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Sequential Continuous Renal Replacement Therapy and Therapeutic Plasma Exchange in Pediatric Necrotizing Hypertriglyceridemia-Induced Pancreatitis with Suspected Familial Chylomicronemia Syndrome: A Case Report

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Abstract

Background: Hypertriglyceridemia-induced acute pancreatitis (HTG-AP) is a severe and underrecognized etiology of pancreatitis, accounting for 1% - 4% of all cases in adults, with extreme triglyceridemia raising the risk of fulminant multi-organ failure. When underlying lipoprotein lipase (LPL) deficiency is suspected—as in familial chylomicronemia syndrome (FCS)—conventional pharmacologic strategies are inherently limited, and therapeutic plasma exchange (TPE) represents the most effective currently available approach for the rapid removal of chylomicrons and triglyceride-rich lipoproteins from the circulation. **Case Summary:** We report a 14-year-old girl presenting with triglycerides > 14,000 mg/dL, severe necrotizing pancreatitis, acute kidney injury (AKI), mild acute respiratory distress syndrome (ARDS), and metabolic encephalopathy. No prior medical history was identified. Despite aggressive pharmacologic therapy with intravenous insulin, heparin, and fibrates, triglyceride levels remained critically elevated. Continuous renal replacement therapy (CRRT) was initiated for AKI, metabolic acidosis, and hemodynamic instability, achieving significant physiologic stabilization. However, because CRRT does not effectively clear chylomicrons, lipid levels remained dangerously high. Two urgent sessions of TPE reduced triglycerides from >14,000 mg/dL to approximately 300 mg/dL, with subsequent normalization of pancreatic enzymes and full recovery of renal, respiratory, and neurological function. The patient was discharged in good clinical condition. **Conclusion:** This case illustrates

that CRRT and TPE fulfill distinct, non-overlapping roles in severe HTG-AP. CRRT provides essential metabolic bridge support, and TPE achieves definitive lipid clearance. When LPL deficiency is suspected, early escalation to TPE is potentially lifesaving. A high index of clinical suspicion and timely decision-making are the key determinants of outcome in this rare but catastrophic condition.

Keywords

Hypertriglyceridemia-Induced Pancreatitis, Familial Chylomicronemia Syndrome, Therapeutic Plasma Exchange, Continuous Renal Replacement Therapy, Pediatric Critical Care, Multi-Organ Dysfunction, Chylomicrons

1. Introduction

Acute pancreatitis is a common and potentially life-threatening gastrointestinal emergency. While gallstones and alcohol are the predominant etiologies in adult populations, hypertriglyceridemia is a recognized and clinically important cause, accounting for approximately 1% - 4% of all cases [1]. In the setting of extreme hypertriglyceridemia—commonly defined as serum triglycerides exceeding 1000 mg/dL—the risk of severe or necrotizing pancreatitis escalates substantially, with reported case fatality rates of up to 20% - 30% in fulminant presentations [2].

The pathophysiological mechanism linking extreme triglyceridemia to pancreatic injury is believed to involve the hydrolysis of chylomicrons and very-low-density lipoproteins (VLDL) by pancreatic lipase, generating toxic free fatty acids and lysophospholipids that directly injure acinar cells and the pancreatic microcirculation. The resulting inflammatory cascade, paralleling other forms of severe pancreatitis, may produce systemic inflammatory response syndrome (SIRS) and multi-organ dysfunction syndrome (MODS) [1] [2].

Severity classification of acute pancreatitis follows the Revised Atlanta Classification, which recognizes moderately severe and severe categories based on the presence and duration of organ failure [3]. In the case described herein, the patient met the criteria for severe acute pancreatitis with persistent multi-organ failure at presentation.

Familial chylomicronemia syndrome (FCS) is a rare autosomal recessive monogenic disorder resulting from biallelic loss-of-function mutations in the gene encoding lipoprotein lipase (LPL) or its obligate cofactors, including *APOC*2, *APOA*5, *LMF*1, and *GPIHBP*1. It is characterized by a near-complete absence of LPL activity, severe chylomicronemia from infancy or childhood, and episodic pancreatitis triggered by dietary fat intake [4]. The global prevalence of FCS is estimated at approximately 1 in 1,000,000, although it is likely underdiagnosed [4] [5].

A critical implication of FCS—and the central clinical challenge in this case—

is that pharmacologic strategies dependent upon LPL activity, including intravenous insulin and heparin infusions, are ineffective in the absence of a functional enzyme [6] [7]. In such patients, TPE represents the most effective currently available mechanism for rapid reduction of circulating chylomicrons, although it should be acknowledged that the evidence base remains observational and predominantly case-based, and no randomized controlled trials exist to guide its use in this rare condition [8] [9].

We report a severe pediatric case in which sequential CRRT and TPE were used in a complementary fashion to achieve multi-organ stabilization and definitive lipid clearance. The case underscores the importance of recognizing the distinct physiological roles of these two modalities and escalating appropriately and without delay.

