Reviewer's report

Title: Clinical and molecular features of an infant patient affected by Leigh Disease associated to m.14459G>A mitochondrial DNA mutation: a case report.

Version: 1 Date: 27 April 2011

Reviewer: Eppie Yiu

Reviewer's report:

This report describes the case of a patient with Leigh syndrome due to a previously reported mutation in the ND6 subunit of Complex 1. The patient and her mother also carry a novel variant in cytochrome b.

Whilst the clinical presentation of Leigh syndrome due to the previously reported ND6 subunit mutation is not novel, it is interesting to note the finding of this additional variant in the cytochrome b gene, although its significance is unclear.

Major compulsory revisions

1. mtDNA is well known to be highly polymorphic and therefore the significance of a new variant obviously requires some consideration. Apart from mentioning that the variant was not present in control samples, little other data has been presented as to the relevance or pathogenicity of this new variant. Also, how was the mother deemed to be ‘healthy’ and unaffected?

2. The discussion and points made seem a little confused and contradictory. On one hand the authors note that marked interfamilial and intrafamilial variation is seen with the m.14459G>A mutation. They postulate that this novel cytochrome b variant could be a secondary mtDNA variant that influences the clinical phenotype. However, they then also reference a family specifically where the clinical phenotype showed marked variability in individuals who share the same mtDNA – in this situation a variant such as the one postulated in the mtDNA would not explain the clinical variability. This needs more clarity.

3. Overall this case report requires some English editing to correct grammatical and spelling errors.

Discretionary revisions

1. A minor point, but I assume BTX is botox? How is this relevant to the case report?

2. The table is very detailed. Can some information be taken out?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being
published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests