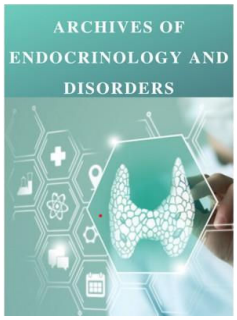

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Case Report

Diabetic Ketoacidosis in a Young Girl with Dorsal Pancreatic Agenesis and Negative Maturity-Onset Diabetes of the Young (MODY) Gene Panel: Expanding the Spectrum of Non-Autoimmune Diabetes: A Case Report

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Abstract

Background: Diabetic Ketoacidosis (DKA) is a potentially life-threatening metabolic emergency typically associated with Type 1 Diabetes Mellitus (T1DM). Structural pancreatic anomalies and monogenic diabetes rarely present with ketosis. Agenesis of the Dorsal Pancreas (DPA) is an exceptionally uncommon congenital anomaly that reduces pancreatic β-cell mass and may result in insulin-dependent diabetes.

Case Presentation: A 15-year-old non-obese girl presented with DKA triggered by pneumonia. Laboratory investigations confirmed severe hyperglycemia (glucose 634 mg/dL), metabolic acidosis (pH 7.18, HCO_3^- 3.7 mmol/L) and elevated HbA1C (12.5%). Autoantibodies for T1DM were negative. Cross-sectional imaging revealed complete dorsal pancreatic agenesis. Stool pancreatic elastase was markedly reduced (64.2 µg/g; normal >200), indicating exocrine insufficiency. A comprehensive MODY gene panel, including PDX1, IPF1, HNF1A and HNF4A, revealed no pathogenic variants. She responded well to insulin therapy and pancreatic enzyme replacement.

Conclusion: This case underscores that DKA can rarely occur in antibody-negative young patients with structural pancreatic anomalies and no identifiable monogenic mutations. Recognition of DPA is crucial for precise diagnosis, targeted management and genetic counseling.

Keywords: Dorsal Pancreatic Agenesis; Diabetic Ketoacidosis; Exocrine Pancreatic Insufficiency; Monogenic Diabetes; MODY-Negative Diabetes

Introduction

Diabetic Ketoacidosis (DKA) remains one of the most serious acute complications of diabetes, predominantly linked to autoimmune β-cell destruction in Type 1 Diabetes Mellitus (T1DM) [1]. However, ketosis-prone diabetes may occasionally occur in atypical clinical settings, including structural pancreatic malformations and monogenic forms of diabetes [2,3]. Maturity-Onset Diabetes of the Young (MODY) represents a heterogeneous group of autosomal-dominant disorders caused by mutations affecting pancreatic β-cell transcription factors [4]. Unlike T1DM, patients with MODY are usually non-obese, antibody-negative and retain some degree of insulin secretion, rarely developing ketosis [5]. Agenesis of the Dorsal Pancreas (DPA) is an exceedingly rare congenital anomaly resulting from developmental failure of the dorsal pancreatic bud, which normally gives rise to the body and tail of the pancreas,

the primary sites of the islets of Langerhans [6-8]. Loss of these structures leads to reduced insulin-producing β-cell mass and exocrine insufficiency. While DPA has been linked to mutations in the PDX1 gene (MODY 4), several reports describe DPA in patients lacking identifiable mutations [9-11]. Here, we describe a rare case of DKA in a young, antibody-negative girl with complete DPA and a negative comprehensive MODY gene panel. This case underscores that early-onset, non-autoimmune diabetes may arise from previously under-recognized structural pancreatic defects, even in the absence of monogenic mutations. Incorporating targeted pancreatic imaging and genetic evaluation into the diagnostic workup of atypical presentations is essential to prevent misclassification, guide individualized management and inform accurate prognostication and genetic counseling.

Case Presentation

A 15-year-old girl presented with high-grade fever for four days, productive cough for three days and progressive breathlessness for one day. There was a two-month history of weight loss, polyuria, polydipsia and genital itching. She was born preterm at 28 weeks with intrauterine growth restriction (birth weight 1.2 kg) and had no prior history of pancreatitis or abdominal pain. Her mother had diet-controlled diabetes diagnosed at 40 years and a maternal uncle was diabetic. On examination, she appeared dehydrated and tachypneic (pulse 150/min, BP 100/70 mmHg, RR 24/min, BMI 14.9 kg/m^2). Chest auscultation revealed bilateral crepitations. Table 1 depicts the summary of investigations (Table 1, Fig. 1-3).