2. Case Presentation

A 14-year-old girl with no documented prior medical history presented to the emergency department in critical condition. She reported a several-day history of worsening severe epigastric and diffuse abdominal pain, nausea, persistent vomiting, and progressive confusion. There was no history of alcohol use, recent dietary excess, or use of lipid-elevating medications (corticosteroids, antipsychotics, or oral contraceptives). There was no known family history of dyslipidemia, recurrent pancreatitis, or inherited metabolic disease in first-degree relatives.

On examination, she was febrile, tachycardic, and hypotensive. She was tachypneic with accessory muscle use and had reduced oxygen saturation on room air. Her abdomen was grossly distended with guarding and absent bowel sounds. Neurologically, she was confused and not fully oriented to time or place.

Laboratory investigations revealed extreme lipemia, immediately apparent from the grossly turbid, cream-colored appearance of drawn blood samples. Serum triglycerides were reported at >14,000 mg/dL. Serum lipase was 12,000 U/L, and amylase was 6000 U/L, confirming severe biochemical pancreatitis. Serum creatinine was 670 μmol/L, indicating severe AKI. Arterial blood gas demonstrated a pH of 7.10, and serum lactate was 10 mmol/L, consistent with profound circulatory insufficiency and severe metabolic acidosis. Serial arterial blood gas monitoring demonstrated progressive correction of acid-base status following initiation of CRRT, with acid-base parameters normalizing after therapeutic plasma exchange in parallel with recovery of organ function. Admission and serial laboratory findings are summarized in **Table 1** [10].

Table 1. Admission and serial laboratory findings.

Parameter	Admission Value	Post-CRRT	Post-TPE
Triglycerides (mg/dL)	>14,000	Persistently critically elevated	~300
Serum Lipase (U/L)	12,000	Decreased but still elevated	Normalized

Continued

Serum Amylase (U/L)	6000	Decreased but still elevated	Normalized
Creatinine (μmol/L)	670	Improved	Recovered/ Near-Normalized
Arterial pH	7.10	Corrected	Normalized
Serum Lactate (mmol/L)	10	Decreasing	Normalized
SpO_2/PaO_2:FiO_2 Ratio	Reduced—consistent with mild ARDS	Improving	Improved
CRP (mg/L)	Elevated	Down-trending	Improved
WBC ($\times 10^9$/L)	Elevated	Down-trending	Improved/ Normalized
Serum Bicarbonate (mmol/L)	Low—severe metabolic acidosis	Corrected	Stable/ Normalized
Total Cholesterol (mmol/L)	Elevated	Improving	Improved

Abbreviations: CRRT = continuous renal replacement therapy; TPE = therapeutic plasma exchange; ARDS = acute respiratory distress syndrome.

Contrast-enhanced CT imaging of the abdomen demonstrated a heterogeneous pancreas with areas of non-enhancement consistent with pancreatic necrosis, together with extensive peripancreatic fat stranding and retroperitoneal inflammatory change extending into the mesenteric fat. No large organized collection or free intraperitoneal air was evident on the provided image. Overall imaging severity was consistent with severe acute necrotizing pancreatitis (CTSI 9-10) (**Figure 1**; see **Table 2** for structured radiological report) [3].

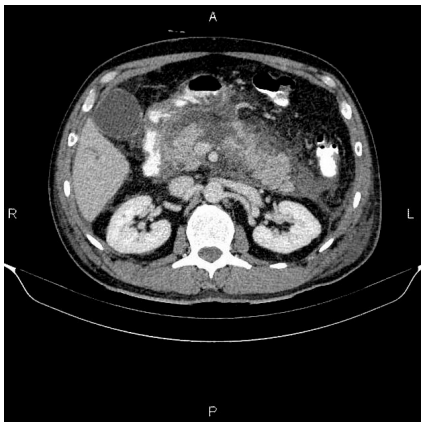

Figure 1. Contrast-enhanced CT abdomen—severe necrotizing pancreatitis.

Axial contrast-enhanced CT of the abdomen demonstrating severe acute necrotizing pancreatitis, with heterogeneous pancreatic enhancement, focal non-en-

hancing areas consistent with necrosis, and extensive peripancreatic and retroperitoneal inflammatory changes. Overall severity was consistent with CTSI 9-10.

Table 2. CT abdomen—structured radiological report.

Section	Findings
Examination	Contrast-enhanced CT abdomen.
Clinical Indication	Severe hypertriglyceridemia-induced acute pancreatitis with multi-organ dysfunction.
Pancreas	Heterogeneous pancreatic enhancement with focal areas of reduced or absent enhancement, consistent with pancreatic necrosis. Extensive peripancreatic fat stranding and marked surrounding retroperitoneal inflammatory changes, with extension into the adjacent mesenteric fat.
Fluid Collections	No large, well-organized fluid collection is evident on the provided image.
Free Air	No visible free intraperitoneal air is present on the supplied image.
Kidneys	The visualized kidneys demonstrate preserved cortical enhancement.
CT Severity Index (CTSI)	Overall radiologic severity is consistent with a CT Severity Index (CTSI) of 9-10, in keeping with severe acute necrotizing pancreatitis.
Impression	CT features are consistent with severe acute necrotizing pancreatitis with extensive peripancreatic and retroperitoneal inflammatory changes. CTSI 9-10. Clinical correlation with evolving organ dysfunction is recommended.

