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The Impact of Hypertriglyceridemia on Recurrent Acute Pancreatitis: A Case Report of a Paediatric Patient with Familial Hyperlipoproteinemia

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Abstract: ***Hypertriglyceridemia (HTG) is a metabolic disorder characterised by elevated serum triglyceride levels, which significantly heightens acute pancreatitis (AP) risk. In paediatric populations, with genetic predispositions such as familial hyperlipoproteinemia, the association between HTG and recurrent AP is noteworthy. This report details the case of a 6-year-old male diagnosed with familial hyperlipoproteinemia type 1. The child was admitted to the paediatric ward with a one-day history of abdominal pain and vomiting. Upon admission, laboratory tests indicated triglyceride levels of 1091 mg/dL, along with elevated serum amylase and lipase levels, which confirmed the diagnosis of acute on chronic pancreatitis. Management protocols were initiated, including intravenous fluid therapy, analgesics, and dietary modifications, and resolving symptoms. A comprehensive management plan emphasising strict dietary adherence was provided upon discharge. This case highlights the critical role of HTG as a risk factor for AP, particularly when triglyceride levels exceed 1,000 mg/dL. The underlying pathophysiological mechanisms involve the hydrolysis of triglycerides, producing cytotoxic free fatty acids that damage pancreatic acinar cells and initiate inflammation. Familial hyperlipoproteinemia type 1, a rare genetic disorder, exacerbates lipid metabolism issues, necessitating lifelong management strategies. Despite the implemented interventions, the genetic nature of this condition requires continuous monitoring and adherence to dietary modifications to mitigate the risk of recurrent episodes of pancreatitis. The early diagnosis and comprehensive management of hypertriglyceridemia in paediatric patients are essential for reducing the risk of recurrent acute pancreatitis. Long-term management strategies should include pharmacological interventions, dietary management, and rigorous monitoring to enhance patient outcomes and prevent complications associated with chronic pancreatic damage.***

Keywords: Acute pancreatitis, Fatty acid, Hypertriglyceridemia**,** Hyperlipoproteinemia

1. Introduction

Hypertriglyceridemia (HTG) is a metabolic disorder characterised by a serum or plasma triglyceride concentration (seTG) exceeding 150mg/dl. HTG can range from mild to severe based on the seTG values.[2] This condition is recognised as a significant risk factor for acute pancreatitis (AP), accounting for approximately 10% of all pancreatitis cases and markedly contributing to its morbidity.[3] Elevated triglyceride levels, particularly those surpassing 1000 mg/dL, may precipitate or exacerbate pancreatitis, especially in individuals with genetic predispositions such as familial hyperlipoproteinemia.[4,5]

The underlying mechanisms that link HTG to AP involve the excessive hydrolysis of triglycerides by pancreatic lipase, resulting in the release of substantial quantities of free fatty acids (FFAs) that are cytotoxic, inflicting damage on pancreatic acinar cells and instigating inflammatory responses, which are central to pancreatic injury.[5]

Two principal theories have been proposed to explain the pathogenesis of HTG-induced AP. The first theory emphasises the pivotal role of FFAs in initiating pancreatic injury through cytotoxic effects and inflammation. [4, 6, 7] The second theory posits that HTG may elevate blood viscosity, impairing pancreatic microcirculation and leading to ischemic damage of acinar cells. [7-9]

In the context of clinical presentation, a young child with familial hyperlipoproteinemia exhibited recurrent episodes of pancreatitis, highlighting the critical importance of early intervention in individuals with elevated triglyceride levels. Effective management of HTG through dietary modifications and pharmacological interventions is essential in preventing the recurrence of acute pancreatitis and enhancing long-term health outcomes.

2. Case Presentation

A 6-year-old male child, previously diagnosed with familial hyperlipoproteinemia (type 1), was admitted to the paediatric ward following a one-day history of abdominal pain and vomiting. He has a documented history of recurrent acute pancreatitis, with initial episode occurring at 45 days of life, correlating with the initial detection of hypertriglyceridemia. During the current admission, the primary concerns included diffuse abdominal pain and non-bilious vomiting, accompanied by diminished oral intake; however, urine output remained stable. No other associated symptoms were reported, such as diarrhoea, fatigue, or weight loss.

