RESPONSE TO COMMENT ON TRINH ET AL.

Successful Treatment of Immune Checkpoint Inhibitor–Induced Diabetes With Infliximab. Diabetes Care 2019;42:e153–e154

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We thank Galligan et al. (1) for their interest in our observation (2) on the successful treatment of immune checkpoint inhibitor–induced diabetes with infliximab.

First, we agree with the commenters that intra-articular steroid injection could have contributed slightly to the development of insulin resistance. However, an intra-articular injection is not expected to have as much impact on insulin sensitivity as systemic corticosteroid treatment. Furthermore, our repeated mixed-meal tolerance tests indicated an impaired insulin secretion capacity—recovered by 3 months after initiation of treatment with infliximab—which points to concurrent β-cell dysfunction. Finally, after publication of our observation and after termination of infliximab, the patient again received intra-articular steroid injections without relapse of his diabetes.

Second, we concur that the presentation of our patient was rather atypical, since the time to onset of diabetes was 37 weeks after initiation of immune checkpoint inhibition and the HbA_{1c} was high at 11.6% (103 mmol/mol), as compared with the reported median of 11 weeks and 7.9%, respectively, in a recent review (3). However, the interquartile ranges for time to onset of diabetes and HbA_{1c} at diagnosis were remarkably wide.

Third, it is true that our patient only presented with positive islet cell antibodies and was negative for anti-GAD, anti–IA-2, and anti-insulin IgG. HLA typing was not done in our case. A recent review of 42 cases of immune checkpoint inhibitor–induced diabetes (4) reported that only 56% of the patients had detectable diabetes-related antibodies as opposed to up to 85% of patients with adult-onset type 1 diabetes (5). Keeping in mind that many reports had only tested for one antibody (3), this could nonetheless support the notion that immune checkpoint inhibitor–induced diabetes might have a different etiology than in type 1 diabetes and could therefore respond differently to systemic immune suppression.

A review on ipilimumab-treated melanoma patients (6) reported that 35% of patients received systemic corticosteroid treatment for immune-related adverse events and 28% received infliximab 5 mg/kg for immune-related diarrhea. Of the latter, only 72% responded to the treatment. To our knowledge, there is only one report about an unsuccessful corticosteroid treatment (7) and no reports about other immune modulatory treatment attempts for immune checkpoint inhibitor–induced diabetes. While the commenters carefully elaborated the potential effects of anti–tumor necrosis factor (TNF) therapy in classic type 1 diabetes, it is unknown whether this applies to immune checkpoint inhibitor–induced diabetes. Therefore, we considered it worthwhile to report our observation of a patient with remission of his diabetes after infliximab therapy. Certainly, further data are needed to assess the success rate of anti-TNF therapy in this probably novel type of diabetes.

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