CTSI = CT Severity Index. The report is based on the available axial contrast-enhanced image; a formal radiologist's report will be appended to the submission as supplementary documentation.

A working diagnosis of severe hypertriglyceridemia-induced necrotizing pancreatitis with suspected FCS was established. The clinical phenotype—extreme chylomicronemia in a previously well adolescent with no secondary causes and poor response to LPL-dependent therapies (detailed below)—was judged consistent with an underlying genetic disorder of LPL pathway function [4] [11]. The principal differential diagnosis was severe multifactorial or polygenic hypertriglyceridemia, which can also produce markedly elevated triglycerides under precipitating conditions. However, the absence of any identifiable secondary cause, the extraordinary magnitude of hypertriglyceridemia, and the failure to respond to LPL-dependent pharmacotherapy were collectively felt to favor a monogenic etiology. Apolipoprotein B (ApoB) levels and formal lipid subfractionation were not available during the index admission; their measurement at follow-up would assist in further characterizing the lipid phenotype. Genetic evaluation for mutations in *LPL*, *APOC*2, *APOA*5, *LMF*1, and *GPIHBP*1 was not available during this admission and was recommended as an outpatient priority. The diagnosis is accordingly classified as suspected FCS rather than genetically confirmed disease.

3. ICU Management

The patient was admitted directly to the pediatric intensive care unit (PICU), requiring immediate multi-organ support. A summary of hemodynamic and supportive care interventions is provided in Table 3.

Table 3. ICU hemodynamic and supportive care summary.

Domain	Detail
Vasopressor	Noradrenaline (norepinephrine)
Approximate Dose	0.05 - 0.1 μg/kg/min
Duration	Early resuscitative phase; tapered after metabolic and hemodynamic stabilization
Respiratory support	Supplemental non-invasive oxygen therapy for mild hypoxemic respiratory dysfunction
IV Fluid Type	Balanced isotonic crystalloid
Fluid Strategy	Titrated to perfusion, urine output, and evolving abdominal physiology
Antibiotic	Meropenem 20 mg/kg IV every 8 hours
Nutrition	Strict lipid restriction; parenteral lipid administration is avoided during the acute phase

IV = Intravenous.

3.1. Hemodynamic and Respiratory Support

The patient required full hemodynamic, metabolic, and respiratory support from the time of admission. Early hemodynamic instability was managed with noradrenaline (norepinephrine) infusion at an approximate dose of 0.05 - 0.1 μg/kg/min, which was subsequently tapered as perfusion and metabolic status improved following initiation of extracorporeal support. Respiratory support consisted of supplemental non-invasive oxygen therapy to manage hypoxemic respiratory dysfunction in the context of mild ARDS; the patient did not require prolonged invasive ventilation [3] [10].

Fluid resuscitation was performed with balanced isotonic crystalloid, titrated according to hemodynamic parameters, urine output, and evolving abdominal physiology. Given the severity of necrotizing pancreatitis and the risk of secondary infectious complications, empiric antimicrobial therapy with meropenem 20 mg/kg intravenously every 8 hours was administered. Nutritional management emphasized strict lipid restriction; parenteral lipid administration was avoided during the acute phase, and nutritional support was advanced cautiously as the patient stabilized.

3.2. Pharmacologic Lipid-Lowering Therapy

Simultaneous and aggressive pharmacologic lipid reduction was initiated. A con-

tinuous intravenous insulin infusion was commenced, targeting euglycemia, with the additional aim of suppressing hepatic VLDL synthesis and stimulating LPL activity [6]. Intravenous unfractionated heparin was administered concurrently to mobilize endothelial LPL into the systemic circulation, consistent with its established use in HTG-AP, although it is acknowledged that this strategy is most effective when residual LPL activity is present and may have limited efficacy in FCS [6]. Oral fenofibrate was commenced via nasogastric tube to enhance LPL expression and reduce VLDL production [12]. Oral fat intake was withheld entirely, and parenteral lipid administration was avoided during the acute phase to eliminate exogenous chylomicron substrate.

Regarding empiric antimicrobial therapy, meropenem was selected, given the severity of necrotizing pancreatitis and the associated risk of secondary infection. It is acknowledged that prophylactic antibiotic use in necrotizing pancreatitis without documented infection remains debated in current guidelines, and the decision to treat empirically in this case was driven by clinical severity and multiorgan compromise rather than microbiological confirmation [3].

Despite this multimodal pharmacologic strategy, repeated serum triglyceride measurements over the ensuing 24 - 48 hours demonstrated no meaningful reduction. This lack of response was clinically interpreted as consistent with absent or severely deficient functional LPL activity, reinforcing the suspicion of FCS [4] [7].

The failure to achieve triglyceride reduction despite maximal pharmacologic intervention was not a failure of supportive care—it was a failure of lipid clearance. This distinction is critical to the subsequent therapeutic decision.