Table 1: Hospital Admissions and Key Lab Findings in Familial Hyperlipoproteinemia

Date of Admission	Age at Admission	Duration of Hospital Stay	Amylase (U/L)	Lipase (U/L)	Triglycerides (mg/dL)	Cholesterol (mg/dL)
18-10-2018	45 DOL	20 Days	-	-	6286	1541
20-02-2021	3 Years	7 Days	103	245	3570	303
29-12-2021	3 Years	6 Days	91	613	2881	318
26-11-2022	4 Years	7 Days	535	1166	N/A	110
18-04-2023	5 Years	5 Days	66	166	5513	51
15-12-2023	5 Years	5 Days	525	1114	4647	566
22-04-2024	6 Years	9 Days	414	900	3856	417
19-07-2024	6 Years	12 Days	428	1425	1251	212
14-08-2024	6 Years	5 Days	884	2495	480	156
27-08-2024	6 Years	5 Days	154	775	1091	343

The patient has consistently undergone management for familial hyperlipoproteinemia, which includes omega-3 fatty acid supplementation and dietary modifications. This condition had resulted in multiple episodes of pancreatitis, necessitating several previous hospitalisations.

Imaging conducted in December 2021 revealed progressive calcifications within the pancreas. Despite ongoing treatment, including dietary adjustments and medication, his lipid levels remained elevated, contributing to recurrent episodes of pancreatitis.

Investigations during this admission indicated elevated serum amylase and lipase levels, as well as hypertriglyceridemia, with triglyceride levels significantly elevated at 1091 mg/dL and cholesterol at 343 mg/dL as shown in **Table 1**. Coagulation studies indicated prolonged clotting time, necessitating the administration of intravenous vitamin K. An abdominal ultrasound confirmed that the body of the pancreas appeared mildly bulky, without evidence of fluid collections or splenomegaly.

The patient was initially managed with intravenous fluids and analgesics, which led to a gradual improvement of symptoms. Lipid levels had decreased by the third day of admission, and he successfully tolerated oral feeds. Subsequent testing demonstrated a marked improvement in triglyceride levels, decreasing to 541 mg/dL and cholesterol normalising to 164 mg/dL, as mentioned in **Table 1**. Due to his stabilisation, the patient was discharged with detailed instructions for home management that included strict adherence to dietary guidelines and continued medication.

The primary diagnosis was determined to be acute on chronic pancreatitis secondary to underlying familial hyperlipoproteinemia. No adverse events were noted during the hospital stay, and the patient is scheduled for follow-up lipid profiling and outpatient review.

The patient responded positively to the prescribed interventions, encompassing pharmacologic management, dietary adjustments, and rigorous monitoring. His symptoms resolved, and significant modifications to the treatment plan were unnecessary during this admission. The family received guidance on the critical importance of adhering to the prescribed management plan to prevent further episodes of pancreatitis.

3. Discussion

HTG is a well-established risk factor for AP, particularly when triglyceride levels exceed 1000 mg/dL. This is evident in the case of a 6-year-old male with familial hyperlipoproteinemia type 1, who experienced recurrent episodes of pancreatitis, highlighting the necessity for early intervention.

The pathophysiological mechanism linking HTG to AP primarily involves the hydrolysis of triglycerides by pancreatic lipase, resulting in the release of FFAs, which have cytotoxic effects on pancreatic acinar cells. This cytotoxicity induces inflammation and cellular damage, observable in progressive calcifications within the patient's pancreas. Such findings are consistent with chronic pancreatitis from recurrent acute episodes [10, 11].

Two prevailing theories elucidate the relationship between HTG and AP, as shown in **Figure 1**. The first theory emphasises the harmful effects of FFAs, which incite an inflammatory cascade and injure acinar cells [12, 13]. The second theory posits that HTG may elevate blood viscosity, impairing pancreatic microcirculation and leading to ischemic injury of acinar cells. However, the hyperviscosity hypothesis lacks substantial experimental support, as mineral oil studies have shown minimal effects on disease progression [2, 14].

