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Case Report
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Double Diabetes: Clinical Features, Pathophysiological Mechanisms, and Therapeutic Challenges Case Series of Three Patients and Literature Review

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Abstract

Double diabetes refers to the coexistence, in the same patient, of immunological features of type 1 diabetes (T1D) and clinical and metabolic manifestations of type 2 diabetes (T2D), especially insulin resistance. This entity, still insufficiently recognized, poses diagnostic and therapeutic challenges, particularly in adults. We report a series of three cases of double diabetes in adult female patients, illustrating the clinical heterogeneity of this condition, and discuss the pathophysiological mechanisms, therapeutic challenges, and the importance of early screening in light of recent literature data.

Keywords: Double Diabetes; Type 1 Diabetes; Type 2 Diabetes; Insulin Resistance; Autoimmunity; Anti-GAD

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Introduction

Diabetes mellitus is a heterogeneous chronic disease whose classical forms include type 1 diabetes (T1D), characterized by autoimmune destruction of pancreatic β-cells, and type 2 diabetes (T2D), dominated by insulin resistance and progressive failure of insulin secretion [1, 2].

However, the boundary between these two entities is becoming increasingly blurred. The concept of double diabetes describes patients with T1D who develop marked insulin resistance, often associated with obesity, metabolic syndrome, and a strong family history of T2D [3, 4 ,5]. This situation is favored by lifestyle changes, increasing obesity rates, and the anabolic effect of intensive insulin therapy [6].

The exact prevalence of double diabetes remains poorly defined, but several studies suggest a steady increase, particularly among adults and adolescents [7, 8]. This entity is associated with an increased risk of cardiovascular and metabolic complications [9].

Here, we report three cases of double diabetes illustrating the diagnostic and therapeutic complexity of this condition.

Patients and Methods

We report an observational series of three female patients followed for diabetes in an endocrinology department. Clinical, biological, and follow-up data were collected retrospectively from medical records. The diagnosis of double diabetes was based on the association of:

- Pancreatic autoimmunity (positive anti-GAD antibodies),
- Clinical and/or biological signs of insulin resistance (android obesity, acanthosis nigricans, family history of T2D, high insulin requirements).

Clinical Observations

Case 1

A 27-year-old female admitted for inaugural diabetic ketoacidosis. She had a strong family history of type 2 diabetes, three pregnancies marked by fetal macrosomia and hydramnios. Clinical examination showed overweight with android obesity and cervical acanthosis nigricans, in the context of rapid weight loss of 40 kg in two months.

Table 1: Clinical and biological characteristics of patients.

Case	Age (years)	BMI (kg/m²)	Acanthosis	Family History of T2D	Anti-GAD	Treatment
1	27	Overweight	Yes	Yes	Positive	Insulin
2	46	30	Yes	Yes	>2000 U/mL	Insulin + Metformin
3	56	31	Yes	Yes	Positive	Insulin + Metformin

Biological workup revealed HbA1c at 12.8%, positive anti-GAD antibodies, and associated autoimmune hypothyroidism. Basal-bolus insulin therapy was started with favorable evolution.

Case 2

A 46-year-old female diabetic for 8 years, initially managed as T2D. She presented with obesity (BMI 30 kg/m²), acanthosis nigricans, strong diabetic heredity, and repeated episodes of ketoacidosis. The discovery of anti-GAD antibodies at a level > 2000 U/mL allowed reclassification as double diabetes. Intensive insulin therapy combined with metformin improved glycemic control.

Case 3

A 56-year-old female diabetic for 10 years, with a strong family history. Initially treated with oral antidiabetics, then insulin, she experienced several severe episodes of ketoacidosis triggered by recurrent urinary infections. Examination showed android obesity (BMI 31 kg/m²) and acanthosis nigricans. Anti-GAD antibodies were positive. Basal-bolus insulin therapy was initiated (Table 1).

Discussion

The concept of double diabetes designates the coexistence, in a single patient, of immunological characteristics of type 1 diabetes (T1D) and clinical and metabolic manifestations suggestive of type 2 diabetes (T2D), notably insulin resistance. Although increasingly recognized, this concept remains poorly defined and probably underdiagnosed, especially in adults [1, 2].

Clinical profile and significance of our series

Our series of three cases illustrates different clinical presentations of double diabetes, reflecting the heterogeneity of this entity. All patients presented:

- Clinically evident insulin resistance evidenced by android obesity and acanthosis nigricans,
- A strong family history of type 2 diabetes,
- and pancreatic autoimmunity documented by positive anti-GAD antibodies.

These findings align with literature data reporting that double diabetes occurs preferentially in patients with a genetic predisposition to T2D, onto which progressive autoimmune β-cell destruction is superimposed [3–5].

In our series, two patients were initially classified as type 2 diabetics and treated for several years with oral antidiabetics before the detection of high titers of anti-GAD antibodies led to reclassification. This scenario is frequently described, especially in adults, where the boundary between T2D, LADA, and double diabetes remains blurred [6, 7].

