

1274 INFLIXIMAB FOR DECOMPENSATED DIABETES FOLLOWING IMMUNE CHECKPOINT INHIBITOR THERAPY

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Background Immune checkpoint inhibitors (CPI) are life-saving cancer therapies but are commonly associated with immune-related adverse events (irAEs). CPI-associated diabetes mellitus (CPI-DM) is rare and thought to be irreversible. The precise pathologic mechanism is unknown but is believed to be an immune-mediated attack against beta cells, analogous to type 1 diabetes mellitus (T1DM).¹ While glucocorticoid therapy is a mainstay treatment for many irAEs, in CPI-DM it is ineffective or even detrimental.

Methods We present the third case to our knowledge using off-label anti-TNF α therapy (infliximab) to treat likely CPI-DM.²⁻³ We assessed efficacy of this therapy by monitoring blood gluces with a continuous glucose monitor (CGM), total daily dose of insulin, c-peptide (a measure of endogenous insulin production) following a mixed meal and c-peptide HOMA-IR⁴ as a proxy measure of insulin resistance.

Results A 71-year-old man with metastatic squamous cell carcinoma of the jaw and a history of diet-controlled diabetes acutely developed weight loss, polyuria, and polydipsia with a rise of his serum glucose to 398 mg/dL following a 9th dose of cemiplimab, an anti PD-1 monoclonal antibody. His hemoglobin A1C had been 5.5% nine months prior to presentation. At presentation, he was not in diabetic ketoacidosis (pH 7.35 by venous blood gas, no urine ketones, anion gap of 8). C-peptide was initially suppressed at 3.5 ng/mL despite glucose elevation (293 mg/dL). Islet autoantibodies were negative. Given the relatively abnormal c-peptide, he was thought to be in early CPI-DM and was started on basal and bolus insulin. Two months later, his total daily insulin dose plateaued at 23 units. Infliximab therapy was then initiated. The patient received four infusions of infliximab dosed at 5mg/kg, spaced 2–3 weeks apart. Within days his insulin needs decreased. By the fourth dose, he was transitioned off insulin and onto metformin and dulaglutide. C-peptide production increased and insulin resistance decreased (figure 1). At seven months of follow-up, he continued on metformin and dulaglutide with a hemoglobin A1C of 5.3% and CGM showing gluces in range more than 98% of the time. His islet autoantibodies remain negative.

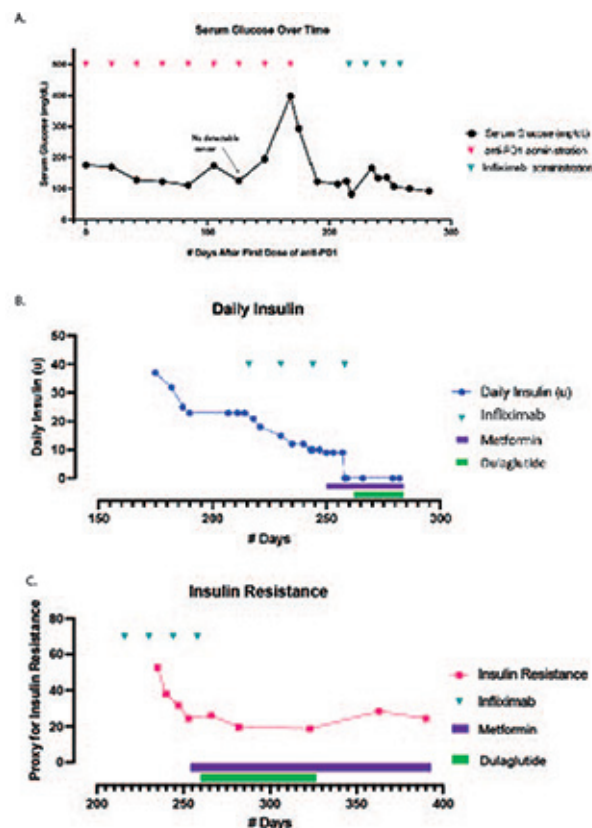
Conclusions CPI-DM was previously considered irreversible with no established interventions aside from initiating insulin. This case suggests that if caught when c-peptide is still present, anti-TNF α therapy might arrest beta-cell loss and that insulin resistance may contribute to CPI-DM, at least in a subset. If true, this would save patients substantial morbidity. We believe this preliminary data warrants further study including randomized controlled trials.

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Ethics Approval This study was approved by the UCSF Institutional Review Board; approval number 10–02467.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.



Abstract 1274 Figure 1 Illustration of evolution of glucose levels, insulin requirements, and insulin resistance over the course of PD-1 inhibitor therapy and infliximab therapy. (A) Random gluces over their course of treatment with PD-1 inhibitor and infliximab, noting that insulin and additional medications were started after presentation with a glucose of 398 mg/dL. (B) Total daily dose of insulin following infliximab therapy and initiation of non-insulin medications. (C) Insulin resistance as calculated by a mixed meal c-peptide with paired glucose after initiation of infliximab and non-insulin agents.

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