Author’s response to reviews

Title: Complete Agenesis of the Dorsal Pancreas Presenting with Diabetic Ketoacidosis – A Case Report and Literature Review

Authors:

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Author’s response to reviews:

Author Responses to editor and reviewers’ comments

Response to editor:

Thanks to your comments. Our answers to your points are as follow.

1. Agenesis of the dorsal pancreas is a rare, but well-known condition. BMC Endocrine Disorders welcomes well-described reports of cases that include "Unexpected or unusual presentations of a disease" or "New associations or variations in disease processes" or "An unexpected association between diseases or symptoms". It is crucial that the authors highlight the novelty, if any, of this clinical case and if it falls in one of the categories described above.

Response: Agenesis of the dorsal pancreas (ADP) is a rare and well-known condition, but diabetic ketoacidosis (DKA) has been never reported as a primary clinical presentation in patients with ADP. What’s more, most of the reported cases were reported by surgeons and radiologists and the β-cell functions were not evaluated. Here, we reported the first case of ADP presented with DKA and evaluated the β-cell function. Our case highlights the β-cell function and rare presentation of DKA for the patient with ADP. We also reviewed the literature and remind the clinicians to consider the diagnosis of ADP for patients presenting with glucose metabolic disorder accompanied by abdominal pain, pancreatitis or steatorrhea.

2. ADP is usually associated to genetic mutations. There are forms of monogenic diabetes resulting in pancreatic agenesis. Please provide the genetic study of this patient.

Response: We agree with the Editor that the genetic study would make the report more persuasive. Unfortunately, we can’t provide the genetic result of this patient. We had followed up with the patient and ask if he will do the genetic test for the study, but the patient was unwilling to do DNA sequencing test for personal reasons.
Response to reviewer 1:
Thanks to your comments. Our answers to your points are as follow.
1. Please, could you use the scientific name for the drugs shown in the clinical case instead of the commercial brand?
Response: Thanks for your suggestions. The commercial brands were replaced by scientific names for the drugs shown in the manuscript (section of Case presentation, pages 4, line 82).

2. Have you thought about the possible cause for the rapid onset of diabetes and DKA in this patient? Could you provide in this section or in the discussion a possible explanation for the onset of DKA? There was a possible infection at the moment of diagnosis or in the previous weeks/months? Other factors as changing in lifestyle, psychic stress, etc.?
Response: Thanks for your comments. We double checked the medical history of the patient and confirmed that the patient took lots of sugared beverages 1 week before the onset of DKA. There was no sign of infection as the patient had no fever, and the creative reactive protein and blood routine were normal. According to the history and lab results, we speculated that the sugared beverages might resulted in high blood glucose, which may contribute to DKA.
Revision: We updated the medical history in the section of Case presentation (page 3, line 55-56) and discussed the possible explanation for the onset of DKA (page 4, line 78-80).

3. The abdominal pain was the main factor that leads to the diagnosis of DKA and diabetes and it remains also after DKA resolution. Could you provide more information about pain resolution? How did you manage it? Did you solve it? If yes, how did you solve it?
Response: The patient had recurrent onset of persistent, mild epigastric abdominal pain, which worsen with eating. After insulin therapy, the DKA resolved but the abdominal pain didn’t stop. As additional images studies indicated the diagnosis of ADP, we believed that the pain may due to dysfunction of the pancreas. A diet low in fat was recommended, and pancreatic enzyme supplements as well as mosapride citrate were given with meals to facilitate the digestive process. The pain gradually resolved and went away in 7 days after the treatment.
Revision: DKA resolved gradually after insulin therapy, but the abdominal pain continued. …… On the basis of these findings, a diagnosis of complete ADP was evident, and we believed that the pain was due to dysfunction of the pancreas. Low-fat diet was recommended, and pancreatic enzyme supplements as well as mosapride citrate were given with meals to facilitate the digestive process. The pain gradually resolved and went away in 7 days after the treatment (section of Case presentation, page 3-4, line 68-74).

