Reviewer’s report

**Title:** Female heterozygotes for the hypomorphic R40H mutation can have ornithine transcarbamylase deficiency and present in early adolescence: two cases

**Version:** 1  **Date:** 26 October 2009

**Reviewer:** Steven Dobrowolski

**Comments to authors:**

1. While the ammonia level is provided in the abstract, the orotic acid is simply described as significantly elevated. Be consistent, either give precise values for both or neither. Both would be preferred.

2. In the introduction correct the following: Femnales and males with “mild”......

3. R40H is not in HGVS approved nomenclature, additionally a cDNA numbered version of the mutation must be provided at least the 1st time the variation is named. Utilizing the standardized nomenclature for sequence variants (both nucleotide and protein) is critical.

4. In the CONCLUSION section of the abstract the following sentence is used: This report expands the clinical spectrum of presentation of this condition to female heterozygotes for the hypomorphic (“mild”) R40H mutation.
   It is not correct to describe a “mutation” as mild, but to say that the mutation is associated with a mild phenotype. Please correct.

5. Many times throughout the manuscript, abbreviations are utilized without being defined. Define all abbreviations at the 1st instance of their use.

6. The following sentence from CASE 2: Although it is not possible to obtain molecular confirmation that she that she was a manifesting carrier of the R40H mutation, her clinical course, biochemical investigations and family history are highly suggestive of this conclusion. Please correct the sentence.

7. The section on Case 2 is very difficult to follow. It is indicated that the patient had 2 episodes nausea and vomiting at age 13. Was one of these during the new year festival or is this something different. Was there no medical follow-up after week-long episodes of nausea and vomiting? Was the mother symptomatically affected with OTC? The manuscript indicates the mother experienced orotic aciduria, thus urine organic acids must have been performed. Overall the entire Case 2 section should be re-composed such as to make it more clear.

Overall the case report is acceptable. Prior to publication, corrections and revisions must be made to clarify the manuscript.