Author’s response to reviews

Title: EXTENDED CLINICAL FEATURES ASSOCIATED WITH NOVEL GLIS3 MUTATION: A CASE REPORT

Authors:
naglaa kamal (nagla.kamal@kasralainy.edu.eg)

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Author’s response to reviews:

Changes were highlighted yellow throughout the manuscript.

We wish the corrections done to improve our manuscript and achieve editors’ and reviewers’ expectations.

Reviewer 1 comment

Very interesting and well written report describing a patient with a novel GLIS3 deletion whose clinical phenotype includes abnormal external genitalia. The authors conclude that infants with neonatal diabetes associated with dysmorphism that includes abnormalities in the external genitalia should be screened for GLIS3 mutations. This conclusion is supported in this case study of a single patient. However, the authors should consider commenting on the occurrence of external genitalia abnormalities (bifid scrotum, bilateral undescended testicles, microphallus, scrotal hypospadias) observed in the absence of GLIS3. This would give a greater perspective in light of the novel and important observation presented by the authors.

Reply to Reviewer 1 :

Thanks for the valuable comment. We included it at the end of the manuscript. It was highlighted yellow and in bold. References 17,18 and 19 were added.

Reviewer 2 comment:

Reviewer 2

This case report describes an infant from a highly consanguineous background with a mutation of the GLIS3 gene and a phenotype that extends the range of abnormalities reported in the literature to include a range of genital abnormalities including hypospadias, chordee and bifid scrotum.

Unfortunately, I don't think this case report is publishable as it is unclear whether this mutation is responsible for the range of genital abnormalities reported in this patient. Such genital abnormalities are relatively common and even though there is no underlying explanation given
the apparently normal endocrine responses to HCG stimulation, the authors do not provide any evidence that these abnormalities are a consequence of the GLIS3 mutation rather than a coincidental finding or a consequence of another genetic abnormality arising from the underlying consanguinity.

Reply to reviewer 2:

Thanks for the valuable comment. We agree that the associated genital abnormalities may be just a coincidental finding.

We agree that we shouldn’t mention that these genital abnormalities extend the spectrum of GLIS3. We changed that in our manuscript and we changed the conclusions. Changes are highlighted yellow in the manuscript.

We believe that this case is important to literature as it reports novel mutation not previously reported in a very rare disease with only 12 reported cases and we adjusted our manuscript and its conclusions so as not to confuse readers or convey unclear information.

We wish the corrections done to improve our manuscript and achieve editors’ and reviewers’ expectations