4. Continuous Renal Replacement Therapy (CRRT)

Because of worsening acute kidney injury, severe metabolic acidosis, hyperlactatemia, and hemodynamic instability, continuous renal replacement therapy was initiated using continuous venovenous hemodiafiltration (CVVHDF) on the Baxter PrisMax platform (**Figure 2**). Treatment was delivered through a right internal jugular 11.5 Fr double-lumen dialysis catheter, using heparin anticoagulation, a blood flow rate of 120 - 150 mL/min, and a prescribed effluent dose of 30 mL/kg/h. Dialysate flow was maintained at approximately 1000 - 1500 mL/h, with pre-filter replacement fluid and net ultrafiltration adjusted according to hemodynamic tolerance and fluid balance targets. CRRT was continued for approximately 48 hours, resulting in progressive correction of acidosis and improved metabolic stability, although triglyceride levels remained critically elevated. Full procedural parameters are detailed in **Table 4** [10] [13].

The Baxter PrisMax system is shown during active continuous venovenous hemodiafiltration (CVVHDF). The extracorporeal circuit demonstrates visibly turbid, lipemic blood consistent with severe chylomicronemia. Real-time hemodynamic and treatment parameters are displayed on the integrated touchscreen monitor.

Figure 2. The Baxter PrisMax CRRT system is in active use.

Table 4. CRRT and TPE procedural parameters.

Parameter	Detail
CRRT modality	CVVHDF (continuous venovenous hemodiafiltration)
CRRT machine	Baxter PrisMax
Filter membrane	PrisMax-compatible high-flux hemofilter
Blood flow rate	120 - 150 mL/min
Prescribed CRRT dose	30 mL/kg/h
Dialysate flow	1000 - 1500 mL/h
Replacement fluid	Pre-filter replacement
Net ultrafiltration strategy	Adjusted according to hemodynamic tolerance and fluid balance goals
Vascular access—CRRT	Right internal jugular double-lumen dialysis catheter, 11.5 Fr
Anticoagulation—CRRT	Heparin
Duration of CRRT	Approximately 48 hours
TPE sessions (number)	2
TPE plasma volume exchanged	~1.0 plasma volumes per session
TPE replacement fluid	5% albumin
TPE access	The same central extracorporeal vascular access was used for CRRT
TPE adverse events	No major procedure-related adverse events were documented

CVVHDF = continuous venovenous hemodiafiltration; CVVHF = continuous venovenous hemofiltration; FFP = fresh frozen plasma; Fr = French.

The primary clinical indications for CRRT in this patient were: 1) severe AKI with creatinine 670 μmol/L and oliguria; 2) refractory metabolic acidosis (pH 7.10, lactate 10 mmol/L); 3) hemodynamic instability with impaired tolerance of volume loading; and 4) the need for continuous fluid balance management in the context of abdominal compartment physiology. CRRT was also anticipated to facilitate drug clearance monitoring and reduce the uremic metabolite burden [10] [13] [14].

Following initiation of CVVHDF, significant physiological improvement was observed. Serial arterial blood gas monitoring demonstrated progressive correction of metabolic acidosis, with lactate decreasing and arterial pH improving substantially over the first 24 hours of extracorporeal support. Fluid balance was corrected, reducing third-space accumulation and abdominal distension. Hemodynamic parameters improved, allowing cautious noradrenaline weaning. Serum electrolytes and bicarbonate stabilized.

However, despite this meaningful metabolic rescue, serial triglyceride measurements demonstrated persistently critical levels. This finding was not unexpected: conventional CRRT membranes, designed for diffusion and convection of small-to-middle-molecular-weight solutes (typically < 50 kDa), are unable to remove chylomicrons, which range from 80 to 1200 nm in diameter and carry molecular weights in the billions of Daltons [13] [14]. The turbid, deeply discolored effluent observed in the CRRT waste collection bag (lipemic effluent; see **Figure 3**) provides a striking visual confirmation of the extreme circulating lipid burden.

Figure 3. Lipemic effluent collection bag—visual evidence of extreme chylomicronemia.

The CRRT effluent waste bag demonstrated profoundly lipemic fluid with a characteristic deep yellow-orange, opaque appearance. This finding is pathognomonic of circulating triglyceride concentrations in the thousands of mg/dL. Despite this striking lipid contamination of the effluent, quantitative chylomicron clearance via CRRT was negligible—confirming that plasma exchange rather than

filtration was required for definitive lipid removal.

CRRT supported and stabilized multi-organ physiology, creating a safer hemodynamic and biochemical platform from which a more invasive lipid-removal intervention could be delivered. It did not, and cannot, remove the causative pathological substrate.

5. Therapeutic Plasma Exchange (TPE)

5.1. Rationale and Indications

Therapeutic plasma exchange operates through the non-selective removal and replacement of a large volume of the patient's plasma. Unlike membrane-based CRRT, TPE separates plasma from cellular blood components using either centrifugation or membrane filtration techniques and replaces it with fresh frozen plasma (FFP) and/or albumin. This process is capable of removing large molecular weight structures, including chylomicrons, VLDL, inflammatory mediators carried by lipoproteins, and other high molecular weight toxins [8] [9] [15].

