Reviewer's report

Title: Acute kidney injury on everolimus in a breast cancer patient: a case report.

Version: 1 Date: 12 September 2014

Reviewer: Hasan Fattah

Which of the following following best describes what type of case report this is?: Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

1. In the first introduction: you mentioned that occurrence of adverse events account for an important percentage of treatment discontinuation and dose reduction, is this statement referring to the BOLERO-2 study, or to clinical practice, and apart of this case of AKI, other major adverse events necessitating treatment discontinuation must be clarified in clinical practice.

2. Case is presented thoroughly, some missing related data, patient presented with peripheral edema, and weight loss, is the 24 hours urine protein measured at presentation or late when GFR was significantly low, other labs like albumin, and liver enzymes are important when dosing MTOR inhibitors, and what is the method the GFR was calculated.
3. it seems that the patient presented with significant hypovolemia associated with ongoing GI volume loss, possibly from medications side effect, patient did not respond to IVF, pointing toward an ischemic ATN, after ruling out sepsis and other nephrotoxic drugs. though the urinalysis was not pretty typical for ATN, the question of whether selective MTOR complex 1 inhibition is the true cause of the renal dysfunction here or this was merely an indirect effect by not allowing renal tissue repair in response to nephrotoxic stress, I agree with author that the etiology of renal dysfunction here is unclear, and can not be causally related to a direct effect of selective MTOR complex 1 inhibition. Especially in this elderly patient with significant other commodities including cardiovascular disease, low GFR, and possibly in association of other nephrotoxic drugs. author must emphasize the idea that this patient presentation is likely a result of hypovolemia of unknown timing, and that there is no direct evidence that mTOR inhibition could be contributing directly here even after the drug was discontinued.

4. In discussion part: It is important to remember that mTOR activity is low or absent in the normal kidney, and although autophagy associated markers were shown to rise in the urine of experimental animals after administrating MTOR inhibitor to an ischemia-reperfusion renal injury model, but this does not necessarily mean that MTOR itself is upregulated after renal injury to initiate regeneration process, on the other hand autophagy seems to play a critical role during renal ischemia period by recycling the macromolecules and providing the needed amino acids for new protein synthesis, which in turn could activate MTORC1.

5. although MTOR inhibitor might be nephrotoxic in expiremental animals, but there is no such evidence in vivo to show a direct drug nephrotoxicity.

6. in Conclusion part:
when prescribing everolimus for clinical indication, vigilance is required in all conditions with existing renal risk factors and not specifically in breast cancer, in addition, most reported cases in literature were not preceded with hypotension or severe hypovolemia like in this case, so avoiding hypovolemia alone may not necessarily prevent AKI, I believe looking at other parameters like elderly age, baseline GFR, other nephrotoxic drugs, heart and liver functions must all be considered when prescribing the drug.

Level of interest:An article of importance in its field

Quality of written English:Acceptable

Declaration of competing interests:
I declare that I have no competing interests
answer 1, no
answer 2, no
answer 3, no
answer 4, no
answer 5, no
answer 6, no