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Case Report

Recurrent acute pancreatitis in a patient with acquired glutaric aciduria type II: a case report

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ABSTRACT

Acquired glutaric aciduria type II (GAII) is an emerging metabolic disorder linked to mitochondrial dysfunction, which may predispose patients to recurrent pancreatitis due to impaired fatty acid metabolism. This report presents the first documented instance of recurrent acute pancreatitis in a patient with acquired GAII. A 30-year-old Caucasian female with a known diagnosis of acquired GAII presented with recurrent episodes of acute pancreatitis, including two episodes during pregnancy and one outside pregnancy. Thorough investigations systematically excluded common causes such as gallstones, alcohol use, hypertriglyceridemia, IgG4-related disease, autoimmune pancreatitis and anatomical anomalies. Management required multidisciplinary collaboration involving surgeons, obstetricians, metabolic specialists and medical physicians. Treatment involved conservative surgical management including intravenous fluid resuscitation, analgesia, anti-emetics and specialized metabolic support, particularly intravenous dextrose while fasting. This case highlights the importance of recognizing acquired GAII as a potential underlying cause of recurrent acute pancreatitis. Awareness among surgical and multidisciplinary teams is crucial for timely diagnosis and effective management to prevent severe complications.

Keywords: Acquired metabolic disorders, Glutaric aciduria type II, Hepatobiliary surgery, Multiple acyl-CoA dehydrogenase deficiency, Pancreatitis

INTRODUCTION

Glutaric aciduria type II (GAII), also known as Multiple Acyl-CoA Dehydrogenase Deficiency (MADD), is a rare metabolic disorder characterized by impaired mitochondrial fatty acid oxidation.[1] GAII typically presents with metabolic crises, muscle weakness, rhabdomyolysis and neurological abnormalities.1 Although pancreatitis is not widely recognized as a common manifestation of GAII, there are limited reports documenting pancreatitis associated with this condition.

The first known case of pancreatitis in GAII was reported by Coşkun et al, in 1997, identifying pancreatitis as a critical, though uncommon, complication in these patients. Subsequent reports, including a case by Liang et al, in 2004 describing recurrent pancreatitis responsive to riboflavin supplementation and a recent case series by Elkhateeb et al, in 2020, have supported the recognition of pancreatitis as a significant and potentially underdiagnosed complication of GAII.[2-4]

Recurrent pancreatitis occurring in patients with acquired forms of GAII remains underreported. The unique pathophysiological mechanisms by which GAII predisposes patients to pancreatitis are not fully elucidated, highlighting the importance of documenting and reporting such cases. This report aims to contribute to the existing surgical and medical literature by presenting a case of recurrent acute pancreatitis in a patient with acquired GAII, providing further clinical insights into this rare and potentially life-threatening condition.

CASE REPORT

A 30-years-old Caucasian female presented to the surgical service at 32 weeks and 4 days gestation with acute onset of abdominal pain localized to the left upper quadrant, accompanied by nausea and vomiting. Clinical examination revealed tenderness in both the left upper quadrant and the left flank without signs of peritonitis. Serum lipase was significantly elevated, initially recorded at 1423 U/l (normal range 0-160 U/l), confirming the diagnosis of pancreatitis.

Imaging investigations, initially an abdominal ultrasound (Figure 1), revealed peripancreatic fluid in keeping with acute pancreatitis. MRI later demonstrated mild generalized pancreatic swelling through the pancreatic body and tail, with peripancreatic edema but no necrosis or fluid collections. There was no evidence of biliary obstruction, gallstones or structural anomalies such as pancreatic divisum (Figure 2). Serum triglycerides were mildly elevated at 2.8 mmol/l (normal 0.5-2.0 mmol/l), although extensive assessments excluded significant hypertriglyceridemia, alcohol use, autoimmune pancreatitis and IgG4-related disease.

This episode represented the patient's third documented occurrence of acute pancreatitis. The first episode occurred during a previous pregnancy at 36 weeks gestation in April 2022, with a significantly higher clinical acuity. At the time she had multiple medical emergency team (MET) calls due to persistent tachycardia and a markedly elevated CRP of 192 mg/l. This prompted an early induction of delivery, after which a computed tomography (CT) scan confirmed pancreatitis (Figure 3). The second episode occurred in April 2024 when she was not pregnant and was comparatively mild. During that episode, she was referred to hepatobiliary surgeons who organized outpatient MRCP imaging. No structural or reversible causes were identified and the patient was subsequently discharged.

