RESPONSE TO COMMENT ON JACKSON ET AL.

Insulitis in Autoantibody-Positive Pancreatic Donor With History of Gestational Diabetes Mellitus. Diabetes Care 2017;40:723–725

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We greatly appreciate the interest of Marchand et al. (1) in our article (2), which we indeed hoped would stimulate interest regarding gaps in knowledge of diabetes during pregnancy. In some cases, gestational diabetes mellitus (GDM) could certainly represent previously undiagnosed/presymptomatic type 1 or type 2 diabetes secondary to β-cell stress during pregnancy.

Indeed, both the case presented in our original article and the example case described by the Thivolet group (1) highlight the need for further studies of GDM to determine the role of type 1 diabetes–associated autoantibodies during pregnancy and postpartum. Our intention was to highlight an interesting presentation of insulitis and autoantibody positivity in a GDM patient to draw further attention to this topic.

A few important differences exist between these two cases. Marchand et al. (1) describe a Caucasian patient with GDM who was positive for a single autoantibody against zinc transporter 8 (ZnT8) during pregnancy. In contrast, the Hispanic donor described in our article was positive for both islet cell antibodies and GAD autoantibodies at the time of her demise, which occurred in the postpartum period. It is now well accepted that nearly all individuals with two or more autoantibodies (i.e., stage 1 type 1 diabetes) will eventually develop symptomatic disease, this compared with those with a single autoantibody, which confers 12.7% 15-year risk of progressing to symptomatic type 1 diabetes (3).

We agree with the assertion that degranulation could potentially explain low β-cell mass assessed by insulin staining; however, it cannot account for insulitis. Insulitis in type 1 diabetes has been defined as a minimum of three islets having six or more $CD3^+$ cells at or within the islet, in conjunction with the presence of insulin-negative islets (4). Indeed, both insulin-negative islets and $CD3^+$ T cell infiltration were observed in our organ donor case. These observations together with the presence of autoantibodies, noted above, support a probable immune-mediated etiology.

Further studies are needed to determine the potential of type 1 diabetes progression following GDM, particularly in those patients who develop multiple autoantibodies during pregnancy. The currently available data indicate that the risk of type 1 diabetes following GDM is especially great when associated with islet autoantibodies (5). Importantly, autoantibody positivity in GDM and subsequent progression to type 1 diabetes may be underreported.

We underscore that autoantibody testing for women with GDM should continue to be investigated as a method to possibly identify those with elevated risk for progressing to type 1 diabetes (6). This could be useful for identifying women who may be at higher risk for diabetic ketoacidosis. The pattern and prevalence of islet autoantibodies are population dependent, and more studies are certainly needed to examine autoantibody and type 1 diabetes incidence by race in the obstetric population.

Again, we thank these authors for their intriguing response, which brings further attention to the important variability in the course of diabetes in women with GDM.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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