal |
| **Bone profile ( Calcium, Magnesium)** | Normal |
| **Electroencephalography** | Multifocal epileptiform discharges |
| **Opthalmological Examination** | No cataract or disc changes |
| **Cardiac Screen** | Normal |
| **Whole Exom Sequencing** | Homozygous mutation in OCLN gene, ENST00000355237.6:c.1324G>T, ENSP00000347379.2:p.Glu442Ter consistent with pseudo-TORCH syndrome 1. |

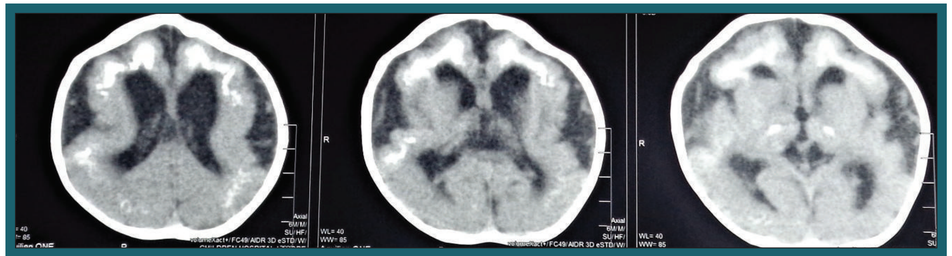


Figure 2: CT Brain showing extensive parenchymal, thalamic calcification with atrophic changes

## Discussion

- Pseudo-TORCH syndrome-1 is an inherited autosomal recessive disorder caused by mutation in the OCLN gene that clinically and radiologically mimics congenital TORCH infection. Mutation leads to ischemic and vascular insults in utero leading to cortical malformations which is unique to PTS contrary to TORCH.
- First described in 1985 in 2 brothers with microcephaly, spasticity, intellectual disability and brain calcification, the disease continued to evolve in terms of new imaging findings of extensive calcification in deep brain structures including thalami, basal ganglia and brainstem as well as associated brain malformation like in our index case .
- The importance of this case report is to create an awareness about the early diagnosis of this genetic disorder that mimics TORCH infection which is highly prevalent in our part of the world. Our index family had 4 deaths including the index patient. This emphasizes that a genetic diagnosis is mandatory in such cases through carrier testing and antenatal screening in subsequent pregnancies which can prevent further morbidity and mortality.

## References

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