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SHORT COMMUNICATION

Fulminant diabetes induced by PD-1 and PD-L1 inhibitors: what about glucose variability?

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We read with interest the paper by Tassone et al., describing difficulties in achieving a good metabolic control and high glucose variability in a subject who presented nivolumab-induced fulminant diabetes (FD) [1]. These issues were not detailed in recent reviews and the large case series of diabetes induced by immune checkpoint inhibitors.

Short-term glucose variability increases the risk of hypo- and hyperglycemia, and can be assed with coefficient of variation (CV) for glucose (the standard deviation divided by the mean). The value of 36% of CV has been found to be a useful cutoff to separate stable and labile diabetes [2, 3].

We previously reported four cases of anti-PD-1/PD-L1-induced FD diabetes (subjects #1, #3, #5 and #6 in a recent study published in this journal [4]). At last follow-up (range 9–25 months), these subjects were treated with multiple daily injections of insulin and wore sensor-based flash glucose monitoring system (FreeStyle Libre). CV was obtained from sensor data (28 days analyzed): the first subject (#1) already experienced two severe hypoglycemic episodes (complicated with traumatic C1-2 dislocation and epileptic seizure) and had a CV of 57%, the second one (#3) a CV of 43%, the third one (#5) a CV of 41% and the last one (#6) a CV of 50%.

This high short-term glucose variability is unusual for diabetes with recent onset, and we speculate that this glucose variability could be related to physiopathological particularities of FD induced by checkpoint inhibitors: completely abolished C-peptide response 1 month after onset despite the use of an ultrasensitive assay; blunted glucagon response for subjects #1 and #6 [4]. It should also be noted that subject #1 presented with nivolumab-induced corticotroph deficiency [5], which could increase the risk of hypoglycemia.

Larger studies are required to confirm these data. But, oncologists should inform patients of the risk to develop FD with PD-1/PD-L1 inhibitors, given the fact that diabetes could cause severe keto-acidosis, and that high glucose variability could be a tough burden to undertake, in addition to the underlying oncological condition.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest associated with this manuscript.

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Human and animal rights All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent Informed consent was obtained from all patients for being included in the study.

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