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TOO LOW FROM A SELF-BLOW: DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN A CASE OF HIRATA'S SYNDROME

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INTRODUCTION

Non-diabetic hypoglycemia in older adults warrants careful evaluation across insulin-mediated and non-insulin-mediated causes. We present a challenging case of insulin autoimmune syndrome (IAS; Hirata's syndrome).

CASE

An 85-year-old female presented with severe hypoglycemia (capillary blood glucose [CBG] 1.8 mmol/L) with reduced consciousness, preceded by 2 months of recurrent dizziness relieved by food intake. Appetite and weight were stable. Past medical history included stage 3 chronic kidney disease and osteoporosis, but no diabetes. Medication review revealed a recent 2-week course of traditional supplement, long-term Neurobion®, but no agents with recognized hypoglycemic potential. Physical examination showed a moderately built elderly female with a body mass index of 24.3 kg/m² and no Cushingoid features.

Recurrent hypoglycemia (CBG nadir 1.5 mmol/L) occurred in both fasting and postprandial states, fulfilling Whipple's triad. Baseline investigations showed an estimated glomerular filtration rate of 42 mL/min/1.73 m², AM cortisol of 700 mmol/L, and unremarkable liver and thyroid function tests. During a hypoglycemic episode (CBG 2.3 mmol/L), plasma insulin and C-peptide were inappropriately raised at 203.6 mU/L (reference interval [RI]: 3.0–25.0) and 33 ng/mL (RI: 0.9–7.1), respectively, confirming endogenous hyperinsulinemic hypoglycemia. Polyethylene glycol precipitation showed 21% insulin recovery, raising suspicion for an autoimmune cause. Elevated insulin autoantibodies (175 AU/mL; RI <20) confirmed IAS. Computed tomography of the abdomen and endoscopic ultrasound excluded a pancreatic neuro-endocrine tumor.

Nutritional management comprising frequent low glycemic index feeds and uncooked cornstarch was commenced. Diazoxide 100 mg TDS caused fluid overload and severe hyponatremia, while hypoglycemia persisted at lower doses, necessitating discontinuation. Subcutaneous octreotide 100 mg QID was required to control hypoglycemia. Prednisolone 30 mg BD improved glycemic stability. Insulin autoantibodies titer remained 175 AU/mL at 2 weeks; reassessment was conducted at 4 weeks with consideration for biologics if persistent.

CONCLUSION

Endogenous hyperinsulinemic hypoglycemia, after excluding insulinoma, should raise suspicion for IAS. Management includes removing triggers, supportive care, and immunomodulatory therapy in severe cases.

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NOT JUST ANOTHER CASE OF TYPE 2 DIABETES IN AN ADOLESCENT

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INTRODUCTION

Cushing's disease (CD) in adolescents may present with subtle clinical features, resulting in a significant diagnostic challenge. We report a case of a young lady whose CD initially masqueraded as Type 2 diabetes (T2D), highlighting the difficulties in differentiating early hypercortisolism from T2D.

CASE

A 12-year-old female was incidentally diagnosed with diabetes during routine medical screening. Examination revealed an overweight female without the classical features of Cushing's syndrome. Due to the presence of acanthosis nigricans, a diagnosis of T2D was initially made. Her diabetes remained well-controlled with a single oral glucose-lowering drug.

The diagnostic challenge became apparent over time. She experienced delayed menarche at the age of 17, and a diagnosis of Cushing's syndrome was suspected when she subsequently developed hypertension and reduced bone mineral density. Biochemical evaluation was consistent with adrenocorticotropic hormone (ACTH)-dependent hypercortisolism, evidenced by the failure of serum cortisol suppression on low dose and overnight dexamethasone suppression tests. Her 24-hour urinary cortisol was elevated twofold, and plasma ACTH was elevated (17.8 pmol/L). MRI demonstrated a right-sided pituitary microadenoma (0.3 × 0.5 × 0.3 cm), and inferior petrosal sinus sampling confirmed the diagnosis of CD. She

underwent endoscopic transsphenoidal surgery 7 years later, which was complicated by panhypopituitarism and cranial diabetes insipidus. Postoperatively, CD was cured, with the resolution of her metabolic comorbidities.