The American Society for Apheresis (ASFA) 2010 guidelines classify TPE as a Category I-II intervention for severe hypertriglyceridemia-induced pancreatitis, representing conditions in which apheresis is accepted as first-line therapy or as second-line therapy when other treatments have failed [16]. Given the persistent critical hypertriglyceridemia and ongoing multi-organ injury despite maximal pharmacological therapy and CRRT, the clinical team escalated management to urgent TPE.

5.2. Procedure and Clinical Response

Given persistent extreme hypertriglyceridemia despite intensive medical therapy and CRRT-supported metabolic stabilization, therapeutic plasma exchange was initiated. Two TPE sessions were performed on consecutive days, each exchanging approximately one plasma volume, with 5% albumin used as the replacement solution. The same central extracorporeal vascular access established for CRRT was utilized for both sessions. No major TPE-related adverse events were documented, including episodes of hypotension, hypocalcemia, citrate-related symptoms, allergic reactions, or circuit interruption [8] [15] [17].

The biochemical response to TPE was rapid and dramatic. Triglyceride levels remained critically elevated despite intensive medical therapy and CRRT, but fell sharply after initiation of therapeutic plasma exchange, decreasing to approximately 3500 mg/dL after the first session and approximately 300 mg/dL after the second session, with subsequent maintenance at <200 mg/dL during recovery—an overall reduction exceeding 98% from admission levels (**Figure 4**; **Table 5**) [8] [9]. Serum lipase and amylase normalized. Clinically, the patient demonstrated progressive improvement across all organ systems:

- Renal function recovered with creatinine trending toward baseline; urine output was restored; CRRT was subsequently discontinued.
- Respiratory status improved with progressive weaning of supplemental oxygen

and resolution of ARDS-pattern changes.

- Neurological function recovered fully—encephalopathy resolved, patient is alert and oriented.
- Hemodynamic stability was maintained without vasopressor requirement.
- Abdominal distension and compartment physiology are resolved.

Follow-up imaging confirmed no further progression of pancreatic necrosis. No secondary pancreatic infection was identified during the admission. At discharge, outpatient follow-up was advised, including gastroenterology and lipid-focused review, strict dietary fat restriction, and ongoing monitoring for recurrence of hypertriglyceridemia or pancreatitis. Genetic evaluation for FCS was recommended as an outpatient priority if accessible.

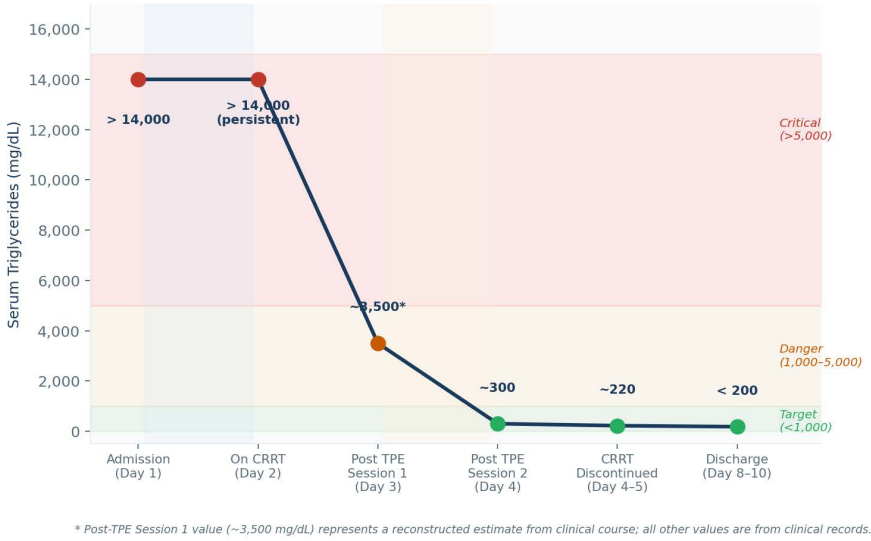

Figure 4. Serial serum triglyceride trend during clinical course.

Serial triglyceride trend showing extreme hypertriglyceridemia (>14,000 mg/dL) at admission, persistent critical elevation during CRRT-supported medical therapy, a marked decline after the first TPE session (~3500 mg/dL), further reduction to approximately 300 mg/dL after the second session, and sustained control to <200 mg/dL by discharge. The post-TPE Session 1 intermediate value is a reconstructed estimate from the clinical course.

Table 5. Clinical timeline—day-by-day summary.

