



COMMENT ON JACKSON ET AL.

Insulinitis in Autoantibody-Positive Pancreatic Donor With History of Gestational Diabetes Mellitus.

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We read with interest the article by Jackson et al. (1) illustrating mild insulinitis in the pancreas of a 28-year-old lean Hispanic female with recent gestational diabetes mellitus (GDM) who died of anoxic encephalopathy of unknown etiology 32 days after cesarean delivery. She was positive for GAD antibody (GADA) and islet cell antibody, while autoantibodies against insulin, IA-2, and zinc transporter 8 (ZnT8A) were negative. This observation, as well as earlier studies (2), raises a possible role of GDM in contributing to anti- β -cell autoimmunity and overt autoimmune diabetes after delivery. It is important not to overinterpret the low β -cell to α -cell ratios found in numerous islets of this woman, which may merely correspond to a situation of metabolic stress with degranulated β -cells. We agree with the words of caution indicating that we have to improve our understanding of the relationship between pregnancy and autoimmune diabetes.

We recently managed a 35-year-old lean Caucasian woman without any medical history who presented GDM treated by insulin during her second

pregnancy. She was GADA and IA-2 autoantibody negative but ZnT8A positive (272 AU/mL with assay cutoff 15) at 33 weeks of amenorrhea (Medizym; Medipan GmbH, Dahlewitz, Germany). Seven months after delivery, this woman was diabetes free with normal fasting blood glucose values and an HbA_{1c} of 5.1% (32 mmol/mol), and ZnT8A levels had returned to normal values.

Autoantibodies (particularly GADA) can be present in obese youths with type 2 diabetes (3,4), suggesting a secondary phenomenon in the context of metabolically stressed β -cells (endoplasmic reticulum stress, unfolded protein response, and chronic inflammatory responses), and GDM has many similar physiopathological features with type 2 diabetes. Reversibility of ZnT8A positivity after delivery as seen in our patient can also be seen with GADA (for 2 out of 11 women who were positive for GADA during GDM and who did not develop type 1 diabetes after pregnancy in the study of Nilsson et al. [2]).

This reinforces the idea shown previously (5) that autoantibodies do not

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always predict β -cell fate in subjects with diabetes.

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