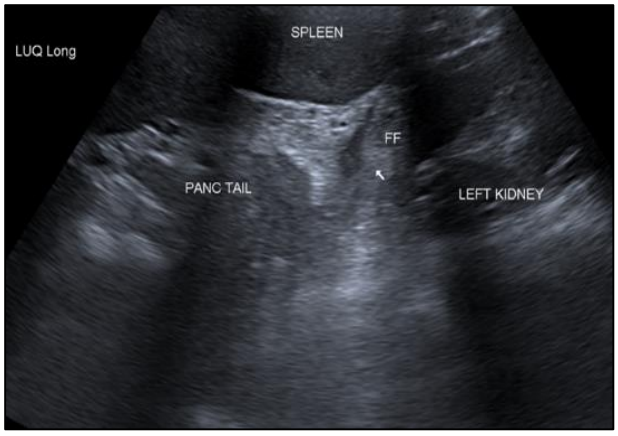

Figure 1: Longitudinal ultrasound of the left upper quadrant demonstrating a small amount of free fluid (arrow) adjacent to the pancreatic tail, consistent with acute pancreatitis.

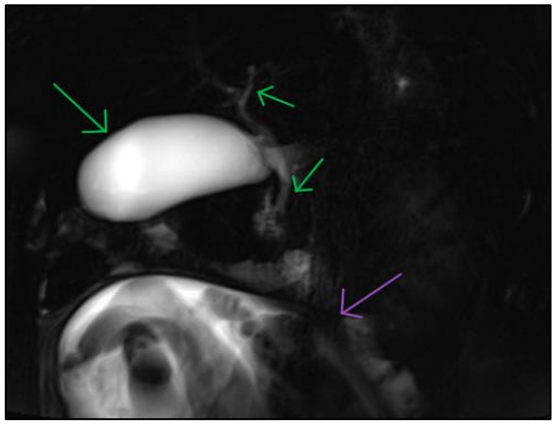

Figure 2: MRCP at time of 3rd episode of pancreatitis. 3D reconstruction in coronal view confirms the absence of gallstones within the gallbladder or biliary system (green arrows). Note intrauterine pregnancy also imaged (pink arrow).

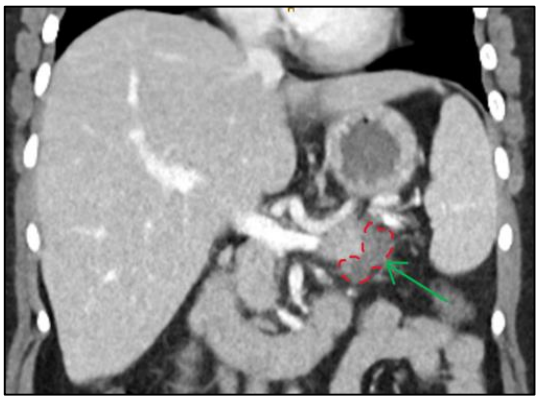

Figure 3: CT Abdomen in coronal view, with portal vein phase contrast, at time of 1st presentation. Scan taken after delivery. Small collection of fluid is seen inferior to pancreatic tail (green arrow).

		Units	Ref Interval
PLASMA CARNITINE PROFILE			
Total Carnitine	87H	umol/L	21-70
Free Carnitine	69H	umol/L	13-56
Acetylcarnitine	10	umol/L	3-23
Tiglylcarnitine	<0.10	umol/L	<0.20
Propionylcarn	0.46	umol/L	<0.66
Isovalerylcarn**	0.15	umol/L	<0.28
3-OHisovalcarn%	<0.10	umol/L	<0.31
Decanoylcarn	2.40H	umol/L	<0.40
Decenoylcarn	0.31	umol/L	<0.50
Tetradecanoylcarn	0.25	umol/L	<0.34
Tetradecenoylcarn	0.42	umol/L	<0.73
Palmitoylcarn	0.28	umol/L	0-0.65
3-OHpalmitoylcarn	<0.05	umol/L	<0.07
Hexanoylcarn	0.48H	umol/L	<0.13
Octanoylcarn	1.60H	umol/L	<0.24
Butyrlcarn*	0.44	umol/L	0.12-0.67
Glutarylcarn	<0.10	umol/L	<0.34
Dodecanoylcarn	0.50	umol/L	<0.62
Oleoylcarnitine	0.29	umol/L	
Stearoylcarn	0.15	umol/L	

COMMENTS:
Acylcarnitine profile by Tandem Mass Spectrometry: This pattern typical of glutaric aciduria type 2. Other causes of this pattern are mitochondrial disorders or valproate therapy.

