

## Management of Severe Hypertriglyceridemia Induced Pancreatitis in Children – A Case Report

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### Abstract

**Introduction:** Hypertriglyceridemia (HTG) is an uncommon but potentially severe cause of acute pancreatitis (AP) in children. Severe HTG may require urgent interventions such as plasma exchange (PEX), and data on pediatric HTG-induced AP and its management is limited.

**Case Presentation:** 15-year-old girl with maturity-onset diabetes of the young type 3 (MODY-3), metabolic syndrome, and obesity, who developed HTG-induced AP shortly after starting oral contraception. Laboratory tests revealed severe hypertriglyceridemia (13102 mg/dL) and elevated lipase (280 U/L). Initial management included the standardized measures of AP. Due to persistently high HTG, infusion of unfractionated heparin and insulin, as well as a session of PEX were administered, resulting in rapid decrease of triglycerides and clinical improvement.

**Discussion/Conclusion:** This case highlights the synergistic effect of genetic, metabolic and hormonal factors in pediatric HTG-AP and underscores the importance of early recognition and aggressive management. Targeted interventions, including PEX, may be justified in high-risk patients to prevent complications and achieve rapid recovery.

**Keywords:** Acute pancreatitis, hypertriglyceridemia, children, plasmapheresis, insulin

**Abbreviations:** TG: Triglycerides; AST: Aspartate Transaminase; ALT: Alanine Transaminase; ALP: Alkaline Phosphatase; ER: Emergency Room; G-GT: Gamma-Glutamyl Transferase, LDH: Lactate Dehydrogenase, TC: Total Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol, CRP: C-reactive Protein; NV: Normal Value

### Introduction

Acute pancreatitis (AP) is an acute inflammatory condition of the pancreas characterized by abdominal pain and elevation of pancreatic enzymes. Its incidence in children is rising, ranging from 3.6 to 13.3 cases per 100000 per year [1]. Hypertriglyceridemia (HTG) is an uncommon but important cause of AP, associated with more severe disease and increased risk of complications [2]. Although HTG-induced AP (HTG-AP) is more common in adults, rare pediatric cases have been reported. In children, HTG may either be congenital due to genetic mutations affecting lipoprotein metabolism, as classified by Fredrickson [3], or acquired and due to poorly controlled diabetes, obesity, alcohol consumption, hypothyroidism or medication use such as estrogens [4-6].

HTG-AP typically occurs when triglyceride levels exceed 1000 mg/dL, with the predicted risk for AP rising to 5% above this threshold and 10–20% when levels surpass 2000 mg/dL [7-9]. There are to date no specific pediatric evidence-based guidelines for HTG-AP. In adults, management of HTG-AP is, similar to other forms of AP, primarily supportive and includes aggressive intravenous (IV) hydration, and adequate pain control. However, in HTG-AP, targeted therapies may rapidly reduce serum triglyceride levels, such as insulin, heparin infusions, or plasma exchange (PEX). After the acute phase, long-term management focus on lifestyle modification, dietary changes, and lipid-lowering therapy to prevent recurrence.

Here we report a case of an adolescent girl with maturity-onset diabetes of the young type 3 (MODY-3) and metabolic syndrome who developed HTG-AP shortly after initiating combined oral contraceptive therapy. Despite the well-recognized association between HTG, estrogens and pancreatitis in adults, reports in pediatric patients are scarce, particularly when multiple risk factors coexist. Moreover, the specific management of severe HTG-AP is poorly defined in children.

