Reviewer's report

Title: Severe Paraneoplastic Hypoglycemia in a Gastrointestinal Stromal Tumor with an Exon 9 Mutation: A Case Report

Version: 1 Date: 7 November 2006

Reviewer: Winette Van der Graaf

Reviewer's report:

General
In this paper a case with a gastro-intestinal stromal tumor with NICTH is described. The only new aspect of the case, adding to the already existing literature (also case histories), is that the patient described has a tumor with an exon 9 mutation.

There are several remarks to be made.
1. The authors talk about non-islet tumor induced hypoglycemia, which is not the right terminology. It should be non-islet cell tumor hypoglycaemia, NICTH. This should be changed throughout the paper.
2. They state in the abstract that they present the fourth case of a GIST with NICTH, but that is not true. It is at least the sixth: ther is also the case described by Hamberg in JCO, 2006 and the paper of Pinks describes 2 patients.
3. It is stated in the abstract that exon 9 mutations are uncommon, but depending on the definition of uncommonness, that is not really the case. Depending on the series that is referred to the incidence in exon 9 KIT mutations is 11-20% (Heinrich JCO 2003; Antonescu Clin Cancer Res 2003, etc).
4. Description of the case (no page numbers..) “Serologic workup etc”..please change what has been written there into: the IGF1 level was below the normal range, insulin, pro-insulin, C-peptide and IGF2 or IGFII (please use the same annotation in text and table!) levels were in the normal range, IGFBP3 was just below normal.
That makes more sense than what is stated now.
5. Description of the case. It would add to the follow-up data apart from that the patient is doing fine, that we are informed about the radiological follow-up status and the glycaemic status 6 months after surgery, as this patient has a very high chance of recurrent disease!
6. Please add IGFBP6 data to the table.

Discussion section:
7. Starts with “Some authors etc…” Please change this and add the paper of Debiec-Rychter, Eur J Cancer 2006. It’s not some. This has been a large study population!
8. The exact incidence of NICTH is unknown and probably exceeds that of insulinomas.
9. Again, change that there are only 3 reports in the literature, see remark 2.
10. NICTH also occurs in hepatocellular carcinomas for example, not only mesenchymal tumors. Please add.
11. In the sentence of Hizuka, please remove “in” after while.
12. Remove “the” before K ATP channels.
13. Finally, the title is somewhat confusing. The patient has hypoglycaemia, not the tumor.

Minor:
It should be C-peptide, in stead of c-peptide.
The “whole” University Medical Center in Utrecht is acknowledged, but it is better to acknowledge someone who did the work or the Department.

References:
In ref 15 only the journal is mentioned, not the page numbers.

Table 1 should be changed, the information about the drugs measured can be summarized in the text after the statement that no evidence for factitious hypoglycaemia was found.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Declaration of competing interests:

I declare that I have no competing interests