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Avelumab-induced autoimmune diabetes mellitus

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Introduction: 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.

Case Presentation: A 67-year-old man with a stage IV renal pelvis urothelial carcinoma (UC), received eight cycles of chemotherapy with cisplatin and gemcitabine (Gem/Cis), ending on July 18, 2023. Then, avelumab immunotherapy was indicated at a dose of 800 mg intravenous infusion every two weeks, receiving the first dose on August 25, 2023. On October 27, a blood glucose of 338 mg/dL was recorded. He reported polyuria and polydipsia. Avelumab administration was discontinued and he was referred to the emergency department. On physical examination: height 181 cm, weight 63 kg, and good general condition. On blood test: creatinine 1.8 mg/dL, venous blood gas: Ph 7.3, HCO3 29 mmol/L, BE 1.4 mmol/L. He was treated with rapid acting insulin and discharged with insulin glargine and repaglinide. As hyperglycaemia persisted, he was referred to the Diabetes Unit. Repaglinide was discontinued and a regimen of insulin glargine and multiple doses of insulin lispro was started. Anti-glutamic acid (anti-GAD) and anti-pancreatic islet antibodies were negative. Basal C-peptide: < 0.1 ng/mL (normal range 0.8-3.9) and HbA1c 8.6%.

Discussion: This patient developed autoimmune diabetes mellitus eight weeks after receiving the first dose of avelumab. 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. Awareness of this form of avelumab-induced autoimmune diabetes mellitus is important to avoid delaying the start of treatment with multiple-dose insulin, as occurred in our case. It is also important to emphasize that, once blood glucose levels are stabilized, immunotherapy should be continued if still indicated, since diabetes mellitus is irreversible.

Biography

Elvira Gea, a specialist in endocrinology at Our Lady of Meritxell Hospital in Andorra, has extensively studied immune checkpoint inhibitors and their side effects. One of her notable research contributions focuses on avelumab-induced autoimmune diabetes mellitus, a rare but serious condition. Avelumab, an anti-PD-L1 monoclonal antibody used in immunotherapy, can trigger autoimmune responses in some patients, leading to diabetes. Dr. Gea's case studies provide crucial insights into the early detection and management of this condition. Her work underscores the importance of monitoring blood glucose levels during immunotherapy and highlights potential interventions to mitigate risks, improving outcomes for cancer patients receiving avelumab treatment.