Figure 4: Plasma carnitine profile taken between initial diagnosis in 2017 and before 1st episode of pancreatitis in 2022. Pattern of carnitine elevation is in keeping with glutaric aciduria type ii, despite negative gene studies.

Importantly, diabetes mellitus was not present during the first two episodes, with normal HbA1c values documented. Gestational diabetes requiring insulin management was only recently diagnosed during the current pregnancy.

Her medical history included acquired glutaric aciduria type II (GAII), initially diagnosed in 2017 during hospitalization for metabolic acidosis, myositis (creatine kinase 4000 U/l, normal range 34-145 U/l), rhabdomyolysis and peripheral neuropathy. Elevated acylcarnitines supported the biochemical diagnosis, despite no genetic variants being identified, suggesting an acquired cause (Figure 4).

Her history was also significant for depression, previously treated with high-dose sertraline, a drug that has recently become associated with acquired GAII. Long-term management involved adherence to a low-fat, choline-rich diet and supplementation with intravenous dextrose 10% during fasting periods.

Multidisciplinary management by surgical, obstetric and metabolic teams successfully provided conservative treatment leading to resolution of this acute episode. Continuous intravenous dextrose 10% was administered due to her inability to tolerate oral intake. Further targeted metabolic support for management of her riboflavin, along with intravenous fluids, analgesia and anti-emetics; resulted in resolution of her symptoms without further complications.

DISCUSSION

Acute pancreatitis typically results from premature activation of digestive enzymes within pancreatic acinar cells, causing autodigestion, inflammation and clinical symptoms.[5] Common causes include gallstones, alcohol use, hypertriglyceridemia, autoimmune factors, anatomical anomalies and medications.[5] Rare causes, such as metabolic disorders like glutaric aciduria type II (GAII), also known as Multiple Acyl-CoA Dehydrogenase Deficiency (MADD), must be considered when common etiologies have been systematically excluded.

The exact pathophysiological mechanisms linking GAII/MADD to pancreatitis are not fully elucidated. However, it is postulated that impaired mitochondrial fatty-acid oxidation could lead to energy depletion and buildup of toxic intermediates in the pancreas, analogous to other mitochondrial disorders or organic acidemias.[6] Due to its high metabolic demands, the pancreas is particularly vulnerable to disordered energy metabolism inherent in GAII. This dysfunction can cause impaired ATP availability in pancreatic acinar cells, resulting in intracellular activation of digestive enzymes, cellular injury and subsequent inflammation.[4] The first documented case of pancreatitis in GAII was identified post-mortem in a paediatric patient, further supporting the association between GAII/MADD and pancreatic involvement.[2] Recurrent pancreatitis has been since reported in a GAII patient responsive to metabolic therapy, suggesting a potential benefit from optimized metabolic control.[3] Additionally, pancreatic involvement was found in approximately 17% of a series of MADD cases, further highlighting this link.[4]

This case highlights a rare presentation of acquired GAII in adulthood, most likely induced by sertraline use. Emerging case reports describe patients developing GAII-like biochemical profiles while on sertraline, with resolution after drug discontinuation.[7] This suggests a reversible, drug-induced mitochondrial dysfunction mimicking inherited GAII.[7] This is clinically relevant to general surgeons, as GAII is classically diagnosed in childhood and managed accordingly by paediatric surgeons. However, acquired GAII due to sertraline exposure manifests in adulthood, shifting these cases to general surgeons when pancreatitis occurs.

Clinicians should maintain a high index of suspicion for rare metabolic causes of recurrent pancreatitis after ruling out more common etiologies. Vigilance is particularly critical regarding interventions that might exacerbate fatty acid oxidation impairment, such as high-fat diets or certain medications.[6] Expert recommendations emphasize routine monitoring of pancreatic enzyme levels during metabolic crises or episodes of acute illness in GAII patients.[2]

CONCLUSION

In conclusion, increased recognition of GAII/MADD as an uncommon yet clinically significant cause of pancreatitis is essential. Multidisciplinary collaboration among surgical, metabolic and medical specialists is pivotal for timely diagnosis, effective management and prevention of recurrent pancreatitis episodes.

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