Day	Key Events	Clinical Status	TG Level
Day 1	ICU admission; insulin, heparin, fibrate, antibiotics, vasopressor support, and full critical care initiated	Critical—severe necrotizing pancreatitis, AKI, acidosis, mild ARDS, metabolic encephalopathy, hemodynamic instability	>14,000 mg/dL
Day 1 - 2	CRRT initiated	Acid-base improving; hemodynamics stabilizing; renal/metabolic support achieved; triglycerides remain markedly elevated	Persistently severely elevated

Continued

Day 3	Lipid-clearance failure recognized; decision to escalate to TPE	Metabolic physiology is more stable; pancreatic and lipid burden remain high; CRRT continues	Still critically elevated
Day 3	TPE Session 1	Significant reduction in visible lipemia; early biochemical and clinical improvement	Falling rapidly
Day 4	TPE Session 2	Further improvement, pancreatic enzymes trending toward normal; multi-organ recovery becoming evident	~300 mg/dL
Day 4 - 5	CRRT was discontinued after stabilization	Renal and metabolic recovery is progressing; vasopressor requirement has resolved	Markedly improved
Day 6 - 7	Step down from PICU/ICU-level care	Neurological and respiratory status improved; no further progression of pancreatic necrosis	<200 mg/dL
Day 8 - 10	Discharge home	Good clinical condition; full recovery from multi-organ dysfunction; outpatient lipidology follow-up arranged	<200 mg/dL

TG = triglycerides; PICU = pediatric intensive care unit.

6. Discussion

6.1. Extreme Hypertriglyceridemia as a Cause of Fulminant Pancreatitis

This case exemplifies the catastrophic potential of extreme hypertriglyceridemia. Triglyceride levels exceeding 10,000 mg/dL, as observed here, are encountered almost exclusively in the context of genetic LPL pathway disorders, particularly FCS [4] [9]. At such concentrations, the pancreatic microcirculation becomes saturated with chylomicrons, which are hydrolyzed by pancreatic lipase to generate high local concentrations of free fatty acids. These lipotoxic intermediates cause direct acinar cell necrosis, microvascular ischemia, and a self-amplifying inflammatory cascade [1] [2].

The severity of organ dysfunction seen in our patient—AKI, ARDS, encephalopathy, and abdominal compartment syndrome—reflects the systemic toxicity of extreme lipemia. Prior published series confirm that triglyceride levels above 5000 mg/dL are associated with a substantially higher rate of severe and necrotizing disease, organ failure, and ICU admission [1] [2] [17].

6.2. Suspected Familial Chylomicronemia Syndrome

We wish to explicitly acknowledge the diagnostic uncertainty inherent in this case. The label of 'suspected FCS' is used deliberately, as confirmatory genetic testing was not available during the index admission. Nevertheless, several clinical features strongly support this diagnosis: extreme chylomicronemia (>14,000 mg/dL) in a 14-year-old with no secondary causes; absence of diabetes, hypothyroidism, alcohol use, or relevant medications; and, crucially, failure to respond to LPL-de-

pendent pharmacologic therapies (insulin, heparin) [4] [5].

FCS must be distinguished from the more common polygenic or multifactorial hypertriglyceridemia, in which LPL activity is reduced but not absent. In multifactorial HTG, insulin and heparin can produce meaningful triglyceride reduction [11]. In true FCS, such treatments are futile. This distinction is not merely academic—it directly determines whether pharmacologic management can be expected to succeed, or whether plasma exchange must be considered the primary therapeutic strategy rather than the last resort [4] [16].

Clinicians should maintain a high index of suspicion for FCS when triglycerides exceed 5000 - 10,000 mg/dL in a young patient without secondary causes, and when pharmacologic treatment fails to achieve triglyceride reduction within 12 - 24 hours [5] [7]. Formal lipidology consultation and genetic testing should be arranged in all such cases, not only for acute management but also for long-term risk stratification and family screening [4].

6.3. Why CRRT Was Necessary and Why It Was Not Sufficient

CRRT served an essential and life-preserving role in this patient. The severe AKI, refractory metabolic acidosis, volume overload, and hemodynamic instability collectively created a physiologic milieu in which undertaking any further intervention, including TPE, would have been hazardous [10] [13]. CRRT normalized the acid-base environment, restored hemodynamic stability, and corrected fluid balance, thereby creating the necessary physiologic platform for safe TPE delivery.

This concept of CRRT as a 'bridge modality' is an important framing for clinicians. In the context of HTG-AP, the goal of CRRT is not lipid clearance—it is organ support and metabolic rescue [13] [14]. The persistence of critical hypertriglyceridemia on CRRT should not be interpreted as treatment failure; it should be interpreted as confirmation that a mechanistically distinct intervention is required.

Several prior reports have described the use of CRRT in severe pancreatitis-associated AKI and have documented its benefit in cytokine clearance and metabolic stabilization [13] [14]. However, chylomicrons, with molecular weights in the billions of Daltons and particle diameters exceeding 80 nm, are physically incapable of passing through standard hemofilter membranes. Their clearance requires plasma removal, not filtration (**Figure 5**) [8] [9].

Schematic diagram illustrating the mechanistic distinction between CRRT and TPE. Left panel: CRRT removes small-to-middle-molecular-weight solutes (urea, creatinine, electrolytes, cytokines) via diffusion and convection, correcting acid-base status, fluid balance, and uremic burden. Chylomicrons (CM; 80 - 1200 nm) are too large to pass through hemofilter membranes and are not removed. Right panel: TPE removes the entire plasma compartment, including chylomicrons, VLDL, and free fatty acids via plasma separation, replacing it with 5% albumin. This directly eliminates the lipotoxic substrate driving pancreatic and end-organ injury.

