**Reviewer's report**

**Title:** Corticosteroid dose increase is a risk factor for nonalcoholic fatty liver disease and contralateral osteonecrosis of the femoral head: A case report

**Version:** 1  **Date:** 23 Oct 2018

**Reviewer:** Satoshi Ikemura

**Reviewer's report:**

Thank you for letting me read and review this case report entitled, "Increasing corticosteroid dose is a potential risk for nonalcoholic fatty liver disease and contralateral osteonecrosis of the femoral head". The manuscript is well written regarding the patient's clinical course and presented images are appropriate.

Page 6, Line 113

As authors mentioned, I agree that individual variability in the level of cytochrome P450 3A activity play an important role for the development of osteonecrosis of the femoral head.

Masada et al. reported that cytochrome P450 3A activity inversely correlated with the incidence of osteonecrosis and extent of the necrotic area. Ikemura et al. (Cytochrome P4503A activity affects the gender difference in the development of steroid-induced osteonecrosis in rabbits. Int J Exp Pathol. 2014;95:147-52) suggested that gender difference in the rate of incidence of osteonecrosis (male > female rabbits) is caused by the gender difference in the cytochrome P450 3A activity (female > male rabbits). Please expand the final paragraph of the Discussion section using above two animal studies.

(e.g.) Several animal studies focused on the correlation between cytochrome P450 3A activity and the incidence of osteonecrosis. Unfortunately, our patient was not examined cytochrome P450 3A activity. Therefore, whether the abnormality of hepatic metabolism could directly play an important role in ONFH occurrence remains unclear. However, recent reports showed the association between cytochrome P450 3A activity and expression in NAFLD as well as between corticosteroid use and NAFLD.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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