### Case Presentation

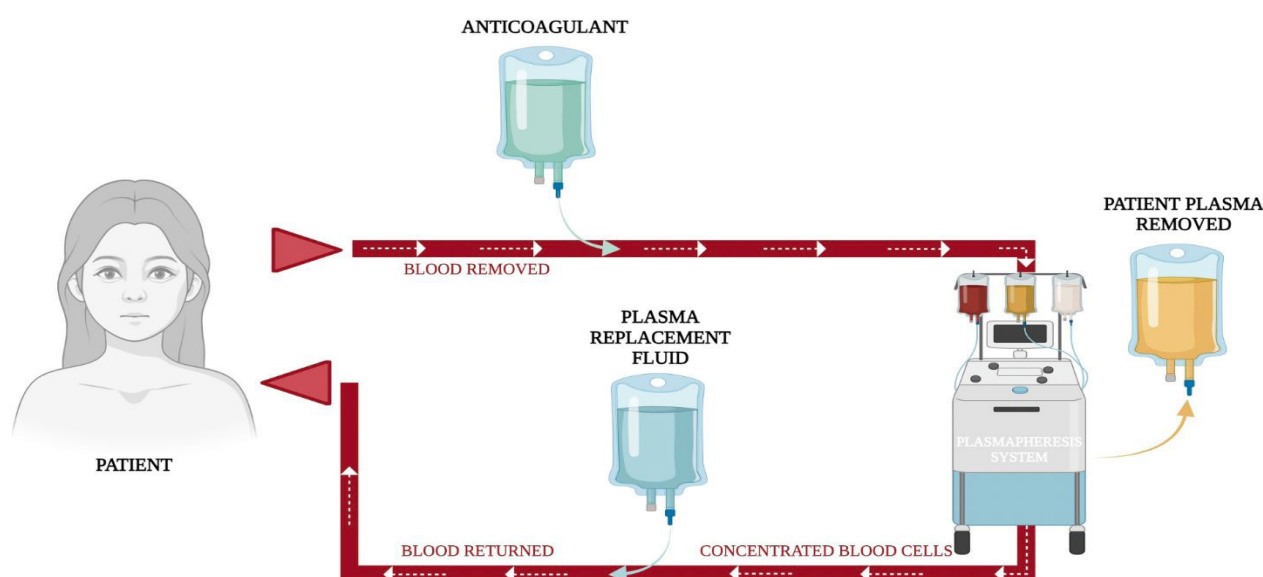
A 15-year-old girl with a past medical history of poorly controlled maturity onset MODY-3, HTG, obesity (BMI: 29.9) and metabolic syndrome presented in the emergency room with a 3-day history of epigastric pain, nausea, and vomiting. Her current medication included metformin, repaglinide, enalapril and oral combined contraception (cyproterone acetate 2 mg - ethinylestradiol 0.035 mg), started 3 months prior to admission. At clinical examination, she was conscious and well hydrated, with painful abdominal palpation in all quadrants, especially epigastrium, without rebound. Vital signs revealed known hypertension (145/70 mmHg), tachycardia (120 bpm), and mild hyperthermia (37.2°C). There were no signs of organ dysfunction. The blood sample was markedly lipemic. Laboratory results revealed severe HTG (13102 mg/dL, NV<150) and elevation of lipase (280 U/L, NV<60), pseudohyponatremia (111 mmol/L), hyperglycemia (173 mg/dL), and an inflammatory syndrome with a CRP of 100 mg/L (NV<5) and a leukocyte count of 17600/μL (neutrophil count 14280/μL). Otherwise, liver enzymes, kidney function and thyroid

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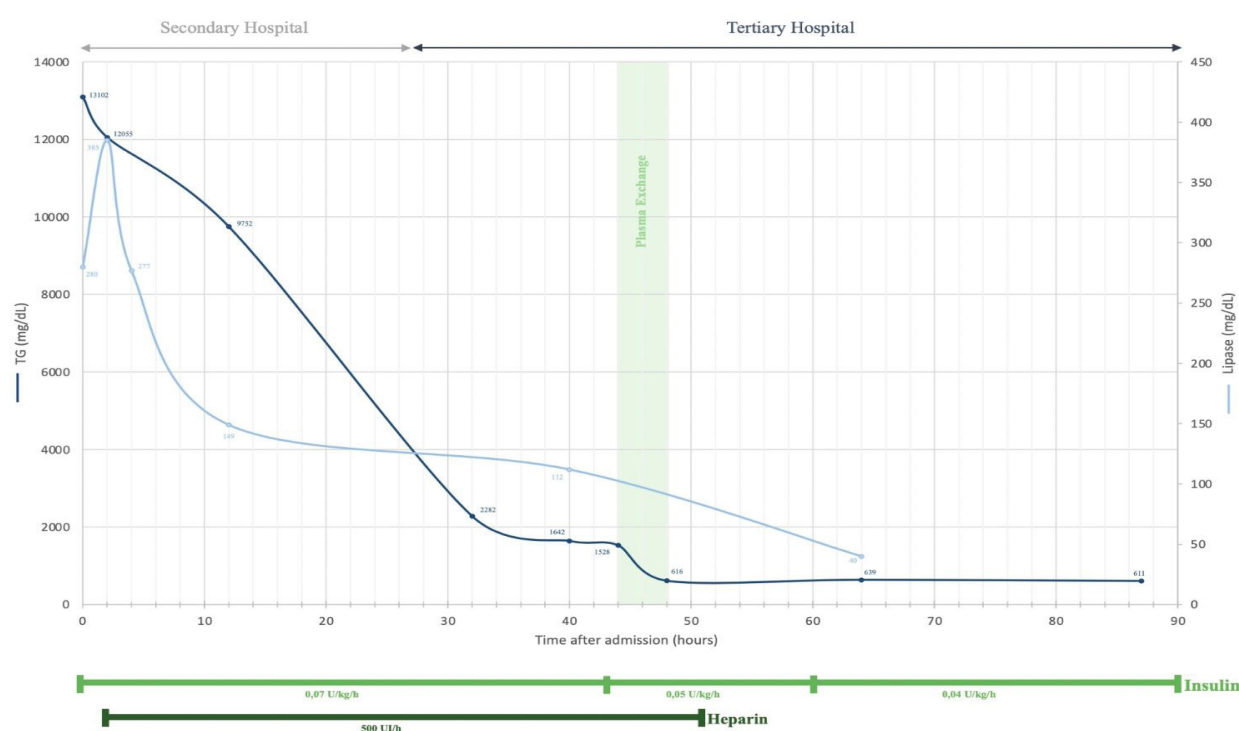
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function were normal. Abdominal ultrasound demonstrated pancreatic swelling with infiltration of peripheral fat and left retroperitoneal fluid collection, consistent with acute pancreatitis. She was initially admitted in the intensive care unit of a secondary

