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Clinical case Seminar

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A case of severe ketoacidosis as the first clinical manifestation of type 2 diabetes mellitus in a youngster

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Abstract

Type 2 diabetes (T2D) is a chronic condition caused by insulin resistance and relative insulin deficiency, leading to disrupted glucose homeostasis. Several genetic, behavioral, and socio-economic factors have been recognized as predisposing factors. The incidence of T2D in the pediatric population is increasing, paralleling the rise in obesity rates among youths. Early diagnosis and initiation of therapy are crucial to preventing or delaying long-term complications. We present the case of a 13-year-old Caucasian boy who presented with respiratory distress and altered consciousness, preceded by fever, cough, polyuria, and polydipsia. Blood gas analysis revealed metabolic acidosis (pH 7.1, Na 129.4 mmol/l, K 3.81 mmol/l, HCO3- 3.4 mmol/l, BE -23.65 mmol/l), ketonemia (4.8 mmol/l), and hyperglycemia (541 mg/dl), consistent with diabetic ketoacidosis. Further investigations, prompted by persistent respiratory distress and increased inflammatory markers, led to the diagnosis of complicated pneumonia. Based on clinical signs of insulin resistance (such as acanthosis nigricans), obesity (BMI 25.6 kg/m^2), family history of T2D (father), and after excluding type 1 diabetes, monogenic, and other forms of diabetes, a diagnosis of T2D was eventually established. Following resolution of diabetic ketoacidosis, therapy with metformin was started, with prompt achievement of satisfactory glucose control. This case underscores the possible association between infections, accelerated metabolic decompensation, and severe diabetic ketoacidosis in individuals predisposed to T2D.

Key-Words: insulin; obesity; pediatrics; type 1 diabetes; type 2 diabetes

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Introduction

Type 2 diabetes (T2D) is a chronic condition caused by insulin resistance and relative insulin deficiency without autoimmune β-cell destruction. Its pathogenesis involves a complex interplay between genetic and environmental risk factors, leading to peripheral insulin resistance and progressive β-cell failure. Although T2D is frequently diagnosed during adulthood, its prevalence among children and adolescents has significantly increased over the past decades, coinciding with rising rates of pediatric obesity [1]. Obesity, family history of T2D, being born small for gestational age (< 2500 g) or macrosomic (> 4000 g), and premature adrenarche in girls are all recognized predisposing factors for T2D [2]. Differential diagnosis between T2D and type 1 diabetes (T1D) in pediatric individuals is often challenging, due to the unavailability of specific biochemical markers of T2D. Diabetic ketoacidosis (DKA) represents the way of presentation of T2D in 5-25% of cases and can occur in newly diagnosed or poorly controlled T2D patients [3].

DKA can also be precipitated by any physiological stress, including infections. Individuals with diabetes are more susceptible to infections due to a hypothesized link between hyperglycaemia and impaired immune response [4]. Moreover, evidence suggests these subjects are more likely to be hospitalized and develop complications during the influenza season compared to healthy subjects [5].

Case Report

We describe the case of a 13-year-old Caucasian boy who presented at the emergency department due to persistent fever and cough, associated with polyuria and polydipsia, without any recent weight loss. The respiratory symptoms had been treated at home with systemic steroid therapy (oral betamethasone). He was born late preterm with a birth weight of 2000 g (appropriate for gestational age) and had a history of recurrent respiratory infections and episodes of wheezing. No concomitant diseases were reported. Upon arrival, he was in poor general conditions with a Glasgow Coma Scale score of 9, Kussmaul breathing, diffuse crackles in both lung fields, and reduced vesicular murmur at the right basal site. Initial laboratory findings revealed metabolic acidosis (pH 7.1, Na 129.4 mmol/l, K 3.81 mmol/l, HCO3 3.4 mmol/l, BE -23.65 mmol/l), hyperglycemia (541 mg/dl), positive ketonemia (4.8 mmol/l), and elevated glycosylated hemoglobin (HbA1c) (11,5 % or 102 mmol/mol), indicating severe DKA. Concurrently, community-acquired pneumonia was confirmed by chest X-ray, demonstrating multiple hazy consolidations tending to confluence and pleural effusion. The DKA correction protocol, consisting of the intravenous administration of regular insulin, fluids, and potassium chloride, was started and continued for 48 hours until the acidosis resolved, followed by multiple daily injection subcutaneous insulin therapy.