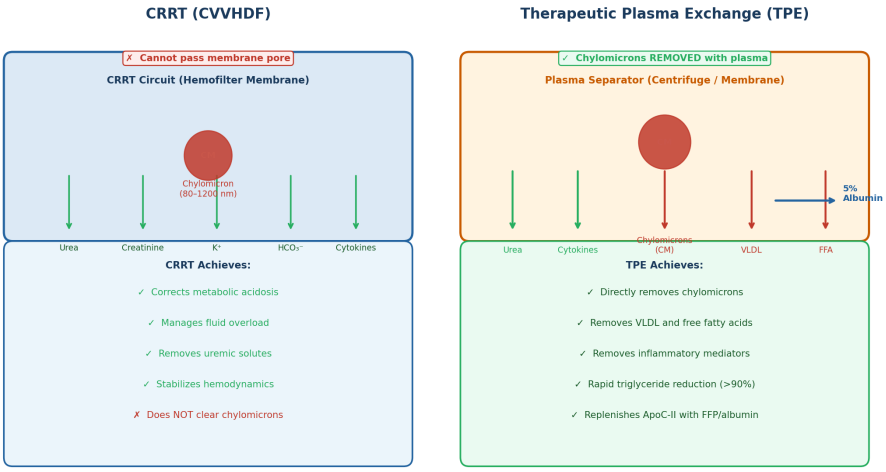

Figure 5. Mechanistic distinction between CRRT and TPE in HTG-AP.

6.4. Therapeutic Plasma Exchange as Definitive Lipid Clearance

The evidence base for TPE in severe HTG-AP, while predominantly retrospective and case-based, is consistent in demonstrating rapid and substantial triglyceride reduction [8] [9] [15] [17]. Chen *et al.* reported triglyceride reductions of >80% per session in a cohort of patients with severe HTG-AP [8]. Gubensek *et al.* demonstrated clinical improvement and reduced organ failure scores following TPE [15]. Kremer Hovinga *et al.* performed a systematic literature review confirming the efficacy and relative safety of TPE in this indication [9].

The mechanism by which TPE produces clinical benefit extends beyond simple triglyceride removal. The exchange of patient plasma with albumin or FFP replenishes coagulation factors and functional LPL cofactors such as ApoC-II, potentially partially restoring LPL activity [8] [15]. It also removes circulating inflammatory mediators, free fatty acids, and lipid peroxidation products, attenuating the systemic inflammatory response [9] [17].

In our patient, the triglyceride reduction from >14,000 mg/dL at admission to approximately 3500 mg/dL after the first TPE session, 300 mg/dL after the second session, and <200 mg/dL at discharge was accompanied by normalization of pancreatic enzymes and progressive multi-organ recovery. While attribution of clinical recovery to TPE alone cannot be made with certainty in a single case—given the concurrent effects of CRRT, pharmacologic therapy, and intensive supportive care—the temporal correlation between TPE initiation and both biochemical and clinical improvement is strongly consistent with the published literature on TPE in severe HTG-AP [8] [14] [17].

6.5. CRRT and TPE as Complementary Modalities

A key conceptual contribution of this case is the explicit framing of CRRT and TPE as non-competing, sequentially complementary interventions in HTG-AP with multi-organ failure (**Figure 6**) [14]. Each modality addresses a distinct physiological domain: CRRT corrects the metabolic and renal consequences of critical

illness, while TPE removes the primary offending pathological substrate. Neither modality alone would have been sufficient in this case.

Clinicians in resource-limited or low-volume settings may default to CRRT as the sole extracorporeal intervention when faced with severe pancreatitis and AKI, without recognizing the concurrent need for TPE. This case serves as a reminder that awareness of the therapeutic ceiling of CRRT—its inability to clear large lipoproteins—is essential for timely decision-making [13] [14].

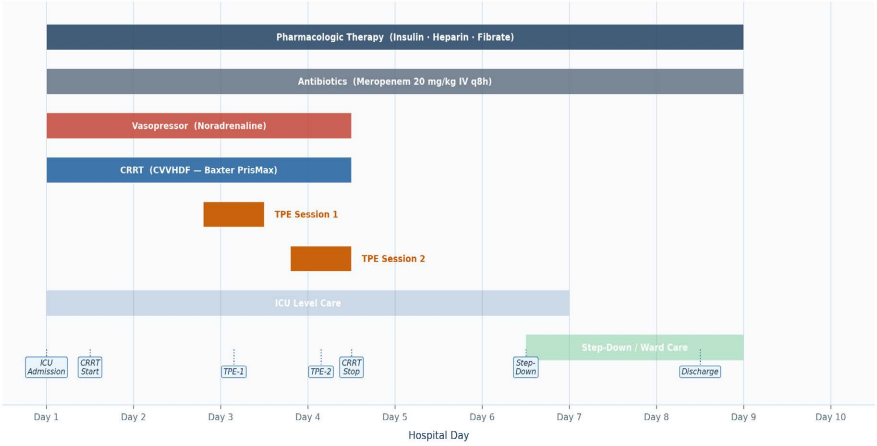

Figure 6. Treatment timeline—sequence and duration of key interventions.