hospital, where she was hyperhydrated (1.5x maintenance), kept NPO, and IV insulin therapy (max 0.07 U/kg/h) was initiated (**Figure 1**).



**Figure 1:** Evolution of serum triglycerides (TG, dark blue line, left y-axis) and lipase (light blue line, right y-axis) levels throughout hospitalization. The x-axis represents the chronological sequence of events, including location of care (Secondary and Tertiary care Hospital) and Therapeutic interventions (plasma exchange, insulin and heparin infusion).



**Figure 2:** Plasma exchange illustration.

TG decreased from 13102 mg/dL to 9752 mg/dL and lipase from 280 U/L to 150 U/L in 12 hours. Analgesia with small doses of piritramide resulted in progressive improvement of the abdominal pain.

Due to persistently severe HTG, the patient was transferred and admitted in our Pediatric Intensive Care Unit. Hyperhydration and insulin therapy were maintained and unfractionated heparin (500 U/h) was commenced for the next 24 hours. Because of the persistently high TG, the patient received one cycle of PEX (1.2x volume of plasma exchanged and restitution with albumin) which resulted in a further drop in serum TG from 1528 to 616 mg/dL. She remained hemodynamically stable with both clinical and biochemical improvement

(Supp Data 1) and could be discharged to the general ward for continued care after 3 days. Genetic testing for hypercholesterolemia and hypertriglyceridemia were negative (Supp Data 2) (**Figure 2**).

## Discussion

This case illustrates the growing societal problem of pancreatitis secondary to dyslipidemic disorders and the successful management of HTG-PA using a combination of insulin, heparin and plasmapheresis to improve HTG. HTG is an increasingly recognized though uncommon cause of AP in children. The exact mechanism of HTG-AP is not clearly understood. Pathophysiology is thought to involve lipase-mediated hydrolysis of TG into free fatty acids (FFA), causing lipotoxic

injury and ischemia [4-6]. Increased blood viscosity in pancreatic capillaries may contribute, though this does not fully explain the pancreas-specific injury.

Metabolic syndrome, characterized by central obesity, insulin resistance, hypertension, and dyslipidemia with elevated TG and low HDL, acts both as facilitator and amplifier in HTG-AP. Obesity promotes increased FFA flux to the liver from high-fat diets, greater very-low-density lipoprotein (VLDL) output by the liver, reduced lipoprotein lipase (LPL) function, and a state of chronic inflammation, all contributing to higher TG levels and more severe pancreatic injury [10]. Estrogen-containing medications are well-documented enhancers of HTG. Estrogens increase hepatic VLDL, reduce hepatic triglyceride lipase activity, and may impair LPL activity [11]. While generally safe in healthy adolescents, these medications can precipitate severe HTG and subsequent AP in patients with underlying metabolic or genetic predispositions. In our patient, these factors converged. She had MODY-3 and metabolic syndrome, both of which predispose to lipid metabolism dysregulation and elevated TG levels. The initiation of estrogen-containing oral contraception likely acted as the precipitating factor, driving TGs to extreme levels and triggering AP. The interplay of monogenic diabetes, metabolic syndrome, and hormonal therapy thus provides a compelling explanation for the clinical presentation [12,13].

