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AVELUMAB-INDUCED AUTOIMMUNE DIABETES MELLITUS

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BACKGROUND

Avelumab is an immune checkpoint inhibitor (ICI) indicated for the treatment of patients with Merkel cell carcinoma and locally advanced or metastatic renal or urothelial carcinoma. ICIs enhance the immune response against cancer cells by activating cytotoxic T lymphocytes, and although infrequent, all ICIs can cause autoimmune adverse effects.

⚠️🚨❗🔔 If activated T lymphocytes infiltrate the pancreas, they destroy its beta cells and lead to type 1 diabetes mellitus.

OBJECTIVE

Description of a case: patient developed autoimmune diabetes mellitus eight weeks after receiving the first dose of avelumab.

METHODOLOGY

WHAT DO WE KNOW?

The incidence of diabetes mellitus in patients treated with ICIs is rare, close to 1%.

Unlike conventional type 1 diabetes mellitus, ICI-induced diabetes is characterized by severe and persistent insulin deficiency from the time of diagnosis, which is manifested by a very low or absent C-peptide level, and which leads to diabetic ketoacidosis if not treated promptly with insulin. It presents between 7 and 17 weeks after the start of immunotherapy, with very high blood glucose levels and difficult metabolic control. HbA1c is usually not very elevated at the time of diagnosis due to the rapid onset of insulinopenia, and pancreatic antibodies are often negative.

2018 Fist case diabetes mellitus induced by the combination of avelumab and utomilumab.

2019 another case in avelumab monotherapy.

THE CASE

A 67-year-old male, with a history of robotic radical prostatectomy for acinar adenocarcinoma in January 2022. The abdominal computed axial tomography (CAT) scan performed in November 2022 revealed a solid tumor measuring 27 × 38 mm in the posterior leaflet of the lower pole of the right kidney, and urothelial thickening hyper-enhancement at the level of the upper calyx and left renal pelvis. Partial right nephrectomy was performed in January 2023, with a pathological diagnosis of adenocarcinoma, and left nephrectomy in March 2023 with a histological diagnosis of urothelial carcinoma (UC) of the renal pelvis, stage IV, T3 N2M0.

On 6 April 2023, he received the first chemotherapy cycle of the cisplatin and gemcitabine (CisGem) regimen, and eight cycles were completed, ending on 18 July 2023.

When a new abdominal CT scan showed that the locally advanced UC had not progressed with the previous chemotherapy, immunotherapy with avelumab monotherapy at a dose of 800 mg by intravenous infusion every two weeks was indicated, with the first dose received on 25 August, followed by 15 and 29 September and 13 October 2023.

ADVERSE EVENT

On 27 October, a blood glucose level of 338 mg/dL was recorded. Reported polyuria and polydipsia.
Avelumab was discontinued and the patient was referred to the emergency department.
On physical examination: height 181 cm, weight 63 kg. Good general condition; creatinine 1.8 mg/dL, sodium (Na) 125 mEq/L, potassium (K) 5 mEq/L, venous blood gases: Ph 7.3, HCO3 29 mmol/L, EB 1.4 mmol/L.
He was treated with rapid insulin and discharged on insulin glargine and repaglinide.

Ethic considerations: patient accepted to publish the case.

RESULTS

CASE RESOLUTION

- As high blood glucose levels persisted, the patient was referred to the Diabetes Unit.
- Repaglinide was discontinued and insulin glargine and multiple doses of insulin lispro were started.
- Results: Anti-glutamic acid (anti-GAD) and anti-pancreatic islet antibodies negative. Basal C-peptide: <0.1 ng/mL (normal value 0.8–3.9) and hemoglobin A1c 8.6%.
- Avelumab treatment was not stopped.

CONCLUSION

✓ Knowing about this form of avelumab-induced autoimmune diabetes mellitus is important in order not to delay the initiation of multi-dose insulin therapy, as was the case here.

✓ It is also important to emphasize that, once blood glucose level has been stabilized, immunotherapy should be continued if still indicated, as diabetes mellitus is irreversible.

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