Parameter	Result	Comment
Random blood glucose	634 mg/dL	Severe hyperglycemia
HbA1C	12.5%	Poor glycemic control
Arterial blood gas	pH 7.18, HCO_3^- 3.7 mmol/L, anion gap 36	DKA
Urine ketones	3+	Positive
CRP	120 mg/L	Infective trigger
Total count	21,300/mm^3 (N80 L18)	Neutrophilic leukocytosis
Stool pancreatic elastase	64.2 μg/g (normal >200)	Exocrine insufficiency
Serum amylase/lipase	Normal	No pancreatitis
Autoantibodies	Negative	Excludes T1DM
Chest X-ray	Multilobar consolidation	Pneumonia
CECT/MRCP abdomen	Complete dorsal pancreatic agenesis	Diagnostic
MODY gene panel	Negative	No pathogenic variants

Table 1: Summary of investigations.

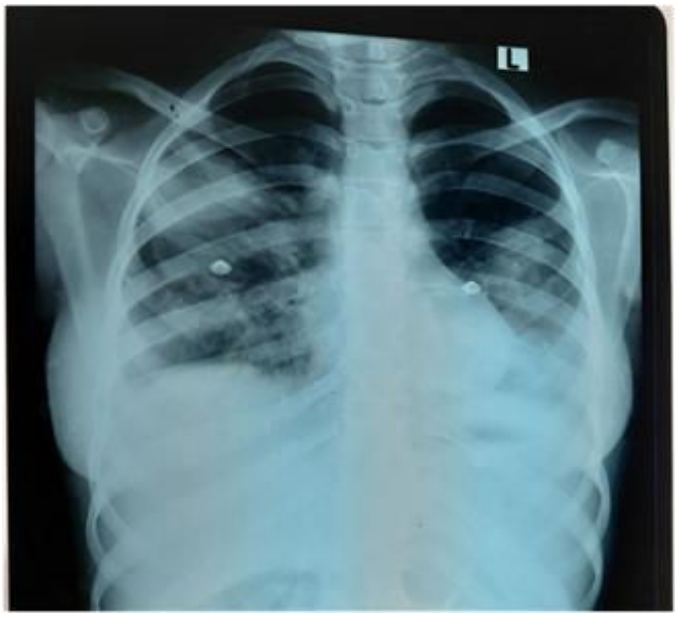

Figure 1: Chest X-ray Showing Multilobar consolidation.

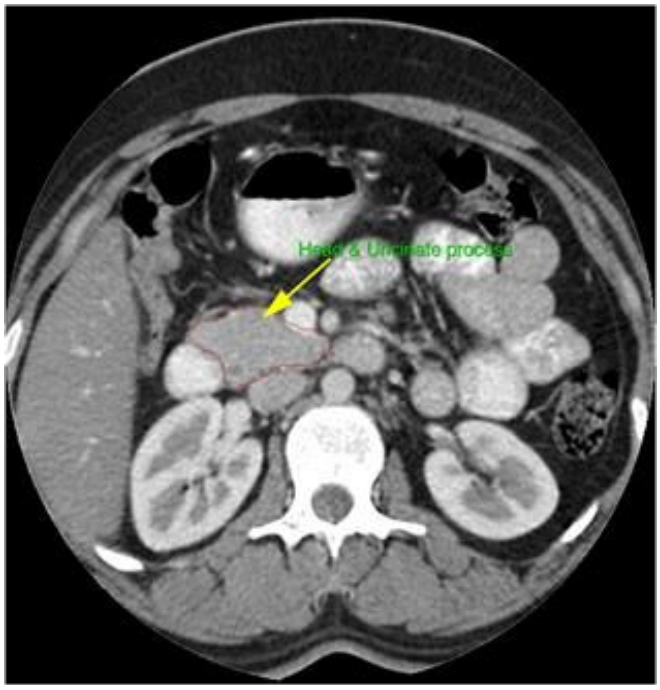

Figure 2: Contrast CT image of abdomen showing dorsal pancreatic agenesis, head and uncinate process seen.

