Correlation of Type II Diabetes Mellitus Glomerulopathy with Pancreatic Morphometry

Lucine Papazian¹ BA | Ernesto Salcedo PhD ¹, ² | Zenggang Pan MD PhD³ Francisco G. La Rosa MD³, Lisa M.J. Lee PhD¹, ²

¹Modern Human Anatomy Program, University of Colorado School of Medicine. Aurora, CO. USA,
²Department of Cell and Developmental Biology, University of Colorado School of Medicine. Aurora, CO. USA,
³University of Colorado Hospital. Aurora CO. USA

Introduction

1. Investigate and correlate pancreatic morphometric alterations with glomerular pathogenesis in patients with type II diabetes.

2. Establish a set of pancreatic histological criteria associated with the progression of type II diabetes.

3. The systemic nature of type II diabetes provides opportunity to use the already established DN staging to classify pancreatic tissue.

4. Aperio Digital pathology images were captured for assessment of pancreatic islet area (Figures 5 and 6).

5. Renal tissues staged I-IV were used for analysis in the study (Figures 6A-C).

6. Aperio ScanScope Microscope was used to digitally capture renal tissues with ImageScope software (Figure 5).

Methods

Pancreatic Analysis

- Methodology:
  - Adipose: class IIa – IIb followed by attenuated decrease in total islet area through DN class III-IV
  - ISLET: progression or DN class IV, using glomerular correlations throughout.

- Staging:
  - Combined renal pancreatic images
  - A. B. Matched pancreatic and renal tissues were organized into matched renal DN samples.
  - Pancreatic and renal tissues were staged DN I-IV.
  - At the onset of DN, diabetic samples exhibit an approximate 33% decrease in pancreatic islet area in response to metabolic demand.

- Staging:
  - Area of pancreatic islets significantly decreases.
  - Intrapancreatic adipose composition significantly increases.
  - Islet area remains static throughout DN progression.

Conclusions

In the pancreas, beta cell deficits and morphological alterations have been observed and documented across the diabetic population. However, the morphometric classification criteria, such as the type I diabetes, or the chronic nature of type II diabetes provides opportunity to use the already established DN staging to classify pancreatic tissue.

Pancreatic islets with lymphoid infiltration have been documented to be a more prevalent feature in diabetic samples. In these cases, the islets exhibit a loss of beta cell mass, leading to impaired glucose metabolism and hyperglycemia.

Results

- Pancreatic islets with apparent amyloid infiltration were included in measured islet area. Amyloid infiltration reduces beta cell functionality and is used to determine beta cell function.

- Islet beta cells are responsible for insulin production in response to metabolic demand (Figure 9A).

- Chronic hyperglycemia stresses beta cells, leading to beta cell apoptosis, depleted insulin production and prolonged hyperglycemia.

- Pancreatic islets with apparent amyloid infiltration were included in measured islet area. Amyloid infiltration reduces beta cell functionality, leading to quantifiable amyloid in the islet.

Inflammation and Diabetes

- Chronic hyperglycemia stresses beta cells, and signals for the production of inflammatory factors.

- The inflammatory response favors apoptotic processes, promoting beta cell death.

- Subsequent lymphatic invasion is likely associated with the removal of apoptotic beta cells (Figure 9A).

- Pancreatic islets with lymphoid infiltration have undergone functional and histologic transitions.

- Immunostaining used to visualize functional beta cells, would provide insight to better understand the role of inflammation in the pancreatic pathogenesis of type II diabetes.

Acknowledgements

Intramural support to the development of this project by the American Association of Anatomists, sponsored by the National Institute of General Medical Sciences, National Institutes of Health, is greatly acknowledged.

INFLAMMATION AND DIABETES

- Chronic hyperglycemia stresses beta cells, and signals for the production of inflammatory factors.

- The inflammatory response favors apoptotic processes, promoting beta cell death.

- Subsequent lymphatic invasion is likely associated with the removal of apoptotic beta cells (Figure 9A).

- Pancreatic islets with lymphoid infiltration have undergone functional and histologic transitions.

- Immunostaining used to visualize functional beta cells, would provide insight to better understand the role of inflammation in the pancreatic pathogenesis of type II diabetes.