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LETTER TO THE EDITOR

Glucose variability in PD-1 inhibitors-induced diabetes mellitus

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We appreciated the short communication by Marchand et al. [1] and their interest in our case report [2]: these authors stressed the importance of glucose variability in our patient similar to those of their patients reported in their present short communication.

We are also in line with them in the peculiar glucose variability of these relatively new type of PD-1 inhibitors-induced diabetes mellitus (DM) that should be further investigated.

Even if we also think that high short-term glucose variability is unusual for DM with recent onset, it should be noted that only in recent years the availability of new technologies (in particular continuous glucose monitoring—CGM and flash glucose monitoring—FGM) have allowed an in deep analysis of these new glucose metrics that could help the clinician, alongside HbA1c assay and self blood glucose monitoring, in the clinical management of diabetic patients. Thus, there are scanty data in the literature about glucose variability (measured with these new techniques) and long-term follow-up of patients affected by type 1 diabetes mellitus (T1DM) and particular in PD-1 inhibitors-induced DM.

In our single case report, FGM revealed a high glucose variability with only 12% of the time spent 'in range' (70–180 mg/dl), 79% above the range (> 180 mg/dl) and 9% under the range (< 70 mg/dl). Since we did not have the possibility to use professional software to download data of FGM, we actually used the Free Style Libre Software® that gave us time in/above/below range and glucose mean; so, unfortunately, we missed the CV of that time of treatment.

Like Marchand et al., however, our relatively long clinical follow-up of the patient allowed us to hypothesize that the particular impairment of insulin secretion, documented by the very low C-peptide levels both at diagnosis and persistent at the 2 year follow-up, could represent a unique feature of this type of DM. Accordingly, another speculative clinical issue could be represented by the absence of the so-called 'honeymoon' phase of type 1 diabetes, i.e. the partial recovery of endogenous insulin production in the first few months after the onset of type 1 diabetes. In our patient, we have not seen this partial restoration of glycaemic control with lower doses of exogenous insulin, frequently observed after the onset of T1DM, and this clinical aspect could be in line with a specific pathophysiology of PD-1 inhibitors-induced diabetes mellitus.

As it was already pointed out, glucose variability could be also affected by other PD-1 inhibitors-induced endocrine comorbidities (not present in our patient) and/or concomitant pharmacological treatments that the clinician should take into account.

In addition, we can speculate that patient's lifestyle could be affected by neoplastic disease and eventually by comorbidities with potential relevant impact on eating behavior and sport activities, resulting in more complexity in diabetes management.

Last, it could be reasonable that patient's attention and commitment in a such difficult situation is focused particularly on the treatment and follow-up of the neoplastic disease, with less adherence to diabetologist recommendations and/or more time required to learn how to manage blood glucose in relationship with all the variables that could affect it.

So, all these potential factors may play a role and contribute to the particular brittle and instable diabetes that characterize the very first phase after the onset of the disease.

In conclusion, Marchand et al. case reports and our case report should be considered "hypothesis-generating data" on extreme glucose variability that could represent a unique feature of PD-1 inhibitors and that should be further investigated.

Managed By Massimo Porta.

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Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Human and animal rights disclosure All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient.

References

1. Marchand L, Thivolet A, Dalle S, Chikh K, Reffet S, Vouillarmet J et al (2018) Diabetes mellitus induced by PD-1 and PD-L1 inhibitors: description of pancreatic endocrine and exocrine phenotype. Acta Diabetol. https://doi.org/10.1007/s00592-018-1234-8
2. Tassone F, Colantonio I, Gamarra E, Gianotti L, Baffoni C, Magro G et al (2018) Nivolumab-induced fulminant type 1 diabetes (T1D): the first Italian case report with long follow-up and flash glucose monitoring. Acta Diabetol 25:1–2. https://doi.org/10.1007/s00592-018-1246-4