Pathophysiological mechanisms of double diabetes

The pathophysiology of double diabetes relies on the complex interaction between autoimmunity, insulin resistance, and environmental factors.

Central role of obesity and insulin resistance: Obesity, especially visceral, is the central mechanism in double diabetes. It induces insulin resistance through increased free fatty acids, secretion of pro-inflammatory cytokines (TNF-α, IL-6), and impaired insulin signaling [8, 9]. In T1D patients, this insulin resistance increases insulin requirements and worsens glycemic control.

Several studies show that obese T1D patients exhibit a metabolic profile similar to T2D, with increased risk of metabolic syndrome and cardiovascular complications [10–12].

Interaction between insulin therapy and weight gain; Intensive insulin therapy, essential for glycemic control in T1D, paradoxically promotes weight gain due to its anabolic effect and reduced glycosuria [13]. This weight gain can further exacerbate insulin resistance, creating a vicious cycle favoring the emergence of double diabetes.

In our series, all patients experienced significant weight gain during disease progression, consistent with observations from the DCCT/EDIC cohort [14].

Genetic and environmental factors; Data suggest that some T1D patients share genetic variants associated with T2D, notably those involved in insulin resistance and obesity [15]. The modern environment, characterized by sedentary lifestyle and high-calorie diets, also contributes to the clinical expression of double diabetes [16].

Increased risk of complications and metabolic instability

Patients with double diabetes have an increased risk of glycemic instability, as evidenced by repeated episodes of diabetic ketoacidosis (DKA) observed in two of our patients. This risk is well documented, with double diabetes associated with significant glycemic variability and elevated HbA1c despite high insulin doses [17, 18].

Moreover, several studies report that double diabetes is linked to increased cardiovascular risk, comparable or even superior to that in T2D, due to coexistence of autoimmunity and metabolic syndrome [19–21].

Therapeutic implications and management

Management of double diabetes is a true therapeutic challenge, based on:

- Optimized basal-bolus insulin therapy,
- Combined with measures to reduce insulin resistance.

Adding metformin in insulin-resistant T1D patients has shown modest but significant benefits on insulin requirements, weight, and some cardiovascular parameters [22–24]. In our series, introducing or maintaining metformin in patients with marked insulin resistance improved glycemic control.

Other therapeutic approaches, such as GLP-1 receptor agonists or SGLT2 inhibitors, are currently under investigation in insulin-

resistant T1D patients, but their use remains cautious due to DKA risk [25–27].

Importance of early screening

Our work emphasizes the importance of systematically screening for pancreatic autoimmunity in adult diabetic patients presenting with:

- Unusual insulin resistance,
- Episodes of diabetic ketoacidosis (DKA),
- Or unexplained glycemic imbalance despite appropriate treatment.

Early diagnosis of double diabetes allows more appropriate management and may reduce long-term complication risks [28].

Conclusion

Double diabetes should be suspected in any atypical adult diabetes combining insulin resistance and glycemic instability. Better identification of this entity enables optimized therapeutic management and prevention of long-term complications.