4. In the background, you stated that: "there are few studies on the involvement of diabetic ketoacidosis (DKA) in ADP. Here, we present the first case of a patient with ADP accompanied by abdominal pain and DKA." and then in the discussion you wrote: "there was no study reporting a correlation between ADP and DKA". Please, could you correct one of the sentences and provide references if "few studies on the involvement of diabetic ketoacidosis (DKA) in ADP" have been published until now?
Response: Thanks for your careful review. According to our literature review, there is no study reported on the involvement of diabetic ketoacidosis (DKA) in ADP in English literature.
Revision: However, there is no study on the involvement of diabetic ketoacidosis (DKA) in ADP. Here, we present the first case of a patient with ADP accompanied by abdominal pain and DKA (section of Background, page 3, line 51-52).

5. In the conclusion, you stated that: "we advise clinicians to consider a diagnosis of ADP for patients
presenting with a glucose metabolism disorder accompanied by abdominal pain or other abdominal symptoms." Please, could you provide which are the "other abdominal symptoms" that you are talking about?
Response: Although most of the ADP patients are asymptomatic, abdominal pain is the most common symptom according to our literature review. Other abdominal symptoms include pancreatitis and steatorrhea have also been reported (please referred to Table-2).
Revision: we advise clinicians to consider the diagnosis of ADP for a patient presenting with a glucose metabolism disorder accompanied by abdominal pain, pancreatitis or steatorrhea. (section of Discussion, page 6-7, line 127-129).

6. In order to better underline the role of abdominal pain in this clinical case, could you provide a brief differential diagnosis between the most common forms of diabetes at the age of your patient (type 1 diabetes, LADA and MODY)? I suggest to refer to the ADA guidelines chapter 2 "Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes2019" and to this review: Nat Rev Endocrinol. 2017 Nov;13(11):674-686. doi: 10.1038/nrendo.2017.99 in order to focus on the differential diagnosis.
Response: Thanks for your suggestions. The patient had no family history of diabetes, and laboratory tests showed negative autoimmune antibody and poor β-cell function. According to the ADA’s standard of Classification and Diagnosis of Diabetes, the diagnosis of “Specific types of diabetes due to other causes” was established.
Revision: According to the ADA’s standard of Classification and Diagnosis of Diabetes, the diagnosis of “Specific types of diabetes due to other causes” was made (section of Case presentation, page 4, line80-81).

7. In order to support your conclusion and give a useful tool to clinicians, could you provide a table that summarizes all the clinical presentation of ADP published so far? The table should highlight the main signs and symptoms and biochemical findings linked to ADP diagnosis reported in your case and in the previous publications in order to give a complete frame to clinicians to suspect an ADP case in clinical practice.
Response: Thanks for your suggestions. We reviewed the articles published between January 2008 and August 2019, and 53 cases reported by Javier A. Cienfuegos were excluded from the study. Clinical presentation, pancreas imaging, and gene mutation results were extracted and summarized in Table-2.
Revision: Please see the Table 2

8. page 4 line 34 and 36 - could you provide in brackets the values of fasting glucose also in mg/dL and switch the values of HbA1c, putting in the test the value expressed as mmol/mol and in brackets the value expressed in %?
Response: Thanks for your suggestions. The measurement units for the values of blood glucose and HbA1c have been changed accordingly (section of Case presentation page3 61-61 and page 4 line 77-78).

9. Could you provide a table with the patient's main anthropometric and serum characteristic at the time of diagnosis of DKA/diabetes?
Response: The suggestions of the reviewer are extremely helpful. We listed the patient’s main anthropometric and serum characteristics in Table 1
Revision: Please see the Table 1

Response to reviewer 2
Response: Agenesis of the dorsal pancreas (ADP) is a rare and well-known condition, but diabetic
ketoacidosis (DKA) has been never reported as a primary clinical presentation in patients with ADP. What’s more, most of the reported cases were reported by surgeons and radiologists and the β-cell functions were not evaluated. Here, we reported the first case of ADP presented with DKA and evaluated the β-cell function. Our case highlights the β-cell function and rare presentation of DKA for the patient with ADP. We also reviewed the literature and remind the clinicians to consider the diagnosis of ADP for patients presenting with glucose metabolic disorder accompanied by abdominal pain, pancreatitis or steatorrhea.