Management of HTG-AP must be prompt and aggressive, especially when TG levels are very high or when there is evidence of severe disease. The pillars of initial therapy include aggressive IV hydration and analgesia. Strategies to lower the TG burden include IV insulin therapy, heparin and in severe situation PEX. Insulin not only activates LPL, which accelerates the degradation of chylomicrons therefore leading to a reduction in TG levels, but also promotes rest in pancreatic tissue and reduces cell apoptosis by upregulating the expression of human leukocyte antigen (HLA) on monocytes. IV heparin, though more controversial, can be also beneficial as heparin releases LPL from endothelial cell, thus lowering TG levels [14].

In severe cases, or when TGs remain high despite medical therapy, PEX is an effective adjunct, enabling rapid removal of TGs and chylomicrons from circulation, effectively removing the inciting factors and halting further inflammation and damage to the pancreas by also removing proinflammatory markers and cytokines. Plasmapheresis is

increasingly being considered for the management of HTG-AP, as it can rapidly reduce serum TG levels (50-80% in one session) [14,15]. Its efficacy in pediatric cases has been demonstrated, with Lutfi et al. reporting successful treatment in a child with HTG-AP, and Ippisch et al. showing favorable outcomes in a pediatric series [16,17]. It requires a central venous catheter (CVC), and should be performed as early as possible (within 24-48h), until TG have been lowered to (ideally) <500 mg/dL [18]. Potential complications include infections and allergic reactions to donor plasma, as well as those related to the use of CVC.

Long-term management should focus on prevention of metabolic decompensation. Dietary modification with restriction of fat and simple carbohydrates, regular physical activity and weight control are essential lifestyle strategies. Tight glycemic control is particularly important in patients with diabetes. Pharmacological therapy, such as fibrates or omega-3 fatty acids, may be considered when TGs remain elevated despite lifestyle measures, although evidence in pediatrics remains limited.

## Conclusion

This case illustrates the complex interplay between genetic, metabolic, and pharmacologic factors in the development of HTG-AP. Early management of AP and specific interventions including IV insulin and heparin therapy followed by plasmapheresis enabled to avoid potential life-threatening complications and achieve rapid clinical improvement. The favorable clinical response supports that in high-risk pediatric patients with multiple predisposing factors, early use of PEX may be justified.

**Conflicts of interests:** authors state no conflict of interest.

**Author contributions:** MN and IS realized the conception and design of the article; MN, TC, CL, BM, GJ, XS, IS collected clinical data; MN and IS drafted manuscript; MN, TC, CL, XS, IS revised manuscript; all authors approved final version of the manuscript.

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**Supplementary Data 1:** Laboratory investigations.

**SUPPLEMENTARY DATA 2:** PANEL OF GENES TESTED BY NGS TO RULE OUT CONGENITAL FORMS OF DYSLIPIDEMIA.

|                                 | ER<br>ADMISSION | ICU<br>H24 post admission | DISCHARGE ICU<br>H72 post admission |
|---------------------------------|-----------------|---------------------------|-------------------------------------|
| Lipase (u/L)<br>NV<60           | 280             | 112                       | 40                                  |
| Triglycerides (mg/dL)<br>NV<150 | 13102           | 2282                      | 611                                 |
| Leukocyte Count (/μL)           | 17600           | 17350                     | 14350                               |
| Neutrophil Count (/μL)          | 14280           | 12880                     | 9620                                |
| Hemoglobin (g/dL)               | 11,7            | 10,7                      | 9,7                                 |
| Platelet (/μL)                  | 382000          | 400000                    | 273000                              |
| Sodium (mmol/L)                 | 111             | 127                       | 135                                 |
| Potassium (mmol/L)              | 4,56            | 4,08                      | 3,5                                 |
| Glucose (mg/dL)                 | 219             | 166                       | 171                                 |
| AST (U/L)                       | <44             |                           | 13                                  |
| ALT (U/L)                       | 34              | 9                         | 6                                   |
| ALP (U/L)                       | 62              | 46                        |                                     |
| G-GT (U/L)                      | 13              | 7                         | 10                                  |
| LDH (U/L)                       | 411             | 415                       |                                     |
| TG (mg/dL)                      |                 | 704                       | 324                                 |
| Non-HDL-C (mg/dL)               |                 |                           | 301                                 |
| HDL-C (mg/dL)                   |                 | 25                        | 23                                  |
| CRP (mg/L)<br>NV <1             | 100             | 125                       | 47,3                                |

ABCG5, ABCG8, APOB, APOE, LDLR, LDLRAP1, LIPA, PCSK9, STAP1, APOC2, APOA5, LPL, LMF1, GPIHBP1