Autoimmune Diabetes As Result Of Immunotherapy For Malignant Melanoma

Eleni Armeni (1); Lucy Walker (2); Efthymia Karra (1); Martin Dumsky (1); Vitalijs Ovcinnikovs (2); Rosenthal Miranda (1); Dipesh Patel (1)

(1) Department of Endocrinology and Diabetes, Royal Free Hospital

(2) Institute of Immunity & Transplantation, UCL Division of Infection and Immunity, Royal Free Campus

Introduction: Immune checkpoint inhibitor therapy has been uncommonly associated with the development of endocrinopathies. This case report describes a patient who developed autoimmune diabetes following treatment with immunomodifiers, in the context of managing malignant melanoma. Case details: A 76 year old female was diagnosed with stage 4 malignant melanoma of the scalp (BRAF-negative), managed with resection and adjuvant radiotherapy. The patient received four cycles of Ipilimumab for systemic metastatic disease with further pembrolizumab treatment planned. Following the first cycle of Pembrolizumab, she was admitted with severe acute hyperglycemia. Hba1c was mildly elevated 48.6mmol/mol, suggesting recent onset glycemic dysregulation. She appeared euglycaemic throughout previous immunotherapy treatment. There was no family history of diabetes mellitus or autoimmune disease. Pancreatic islet cell and glutamic acid decarboxylase antibodies were positive. Cortisol levels, thyroid and pituitary function were normal. Blood lymphocyte immunophenotyping identified that the frequency of the patient's Treg cells was increased, complemented by an overall skewing of CD4 cells towards a CD45RA-negative memory phenotype. This was deemed be compatible with unrestricted, co-stimulation as a result of aCTLA-4 (anti-CTL-associated antigen-4) and aPD-1 (anti-programmed cell death protein 1). The CD4/CD8 ratio was similar to age-matched T1DM controls, indicating no preferential expansion of CD8 cells. The endocrinopathy was presumed immunotherapy-related autoimmune toxicity. Discussion: Combination immunotherapy is a risk factor for the development of endocrinopathies. Immunophenotyping may allow further insight into understanding changes involved in autoimmune disease. Regular monitoring following the initiation of such treatments would enable early detection and appropriate management of endocrinopathies.

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