Author’s response to reviews

Title: Efficacy of combined treatment with pasireotide, pegvisomant and cabergoline in an acromegalic patient resistant to other treatments: a case report.

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Reviewer reports:

Marinela Tzanela (Reviewer 1):

Dear colleagues, I read your manuscript carefully. My only comment is that the patient described here must take two very expensive drugs for the rest of his life. Do you plan to try any alternative therapeutic modality in the future (2ND SURGERY OR IRRADIATION)?? please add a paragraph in the discussion addressing the health economics issue, as well as the latent effects on glucose metabolism.

Authors’ reply: In agreement with these suggestions, we added a comment about other future therapeutic options (page 6, line 221-225) and the latent effects of pasireotide on glucose metabolism (page 6, line 226-233).

Adriana Ioachimescu (Reviewer 2):

This a case report of a 41 year old man with acromegaly who underwent several regimens of medical therapy and surgery and achieved biochemical control for the first time on a combination of pasireotide LAR/pegvisomant.

I have the following comments:

- Abstract: Include patient's age instead of "young acromegalic". Also the fact this was a mixed GH/PRL pituitary adenoma.

Authors’ reply: As suggested, we added in the Abstract the age of patient and the nature of the pituitary adenoma.
Background: the long sentence on lines 79-82 requires streamlining.

Authors’ reply: In agreement with this suggestion, we reorganized the sentence (page 3, line 79-86).

Sentence on lines 86-87 would me more informative if it included a range of IGF-1 normalization from several published studies rather than "up to 97%".

Authors’ reply: As suggested, we specified in the text the range of IGF-1 normalization reported by major studies (page 3, line 90-93).

Case presentation:

What happened to the prolactin level in absence of dopamine agonist regimen?

Authors’ reply: We thank the reviewer for this observation, which has led us to better specify that cabergoline therapy has never been suspended. In agreement with this comment, we added in the text the trend of PRL levels during the follow-up (page 4, line 156-158).

Line 108, replace "from some months" with "for some months". Line 114: replace "objectivity" with "exam". Line 122: replace "larger diameter" with "largest diameter". Line 129: "slight increase in fasting glucose and HbA1c" is not quite accurate as HbA1c increased from 5.9 to 6.5%.

Authors’ reply: All these suggestions have been carefully addressed (line 113, 120, 128 and 135, respectively).

Line 138: "Surgery proved unsuccessful" could be replaced with something more adequate. The tumor was invasive to the cavernous sinus, so surgery had a debulking rather than a curative purpose. In addition, it did significantly improved the biochemical parameters of acromegaly, which increased the likelihood of control on postoperative medical treatment, which is what actually happened.

Authors’ reply: We agree with this observation and, accordingly, we modified the sentence (page 4, line 145-146).

Line 151: replace "highlighted" with "seen". Line 158: replace "with more colliquative outcomes" with something more appropriate that reflects changes in signal on the MRI. - Discussion: line 199: Delete "Surprisingly" because doses of pegvisomant were not escalated to the maximally-allowed and injections were not daily.

Authors’ reply: All these suggestions have been carefully addressed (line 159, 165-167 and 208, respectively).