Gantt-style treatment timeline illustrating the sequence and approximate duration of key interventions across the ICU admission. Pharmacologic therapy (insulin, heparin, fibrate, meropenem) was initiated on Day 1 and continued throughout. CRRT (CVVHDF on Baxter PrisMax) ran for approximately 48 hours (Days 1 - 4). TPE sessions were performed on Days 3 and 4. Vasopressor support was tapered and discontinued by Day 4 - 5. The patient was stepped down to ward care on Days 6 - 7 and discharged on Days 8 - 10.

6.6. Timing and the Decision to Escalate

Perhaps the most clinically instructive lesson of this case is the challenge of knowing when to escalate. In the acute phase, it is tempting to continue optimizing supportive care when the patient shows some improvement—particularly when pharmacologic lipid-lowering therapy and CRRT are producing measurable physiologic benefits. However, the persistence of triglycerides at dangerous levels despite 24 - 48 hours of maximal therapy should be recognized as a decisive indicator for TPE escalation [8] [16].

Published guidance and case series suggest that when triglycerides fail to fall below 5000 mg/dL (or ideally 1000 - 2000 mg/dL) within 12 - 24 hours of pharmacologic therapy, particularly in cases where LPL deficiency is suspected, TPE should be initiated without further delay [9] [15] [16]. Delays in escalation risk compounding pancreatic necrosis, irreversible organ injury, and death.

Multidisciplinary coordination—between intensivists, nephrologists, apheresis specialists, and lipidologists—is essential for achieving timely TPE access in the ICU setting. Institutional protocols for this indication are warranted [16] [18].

6.7. Limitations

Several limitations of this report warrant explicit acknowledgment. First, the diagnosis of familial chylomicronemia syndrome was not genetically confirmed; the classification of 'suspected FCS' is based on clinical and biochemical criteria only, and multifactorial severe hypertriglyceridemia cannot be entirely excluded. Second, this is a single-patient case report, which precludes generalization of findings or causal inference. Third, several supportive data points—including exact serial triglyceride values between treatment phases, formal lipid subfractionation, ApoB levels, and serial creatinine and enzyme values at defined time points—were not available, limiting the precision of the reported treatment response. Fourth, the intermediate arterial blood gas values in Table 6 represent a clinically reconstructed trajectory rather than directly measured chart data and should be interpreted accordingly. Fifth, long-term follow-up data are limited; the patient's lipid profile, recurrence risk, and response to dietary and pharmacologic management beyond discharge are not reported. Genetic evaluation and specialist lipidology follow-up were recommended, but outcomes are not yet known.

Table 6. Serial arterial blood gas trend.

Time Point	pH	$PaCO_2$ (mmHg)	HCO_3^- (mmol/L)	Lactate (mmol/L)	Interpretation
Admission	7.10	28	9	10	Severe metabolic acidosis with partial respiratory compensation
12 h after CRRT	7.21	30	12	7.2	Partial correction of metabolic acidosis
24 h after CRRT	7.30	32	16	4.8	Improving acid-base status and tissue perfusion
Pre-TPE/Day 2	7.34	34	19	3.1	Metabolically improved, but the patient remains critically ill
After TPE Session 1	7.38	36	22	2.1	Near normalization
After TPE Session 2	7.41	38	24	1.5	Normalized acid-base profile

Serial ABG values after admission are presented as a clinically reconstructed improvement trajectory based on the documented course of severe metabolic acidosis, CRRT-supported correction, and post-TPE recovery. Admission pH 7.10 and lactate 10 mmol/L were directly confirmed; intermediate values are included to reflect the physiologic trend.

7. Conclusions

This case documents a successful outcome in catastrophic hypertriglyceridemia-

induced necrotizing pancreatitis with multi-organ failure in a 14-year-old girl with suspected FCS, achieved through a deliberately sequenced therapeutic approach. Aggressive pharmacologic therapy established the initial management framework. CRRT provided essential metabolic stabilization, renal support, and hemodynamic correction. Therapeutic plasma exchange provided the definitive, mechanistically appropriate lipid clearance that conventional and filtration-based therapies cannot achieve.

The central practical lesson is not how to perform either CRRT or TPE—it is recognizing which problem each modality is designed to solve. In severe HTG-AP with suspected FCS, the dominant challenge is lipid clearance failure, and TPE represents the most effective currently available intervention for achieving rapid reduction of circulating chylomicrons. While this conclusion is based on a single case and an unconfirmed genetic diagnosis, it is consistent with the broader observational literature and with the physiological reasoning that underpins TPE's mechanism of action [8] [9] [14] [16].

Clinicians managing critically ill patients with extreme hypertriglyceridemia should consider early lipidology and apheresis consultation, maintain a low threshold for escalation to TPE when pharmacologic lipid-lowering fails within 12 - 24 hours, and treat CRRT and TPE as complementary tools rather than alternatives. We advocate for the development of institutional protocols and international registry data to further characterize optimal management strategies in this rare but lethal condition.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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