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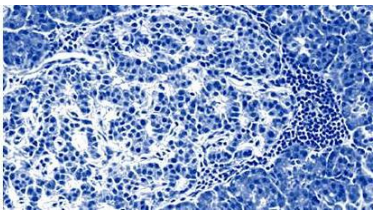

Islet amyloidosis in a child with type 1 diabetes

AUTHORS

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PURPOSE

Islet amyloidosis represents a histopathological feature classically ascribed to patients with type 2 diabetes. Herein, the occurrence of islet amyloidosis and its severity are reported in a child with type 1 diabetes along with histological comparisons of islet amyloidosis in two young adults with recent-onset type 1 diabetes.

METHODS

Histopathology reviews were conducted on hematoxylin and eosin (H&E) and immunohistochemistry (insulin, glucagon, Ki67, CD3) stained pancreas slides. When islet amyloid was detected during initial histopathology reviews, additional pancreas sections (8 µm thick, N = 4–7 sections/patient) were stained using Congo Red (S7441, Cardinal Health, Dublin, OH) to confirm islet amyloidosis. Three age-, BMI-, and sex-matched control donors to the three patients with type 1 diabetes described herein were selected and paraffin sections similarly stained with Congo Red. Amyloid area was automatically quantified using the tissue classifier function in HALO after total tissue, islet count and amyloid positive islet areas were calculated following manual annotations.

SUMMARY OF RESULTS

Islet amyloidosis was infrequent yet widely distributed throughout the pancreas in the child with type 1 diabetes and both adults with type 1 diabetes, with no such pathology seen in matched control donors. Congo Red staining showed a wide range in numbers of amyloid-positive islets per section with variable degrees of regional islet amyloidosis in all three patients. No amyloid was detected by Congo Red staining in three matched controls. Islet amyloid prevalence ranged from 0–9.3%, 0–12.6%, and 0–4.7% in donors 6371, 6414, and 6362, respectively. Islet amyloid severity within only amyloid positive islets per section ranged from 0–41.2%, 0–15.1%, and 0–39.0% in donors 6371, 6414, and 6362, respectively. In donors 6371 and 6362, amyloid-positive islets were distant from each other and rare (0–8 islets/section), with minimal to moderate islet amyloidosis (12 islets with 0.4–19% amyloid area; 7 islets with 25–48% amyloid area). Donor 6414 had a higher frequency of amyloid-positive islets (4–35/section) with minimal to moderate amyloidosis (41 islets with 1.5–23% amyloid area, two islets with 25–43% amyloid area, respectively). A clustering of

amyloid positive islets was observed in two lobules from donor 6414 but not in the other two donors with type 1 diabetes. This lobular pattern of islet amyloid was unevenly distributed across the pancreas, largely being concentrated in the tail with a few foci identified in the head region. All three donors with type 1 diabetes had insulitis; however, insulitic islets did not show amyloidosis

CONCLUSIONS

Analysis of these cases add to the increasing appreciation of islet heterogeneity in children and young adults with type 1 diabetes. Our finding of islet amyloid in two young adults with recent onset type 1 diabetes is in keeping with the report by Westermark et al. The child with type 1 diabetes showed a very similar pattern to the two young adults in terms of islet amyloid prevalence and severity. Notably, however, the child and one of the young adults (6362) showed a scattered distribution of amyloid-containing islets whilst in the other young adult (6414), lobular clustering of amyloid-containing islets was seen. This lobular clustering of amyloid was also noted in the 2 subjects with recent onset type 1 diabetes in the Westermark report. Such knowledge supports a notion that multiple pathophysiological mechanisms underlie the loss of functional β-cell mass in the spectrum of clinical phenotypes in patients with type 1 diabetes.