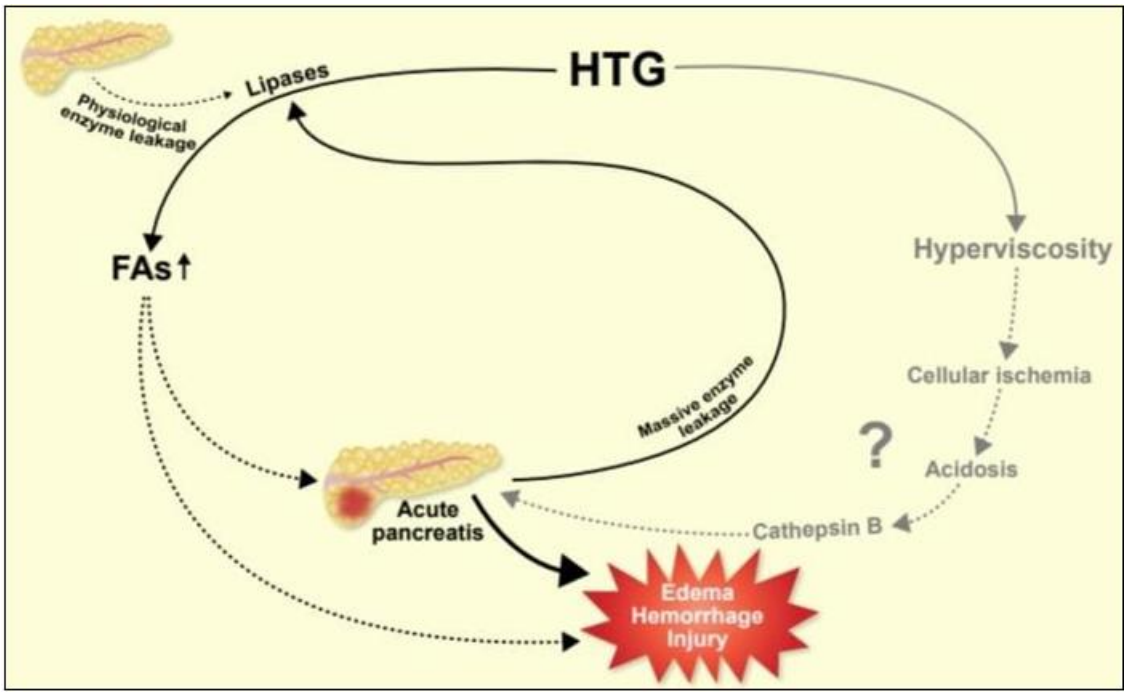

Figure 1: The potential mechanism for hypertriglyceridemia (HTG) to induce pancreatic injury has been investigated. There are two prevailing theories concerning the relationship between HTG and acute pancreatitis (AP) or the exacerbation of this condition: (A) the liberation of fatty acids (FAs) resulting from the excessive hydrolysis of triglycerides (TGs) by lipases (indicated in black text), and (B) the increased blood viscosity associated with HTG (noted in grey text). Fatty acids induce and aggravate tissue injury related to acute pancreatitis. The impact of HTG-induced hyperviscosity remains a topic of debate. While it is theoretically plausible that hyperviscosity could contribute to adverse effects linked to HTG, current experimental data involving mineral oil and hyperviscosity syndromes do not substantiate this hypothesis.

Familial hyperlipoproteinemia type 1, a rare monogenic disorder underlying severe HTG, is central to this patient's condition. Monogenic HTG syndromes, such as familial chylomicronaemia, typically manifest with early onset and severe complications, including recurrent pancreatitis. These disorders are linked to mutations in genes like LPL and APOC2, which disrupt lipid metabolism and heighten the risk of AP, particularly in paediatric populations [15, 16].

In familial hyperlipoproteinemia, mutations hinder the clearance of triglyceride-rich lipoproteins, resulting in persistent HTG. This persistence facilitates the excessive release of FFAs during lipolysis, which damages pancreatic acinar cells and instigates AP [10, 14]. The recurring episodes of pancreatitis in this child align with familial chylomicronaemia syndrome, wherein genetic predisposition leads to severe lipid metabolism disorders.

A notable strength of this case report is its comprehensive account of clinical management over time. However, the absence of genetic testing to confirm specific mutations and the limited discourse on long-term treatment adherence are significant limitations.

4. Conclusion

This case report highlights the imperative of early diagnosis and effective management in preventing recurrent acute pancreatitis in paediatric patients diagnosed with familial hyperlipoproteinemia type 1. A triglyceride level exceeding 1000 mg/dL is identified as a significant risk factor for the onset of pancreatitis. Long-term management strategies must encompass dietary modifications, pharmacological interventions, and stringent monitoring protocols. Despite the implementation of these interventions, the inherent genetic predisposition associated with familial hyperlipoproteinemia necessitates a commitment to lifelong care aimed at reducing both the frequency and severity of pancreatitis episodes, as well as mitigating the progression of chronic pancreatic damage. Early and consistent adherence to the established management plan is crucial for enhancing patient outcomes.

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