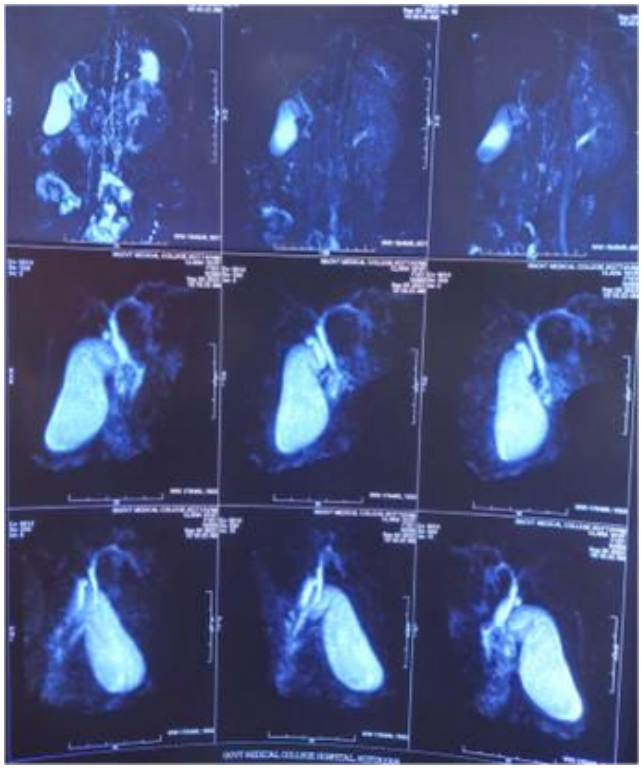

Figure 3: MRCP image showing dorsal pancreatic agenesis.

Hospital Course

The patient was admitted to the intensive care unit and managed per standard DKA protocol with intravenous fluids, regular insulin infusion and empirical antibiotics (ceftriaxone and azithromycin). Her acidosis resolved within 48 hours (repeat ABG pH 7.46, HCO_3^- 26.7 mmol/L). She was transitioned to basal-bolus insulin therapy and started on pancreatic enzyme replacement. At three-month follow-up, she had gained 3 kg, maintained good glycemic control and remained asymptomatic.

Discussion

Dorsal Pancreatic Agenesis (DPA) is an exceptionally rare congenital anomaly characterized by the absence of the pancreatic body and tail due to failed development of the dorsal pancreatic bud, with fewer than 100 cases reported globally [6,7,11]. Because the dorsal pancreas contains a substantial proportion of islet cell mass, its agenesis predisposes individuals to both endocrine and exocrine dysfunction. In our patient, cross-sectional imaging Contrast-Enhanced Computed Tomography (CECT) and Magnetic Resonance Cholangiopancreatography (MRCP) confirmed complete agenesis of the dorsal pancreas and the markedly reduced stool pancreatic elastase (64.2μg/g) indicated severe exocrine insufficiency, consistent with previous reports [1,8,12]. At presentation, the patient fulfilled diagnostic criteria for DKA with severe hyperglycemia (634 mg/dL), elevated HbA1c (12.5%), high-anion gap metabolic acidosis and ketonuria. Although DKA is classically associated with autoimmune type 1 diabetes, it is distinctly uncommon in structural pancreatic anomalies or monogenic diabetes because residual β-cell reserve generally suppresses ketogenesis [3,5]. In this case, multilobar pneumonia, evidenced by chest radiograph, elevated CRP and neutrophilic leukocytosis, acted as a potent physiologic stressor precipitating metabolic decompensation. Infection-related DKA has similarly been documented in other cases of DPA and in non-type 1 diabetes phenotypes [3,4,13,14].

The absence of pancreatic autoantibodies effectively excluded autoimmune T1DM, prompting evaluation for alternative etiologies. The negative MODY gene panel, which included PDX1, HNF1A, HNF4A and other β-cell transcription factor genes, ruled out known monogenic diabetes forms. Although PDX1 (IPF1) mutations are well recognized in MODY 4 and pancreatic hypoplasia or agenesis multiple studies have reported DPA in patients without identifiable genetic variants [9,10,15]. Increasing evidence implicates additional developmental genes such as PTF1A, RFX6, GATA6 and NEUROD1 in pancreatic organogenesis and agenesis phenotypes [16-18]. Our findings therefore highlight the limitations of currently available genetic panels and underscore the need for expanded genomic approaches, including whole-exome and whole-genome sequencing.

The patient's hospital course reinforces the functional consequences of the structural defect identified. Early DKA management led to resolution of acidosis within 48 hours and initiation of pancreatic enzyme replacement addressed exocrine insufficiency. At three months, the patient exhibited weight gain, improved glycemic control and absence of recurrent symptoms, demonstrating the importance of timely recognition and targeted management of DPA-related metabolic derangements.

Overall, this case expands the phenotypic spectrum of non-autoimmune diabetes in adolescents and emphasizes that DPA should be considered in young, non-obese, antibody-negative individuals presenting with DKA, especially when accompanied by exocrine insufficiency or atypical features. Comprehensive structural imaging and functional pancreatic assessment are critical components of evaluation. Even when MODY gene testing is negative, congenital anomalies such as DPA remain important etiologies and ongoing genomic research is likely to reveal additional developmental pathways implicated in these rare presentations (Table 2).

