Introduction:
Mitochondrial amino-acid tRNA synthetase deficiencies were first recognized in patients with Leigh syndrome, in whom mutations in genes involved in tRNA synthetase disorders were found. EARS2 is one of the genes responsible for this syndrome. It encodes for elongin A, a subunit of the elongation factor 1A (Elongin 1A), which is involved in the translation of amino acids into proteins. Patients with EARS2 mutations typically present with neurological and developmental disabilities, as well as metabolic abnormalities.

Case Description:
A 6-month-old boy was born in 2015 to Pakistani parents. His birth was uneventful, and his development was normal. He presented at 11 weeks of age with a febrile illness. At 5 months of age, he had a similar clinical presentation. The patient was diagnosed with tRNA synthetase deficiency associated with high lactate (LTBL) caused by EARS2 mutations. The hallmark features of this condition include high lactate levels, metabolic acidosis, and neurological symptoms.

Genetic Variants:
SNP microarray showed no significant copy number changes but multiple long contiguous stretches of hemizygosity. Whole Exome Sequencing identified a previously reported homozygous pathogenic missense variant in EARS2 on chromosome 16: NM_00138614.1, c.952C>T, p.(Gly317Ala).

Progress:
At 6 months of age, the infant presented with tachypnoea in the context of a mild febrile illness. She developed severe refractory metabolic acidosis with pH of 6.9 and lactate levels >25 mmol/L. There was no improvement despite bicarbonate infusions. After multidisciplinary discussions, it was considered that if life-saving intervention with haemofiltration was offered and effective, it would be likely that she would develop respiratory failure and fail to improve, remaining severely disabled. There was persistent lactate elevation. MR features are of progressive atrophy of the affected structures.

In the mild form, early development is normal. Clinical onset manifests after six months of age with spasticity, psychomotor regression, seizures, and irritability. However, clinical and biochemical improvement takes place from the second year of life without further deterioration. Some milestones can be regained or progress. Lactate levels reduce. MR shows significant improvement without new lesions.

Discussion:
In addition to the mild and severe biphasic neurological, biochemical and radiological presentations previously published, a multisystem, rapidly progressive fatal version of the severe form has also been described. As with our patient, the patient in that case report also had elevated liver enzymes and hepatomegaly.

Conclusion:
The patient presented here highlights the lack of genotype-phenotype correlation. It may be that associated liver involvement predicts a more rapidly progressive fatal outcome. With increasing awareness of the clinical and radiological presentation from variants in the EARS2 gene and with multidisciplinary-guided genomic testing, more patients may be identified with nuclear encoded mitochondrial glutamyl-tRNA synthetase deficiency. Our ability to prognosticate may be more refined with increasing knowledge from natural history outcomes.