CONCLUSION

Despite the increasing prevalence of T2D in adolescents, clinicians must recognize the diagnostic challenge of CD in this age group. Atypical manifestations in a presumed T2D patient should prompt consideration of Cushing's syndrome.

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INSULIN-RECALCITRANT HYPERGLYCEMIA FOLLOWING CAPIVASERTIB THERAPY: A NOVEL CHALLENGE IN A NON-DIABETIC PATIENT

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INTRODUCTION

Capivasertib is a selective oral AKT inhibitor approved for hormone receptor-positive, HER2-negative advanced breast cancer with AKT pathway mutations. As AKT is integral to insulin signaling, its inhibition predisposes patients to hyperglycemia. We report a case of severe capivasertib-induced hyperglycemia with profound insulin resistance in a non-diabetic patient.

CASE

A 56-year-old female with metastatic breast cancer (ER/PR-positive, HER2-negative, AKT1- and ESR1-mutated, TMB-high) presented with severe hyperglycemia following capivasertib initiation. She had no prior diabetes history, with a baseline hemoglobin A1c of 5.6%. Her first cycle (200 mg twice daily, 7 April 2025) was uncomplicated metabolically. The second cycle was escalated to 400 mg twice daily on 21 April 2025. By Day 3, blood glucose rose significantly. Premixed insulin 20 units failed to achieve glycemic control, necessitating intravenous insulin infusion. Despite escalation to 30 units per hour, euglycemia could not be achieved. Notably, there was no biochemical evidence of diabetic ketoacidosis or hyperosmolar hyperglycemic state, and the patient remained hemodynamically stable. No corticosteroids or other contributing medications were administered. Blood glucose normalized spontaneously approximately 36 hours after the last capivasertib dose, and all insulin was weaned and discontinued by 26 April 2025. She remained euglycemic without antidiabetic therapy thereafter. The patient and family opted for palliative care, and she passed away on 6 May 2025.

CONCLUSION

Capivasertib can precipitate severe, insulin-resistant hyperglycemia even in non-diabetic patients, without progression to overt hyperglycemic crisis. Spontaneous resolution upon drug cessation supports a direct drug-mediated mechanism via AKT-disrupted insulin signaling. Clinicians should monitor glucose closely during therapy and consider drug cessation in refractory cases. Further studies are warranted to guide optimal glycemic management.

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THE VARIABLE NATURE OF BIOPSY-PROVEN VILDAGLIPTIN-INDUCED BULLOUS PEMPHIGOID IN AN ELDERLY PATIENT: A CASE SERIES

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INTRODUCTION

Bullous pemphigoid (BP) is the most common autoimmune blistering disease. Drug-induced BP has been increasingly reported, with dipeptidyl peptidase-4 (DPP-4) inhibitors, particularly vildagliptin, emerging as a notable cause. The pathogenesis is thought to involve the disruption of immune tolerance and epitope spreading, leading to a broader autoimmune response against basement membrane antigens beyond the classic NC16A domain of BP180. This case series highlights the variable clinical spectrum and therapeutic challenges in vildagliptin-induced BP.

CASES

A 74-year-old male with type 2 diabetes mellitus (T2DM), hypertension, dyslipidemia, and a history of stroke presented with a 2-month history of recurrent, pruritic, tense bullae. He had been on vildagliptin for 36 months. Histopathology confirmed subepidermal blistering, and direct immunofluorescence demonstrated linear IgG/C3 deposition at the dermo-epidermal junction, with positive anti-BP180 antibodies, diagnosing BP. Discontinuation of vildagliptin and initiation of systemic corticosteroids resulted in significant clinical improvement, allowing a rapid prednisolone taper to 5 mg daily without new bullae formation.

A 62-year-old female with T2DM and dyslipidemia presented with bullous eruptions 3 months after initiating vildagliptin. Skin biopsy confirmed BP, revealing subepidermal blistering with eosinophils and linear C3/IgG deposition at the basement membrane zone. Vildagliptin