Viral Etiology

Detection of Enteroviruses in Tissue Samples of Cadaver Organ Donors with Type 1 Diabetes

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Purpose: Epidemiological studies have showed an association between enterovirus (EV) infections and type 1 diabetes (T1D). Prospective studies have suggested that EVs may initiate the beta-cell damaging process. Potential causal relationship has got support from studies showing enterovirus in the pancreatic islets and intestinal mucosa of T1D patients. The aim of the present study was to analyze the presence of enterovirus in the pancreas, spleen, duodenum and pancreatic lymph nodes (PLN) of T1D patients, islet-autoantibody-positive (auto-ab+) individuals and healthy controls.

Methods: Tissues were collected from cadaver organ donors in the Network for Pancreatic Organ donors with Diabetes (nPOD) study. Formalin-fixed paraffin-embedded tissue samples were analyzed using enterovirus-specific *in situ* hybridization (ISH) and immunohistochemical (IHC, clone 5-D8/1, DakoCytomation) assays. Study series included 18 T1D patients from whom 21 pancreas sections (two sections from one patient and three from another patient taken from different parts of the pancreas), 15 spleen, 10 duodenum and 2 PLN sections were available. Similar samples were available from 3 auto-ab+ individuals including 4 pancreas sections (2 from same individual), 3 spleen, 2 duodenum and 1 PLN sections. Samples from 23 non-diabetic controls included 25 pancreas sections (two sections were available from two individuals), 17 spleen and 1 duodenum sections.

Summary of Results: Altogether 43 % of all samples of T1D patients and 40 % of all samples of auto-ab+ individuals compared to only 9 % of all samples of control donors were positive for EV genome in ISH. Virus protein was found by IHC in 29 % of T1D patients, 38 % for auto-ab+ individuals and 5 % of healthy controls. EV was detected more frequently in the pancreas (30 % vs. 4 %; p=0,017) and spleen (53 % vs. 18 %; p=0,034) of T1D patients than control subjects using ISH. IHC showed enterovirus in 33 % of the pancreas samples of T1D patients but in only 5 % of control subjects (p=0,015). One T1D patient was positive in only one part of the pancreas in ISH and one in IHC. Virus isolation was carried out from 9 pancreas and 11 spleen samples, and EV RT-PCR from 8 pancreas, 10 spleen and 2 duodenum samples, but none were positive.

Conclusions: EV was detected more frequently in the pancreas and spleen of T1D patients than in control subjects using ISH and IHC. The results support the role of enteroviruses in the pathogenesis of T1D and fit with persisting slowly replication infection.