Author's response to reviews

Title: Electrical short-circuit in beta-cells from a patient with non-insulinoma pancreatogenous hypoglycemic syndrome (NIPHS): A case report

Authors:

Robert Bränström (robert.branstrom@ki.se)
Erik Berglund (Erik.Berglund@ki.se)
Pontus Curman (pontus.curman@sodersjukhuset.se)
Lars Forsberg (larsforsberg65@gmail.com)
Anders Höög (anders.hoog@karolinska.se)
Lars Grimelius (lars.grimelius@genpat.uu.se)
Per-Olof Berggren (Per-Olof.Berggren@ki.se)
Per Mattsson (Per.Mattsson@karolinska.se)
Per Hellman (per.hellman@surgsci.uu.se)
Lisa Juntti-Berggren (Lisa.Juntti-Berggren@ki.se)

Version: 3  Date: 9 May 2010

Author's response to reviews:

Dear Editor-in-Chief.

We have read the comments from the two reviewers and made changes in the manuscript according to their suggestions. All changes made in the manuscript are labeled red.

We hope that you will find that this version of our manuscript fulfills the criteria for publication in Journal of Medical Case Report (JMCR).

Yours sincerely,

Robert Bränström
MD, PhD, Assoc professor

Responses to reviewers

Dr Rodrigo RM Moreira

1. We agree that there is an ambiguity when you read the literature. In some articles NIPHS and Nesidioblastosis are consider as synonymous, but to eliminate any confusion we have changed in our manuscript and use NIPHS, because what is really true is that the patient had pancreatic hyperinsulinemia, but no insulinoma.
2. The membrane potential in normal cells under resting and stimulatory conditions is well defined and characterized. From this patient all the cells we measured were depolarized at low glucose, giving an explanation why he secreted insulin at non-stimulatory concentrations of glucose. We have included the membrane potential values for normal cells in the revised manuscript to make it more clear for readers not so familiar with electrophysiology.

3. We have, as suggested by the reviewer, moved the last paragraph from the “Case Presentation” part to the “Conclusion” part.

4. We have changed and added a new section to the conclusion part.

Dr Patrick Manning

In the revised manuscript we have, as suggested by the reviewer, included an example of actual values of insulin, C-peptide, glucose and pro-insulin taken from the patient.

A graph of the two Calcium stimulation tests that were performed are now included as Fig. 1 in the manuscript to clearly show that in this particular patient we did not have any help to localize a specific area of the pancreas with hypersecretion of insulin.

In our manuscript we have written on page 4 The condition worsened, resulting in the need of food intake every hour, day-and-night, which however did not prevent the continuation of severe hypoglycaemic episodes, leading in turn to a need for glucose infusions.” This makes it clear for the reader that this patient had hypoglycaemia without postprandial relationship.

The histopathological and immunohistochemical examination of the removed (80%) part of the pancreas showed an increased number of islets of different sizes evenly distributed in the gland. No remarkable islet-cell hyperplasia in relation to ducts. The last sentence has been added to the manuscript. The patch clamp data have been explained more in detail as this was suggested by both reviewers.