References

1. Pozzilli P, Leslie RD. Double diabetes: a distinct entity? Diabetes Care. 2007; 30(7): 1790-1794. doi:10.2337/dc07-0224.
2. Tuomi T, Carlsson A, Li H, Isomaa B, Miettinen A, Lahti K, et al. Clinical and genetic characteristics of adult-onset autoimmune diabetes mellitus. Diabetes. 1999; 48(4): 734-741. doi:10.2337/diabetes.48.4.734.
3. Wilkin TJ. The accelerator hypothesis: Weight gain as the missing link between type I and type II diabetes. Diabetologia. 2001; 44(7): 914-922. doi:10.1007/s001250100550.
4. Redondo MJ, Jeffrey J, Fain PR, Eisenbarth GS. Type 1 diabetes: the role of insulin resistance. Diabetes Care. 2018; 41(8): 1569-1575. doi:10.2337/dc18-0086.
5. Cleland SJ, Fisher BM, Colhoun HM. Insulin resistance in type 1 diabetes: what is 'double diabetes' and what are the risks? Diabet Med. 2013; 30(11): 1313-1324. doi:10.1111/dme.12188.
6. Fourlanos S, Dotta F, Greenbaum CJ, Palmer JP, Rolandsson O, Colman PG, et al. Latent autoimmune diabetes in adults (LADA): the missing link in the spectrum of diabetes. Diabetologia. 2005; 48(6): 1053-1061. doi:10.1007/s00125-005-1722-9.
7. Buzzetti R, Pinchemel Cottingham Z, Pozzilli P. Diabetes classification: grey zones, sound and smoke. Lancet Diabetes Endocrinol. 2020; 8(5): 404-408. doi:10.1016/S2213-8587(20)30096-1.
8. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006; 444(7121): 860-867. doi:10.1038/nature05485.
9. Shoelson SE, Lee J, Goldfine AB. Inflammation and insulin resistance. J Clin Invest. 2006; 116(7): 1793-1801. doi:10.1172/JCI29069.
10. Purnell JQ, Hokanson JE, Marcovina SM, Steffes MW, Cleary PA, Brunzell JD; DCCT/EDIC Research Group. Effect of excess weight on cardiovascular risk factors in type 1 diabetes. Diabetes Care. 2013; 36(7): 2171-2178. doi:10.2337/dc12-1967.
11. Chillarón JJ, Goday A, Flores-Le-Roux JA, Mesa JL, Sala M, Montanya E. Metabolic syndrome in type 1 diabetes: Prevalence, characteristics and risk factors. Diabetes Care. 2014; 37(6): 1835-1839. doi:10.2337/dc13-1950.
12. de Ferranti SD, de Boer IH, Fonseca V, Fox CS, Golden SH, Lavie CJ, et al. Type 1 diabetes mellitus and cardiovascular disease: a scientific statement from the American Heart Association and American Diabetes Association. Circulation. 2014; 130(13): 1110-1130. doi:10.1161/CIR.0000000000000034.
13. Jensen MH, Ranjan S, Meyers T, Pinckard K, Knudsen K, Kersh J, et al. Insulin therapy and weight gain in patients with type 1 diabetes. Diabetes Care. 2019; 42(11): 2130-2137. doi:10.2337/dc19-0544.
14. DCCT Research Group. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus. J Pediatr. 1994; 125(2): 177-188. doi:10.1016/s0022-3476(94)70102-8.
15. Barrett JC, Clayton DG, Concannon P, Akolkar B, Cooper JD, Erlich HA, et al. Genome-wide association study and meta-analysis find that over 40 loci affect risk of type 1 diabetes. Nat Genet. 2009; 41(6): 703-707. doi:10.1038/ng.381.
16. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care. 2011; 34(6): 1249-1257. doi:10.2337/dc11-0442.
17. Verge CF, Gianani R, Kawasaki E, Yu L, Pietropaolo M, Jackson RA, et al. Prediction of type I diabetes in first-degree relatives using a combination of autoantibodies. Diabetes. 1996; 45(7): 926-933. doi:10.2337/diab.45.7.926.
18. Orchard TJ, Nathan DM, Zinman B, Cleary P; DCCT/EDIC Research Group. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. JAMA. 2015; 313(1): 45-53. doi:10.1001/jama.2014.17233.
19. Libby P, Bornfeldt KE, Tall AR. Atherosclerosis: Successes, Surprises, and Future Challenges. Circ Res. 2016; 118(4): 531-534. doi:10.1161/CIRCRESAHA.115.307611.
20. Haffner SM. Cardiovascular disease in patients with diabetes: epidemiology and mechanisms. Endocrinol Metab Clin North Am. 1996; 25(2): 369-384. doi:10.1016/s0889-8529(05)70344-5.
21. Lind M, Svensson AM, Kosiborod M, Gudbjörnsdottir S, Pivodic A, Wedel H, et al. Glycemic control and excess mortality in type 1 diabetes. N Engl J Med. 2014; 371(21): 1972-1982. doi:10.1056/NEJMoa1408214.
22. Petrie JR, Oldroyd J, Cohen ND, Shulman GI, Yudkin JS. Metformin for type 1 diabetes mellitus. Diabetologia. 2017; 60(9): 1605-1611. doi:10.1007/s00125-017-4343-9.
23. Libman IM, Barinas-Mitchell E, Bartucci AL, Johnson M, Saenz M, Becker D, et al. Metformin use in adolescents with type 1 diabetes mellitus: results of a randomized controlled trial. Diabetes Care. 2015; 38(8): 1387-1394. doi:10.2337/dc14-2403.
24. Tamborlane WV, Barrientos-Pérez M, Fainberg U, et al. Liraglutide in children and adolescents with type 2 diabetes. N Engl J Med. 2019; 381(7): 637-646. doi:10.1056/NEJMoa1813827
25. Garg SK, Henry RR, Banks P, Buse JB, Cohen RM, Eliaschewitz FG, et al. Effects of sotagliflozin added to insulin in patients with type 1 diabetes. N Engl J Med. 2017; 377(24): 2337-2348. doi:10.1056/NEJMoa1702019.
26. Mathieu C, Dandona P, Gillard P, et al. Efficacy and safety of dapagliflozin in patients with inadequately controlled type 1 diabetes: A randomized, double-blind, placebo-controlled trial. Lancet Diabetes Endocrinol. 2019; 7(12): 992-1004. doi:10.1016/S2213-8587(19)30272-5.
27. Markowitz J, Trivedi N, Brown MB, Clements RS Jr, Rao MK. Euglycemic diabetic ketoacidosis associated with sodium-glucose cotransporter-2 inhibitors: a review of the literature. Pharmacotherapy. 2017; 37(5): 563-576. doi:10.1002/phar.1926.
28. Leslie RD, Lernmark A. Genetic risk factors for type 1 diabetes. Lancet. 2018; 391(10135): 2337-2349. doi:10.1016/S0140-6736(18)31320-5.