Evaluation of an Young Patient with Diabetes
Age <25 years, non-obese, mild-moderate hyperglycemia, preserved C-peptide
Initial Assessment for Autoimmune Diabetes
Test pancreatic auto antibodies: GAD65, IA-2, ZnT8, ICA Auto antibodies positive → Type 1 Diabetes → STOP; Auto antibodies negative → Proceed
Evaluate Clinical Indicators Suggestive of MODY
Family history of diabetes across ≥2 generations>; Normal BMI or mild overweight • Absence of ketosis; No signs of insulin resistance (acanthosis, hypertension, dyslipidemia); Stable insulin requirement or good control with low-dose insulin
Measure C-peptide (fasting or stimulated)
C-peptide <0.2-0.4 ng/mL → Insulinopenia → unlikely MODY → consider T1DM, DPA, pancreatogenic DM; C-peptide preserved → MODY likely
Biochemical Clues toward Subtypes
High-sensitivity CRP very low → Suggests HNF1A-MODY; Glycosuria with normal glucose → SGLT mutation → HNF1A-MODY; Progressive hyperglycemia post-puberty → HNF4A-MODY; Early onset (neonatal/infant) → KCNJ11/ABCC8 (neonatal diabetes); Pancreatic hypoplasia/agenesis → PDX1-MODY, GATA6, PTF1A
Targeted MODY Gene Panel Testing

Order multi-gene panel including: HNF1A, HNF4A, HNF1B, GCK, PDX1, NEUROD1, KCNJ11, ABCC8, RFX6, GATA6, PTF1A
Interpretation of Genetic Testing Results
Pathogenic variant identified → CONFIRMED MODY → subtype-specific management
No variant identified →Consider rare regulatory region variants; Consider expanded sequencing (exome/genome); Evaluate for structural cause (e.g., DPA, pancreatitis-related damage)
Management According to MODY Subtype
GCK-MODY → No treatment needed except pregnancy; HNF1A/HNF4A-MODY → Sulfonylurea preferred: excellent response; HNF1B-MODY → Requires lifelong insulin, consider renal evaluation; PDX1/NEUROD1/GATA6 → Often mixed endocrine-exocrine defects
Follow-up and Genetic Counseling
Family screening of first-degree relatives; Long-term monitoring for complications

Table 2: A flow chart showing evaluation of an young patient with diabetes.

Conclusion

Dorsal pancreatic agenesis is an uncommon but clinically important structural cause of non-autoimmune diabetes in adolescents. This case demonstrates that diabetic ketoacidosis, although rarely described in congenital pancreatic anomalies, can occur when limited β-cell reserve is compromised by acute metabolic stress such as infection. The strength of this report lies in its comprehensive evaluation combining autoantibody testing, exocrine function assessment, advanced imaging and extensive MODY gene analysis which allowed precise etiological classification and avoided misdiagnosis as type 1 diabetes. This integrated approach reinforces the need to consider anatomical abnormalities in young patients presenting with atypical, antibody-negative hyperglycemia. However, as a single-patient observation, broader generalizability is limited and the absence of extended genomic studies (such as whole-exome or whole-genome sequencing) limits exploration of the underlying developmental genetics. Likewise, the relatively short follow-up period restricts long-term insights into metabolic and exocrine outcomes. Despite these limitations, this case expands the phenotypic spectrum of MODY-negative, non-autoimmune diabetes and underscores the need for heightened clinical vigilance. Early recognition of dorsal pancreatic agenesis can guide targeted therapy, inform genetic counseling and improve long-term management in similar atypical presentations.

Learning Points

- Dorsal Pancreatic Agenesis (DPA) is a rare but important structural cause of non-autoimmune diabetes and should be considered in adolescents presenting with antibody-negative hyperglycemia
- Diabetic ketoacidosis can occur in DPA, especially when limited β-cell reserve is stressed by intercurrent illness such as infection
- Comprehensive evaluation including pancreatic imaging and stool elastase is essential to differentiate structural pancreatic defects from type 1 diabetes, type 2 diabetes and monogenic diabetes
- A negative MODY gene panel does not exclude congenital pancreatic anomalies, as several developmental genes remain under-recognized or not covered in standard sequencing platforms
- Management must address both endocrine and exocrine insufficiency, with insulin therapy and pancreatic enzyme replacement improving clinical outcomes
- Early diagnosis enables accurate counseling, long-term monitoring and appropriate family screening, particularly in atypical presentations with preserved C-peptide and absent autoimmunity

Conflict of Interest

The authors declare that they have no conflict of interest.

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Authors Contributors

All the authors have made contributions in their own way.

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