Author's response to reviews

Title: Secondary amenorrhea in patient with spinocerebellar degeneration treated with thyrotropin-releasing hormone (TRH): a case report and in vitro analysis

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Author's response to reviews: see over
Dear Sir,

RE: MS 6160967635754670

Thank you for your letter dated October 7, 2011 with the reviewer comments on our manuscript entitled “Does continuous administration of thyrotropin-releasing hormone induce hyperprolactinemia? A case report of spinocerebellar degeneration treated with thyrotropin-releasing hormone and results of in vitro analysis” by H Kanasaki, A Oride, T Mijiddorj, I Purwana and K Miyazaki. We have carefully considered the comments and criticisms and have revised the manuscript accordingly.

We hope that the revised manuscript is now suitable for publication in Journal of Medical Case Reports. Thank you for your time. We look forward to hearing from you soon.

Yours sincerely,

Haruhiko Kanasaki, MD, PhD
Answer to reviewer

We agreed reviewer’s comment. There is no criteria for the diagnosis of latent hyperprolactinemia by recent chemiluminescence immunoassay (CLIA) for PRL. Based on the observations that serum PRL increased to more than 140 ng/ml after the TRH provocation test, serum PRL was increased more than 20-fold by TRH, and that the patient had symptoms associated with hyperprolactinemia, we diagnosed latent hyperprolactinemia.

We added this description in discussion section, as follow,

(P7, line 4-11)

What are considered normal values for serum PRL differs according to the assay system used. The chemiluminescence immuno assay (CLIA) we currently use defines normal serum PRL levels as 3.2–26.2 ng/ml. Although there are no standard criteria for the diagnosis of latent hyperprolactinemia using recent assay systems, we diagnosed latent hyperprolactinemia based on the observation that serum PRL increased to more than 140 ng/ml after the TRH provocation test, serum PRL was increased more than 20-fold by TRH, and that the patient had symptoms associated with hyperprolactinemia.

Following reviewer’s suggestion, we revised conclusion of this manuscript, as follow,

(P2, line22-)

Physicians should be cognizant of hyperprolactinemia-associated side effects in patients receiving TRH treatment. Long-term treatment with a TRH preparation might cause a large amount of PRL to accumulate in PRL-producing cells and be released in response to exogenous TRH stimulation.

(P9, line16-)

We experienced a patient who was treated with a TRH preparation for spinocerebellar degeneration (SCD) and who developed amenorrhea following a dose increase. The patient had a normal PRL level but showed a response pattern suggestive of latent hyperprolactinemia following stimulation with TRH. Physicians should be cognizant of hyperprolactinemia-associated side effects in patients receiving TRH treatment. The experiment using PRL-producing cells demonstrated that long-term exposure to TRH resulted in increased basal activity of PRL synthesis and decreased responsiveness to TRH. Thus, different responses to TRH were observed in vivo and in vitro following the long-term administration of TRH.
This manuscript was re-corrected by native English speaker