Further investigation of the pneumonia via chest computed tomography revealed cavitary pneumonia. Tests for tuberculosis, including Mantoux's intradermal reaction and Quantiferon test, were negative. However, sputum cultures identified infections by Acinetobacter baumannii, Streptococcus mitis, and Stenotrophomonas maltophilia. Consequently, broad-spectrum antimicrobial therapy with meropenem and linezolid was started, leading to near-complete resolution of the pneumonia within 30 days.

Serum C-peptide measurements at fasting and after glucagon stimulation test were performed, showing preserved β-cell function (basal C-peptide 2.30 ng/ml; stimulated C-peptide 3.28 ng/ml), while T1D-specific autoantibodies and genetic tests for monogenic diabetes were negative. Given the patient's history of recurrent severe pulmonary infections, cystic fibrosis was ruled out through sweat and genetic testing. Considering the laboratory results, family history of T2D (father), obesity (BMI 25.6 kg/m2; +2.25 Z-score) and clinical signs of insulin resistance (acanthosis nigricans), a diagnosis of T2D was established, and therapy with metformin was started at a dosage of 500 mg twice daily. Over the subsequent weeks, glycemic control improved gradually, accompanied by progressive weight loss.

Following discharge, the patient maintained satisfactory glucose control as evidenced by continuous glucose monitoring, with no further respiratory infections reported.

Discussion

DKA is an acute, life-threatening complication of hyperglycaemia that commonly occurs in children and adolescents with T1D and, occasionally, T2D [6]. It is characterized by hyperglycaemia (serum glucose >200 mg/dl), ketonemia (β-hydroxybutyrate concentration > 3.0 mmol/L) and/or ketonuria, and acidosis (venous pH < 7.3 and/or bicarbonate < 18 mmol/L). Clinical manifestations typically include dehydration, tachypnea, gastrointestinal symptoms, and reduced level of consciousness, following early symptoms such as polyuria, polydipsia, and weight loss.

Early diagnosis, prompt intervention, and intensive monitoring are imperative to manage DKA and to prevent further complications [3].

Upon admission, our patient presented with severe DKA. Although initial clinical characteristics suggested T1D, the absence of T1D-specific autoantibodies necessitated the exclusion of other forms of diabetes. Considering the family history of T2D, genetic investigations for maturity-onset diabetes of the young (MODY) were conducted but returned negative. The patient's susceptibility to infections caused by atypical bacteria also warranted ruling out cystic fibrosis-related diabetes (CFRD).

Ultimately, the clinical presentation suggested T2D, indicated by obesity (BMI 25.6 kg/m^2) and signs of insulin resistance such as acanthosis nigricans.

Infections are known precipitating factors for DKA due to their role in glucose derangement and accelerated metabolic decompensation. Conversely, diabetes impairs immune response, making individuals more vulnerable to infections [4].

Severe respiratory infections, including pneumonia caused by pathogens like Streptococcus pneumoniae, Legionella pneumophila, Klebsiella pneumoniae, Candida albicans, and Mucorales, have been reported to cause respiratory failure in people with diabetes. Pneumonia has been recently recognized as a predictor of short-term mortality in subjects with DKA. Therefore, early diagnosis and treatment of pulmonary infections are essential in managing DKA [7].

Conclusions

This case underscores that, in addition to T1D, DKA can also be a modality of presentation of T2D. The inflammatory state associated with pneumonia may have accelerated metabolic decompensation, revealing an overlooked diabetes. Conversely, chronic hyperglycemia might have contributed to the development of such a complicated pulmonary infection.

Conflicts of Interest: The authors declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

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