

Case Report

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ACUTE NECROTISING PANCREATITIS CAUSED BY SODIUM VALPROATE: A CASE REPORT



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Abstract

Valproic acid (sodium valproate; VPA)-associated pancreatitis is an uncommon but potentially life-threatening adverse event, particularly in children. Although pancreatitis related to valproate therapy is reported more frequently in pediatric patients than in adults, necrotizing pancreatitis remains exceptionally rare. We report a 5-year-old male patient who developed acute necrotizing pancreatitis following short-term sodium valproate therapy. He presented with lethargy, altered mental status, nausea, vomiting, fever, and abdominal tenderness. Laboratory investigations demonstrated markedly elevated pancreatic enzyme levels, and contrast-enhanced computed tomography confirmed necrotizing pancreatitis. Following prompt discontinuation of sodium valproate and initiation of supportive treatment, including aggressive intravenous fluid resuscitation, bowel rest, analgesia, and antimicrobial therapy, the patient recovered without complications. This case highlights the importance of considering acute pancreatitis in children receiving sodium valproate and emphasizes the critical role of early diagnosis and timely intervention in improving clinical outcomes.

Keywords Acute pancreatitis · Sodium valproate · Necrotizing pancreatitis · Pediatric patient

INTRODUCTION

Acute necrotizing pancreatitis (NP) is a life-threatening form of acute pancreatitis (AP) characterized by extensive necrosis of the pancreatic parenchyma or peripancreatic tissues, leading to systemic inflammation and multi-organ failure. It represents a critical complication of AP, occurring in approximately 7%–10% of all cases (1). Although the exact pathogenesis of VPA-induced injury remains unclear, metabolic and cellular disturbances drive the process (2, 3). VPA exposure is thought to prompt significant pancreatic oxidative

stress, accelerating free radical generation and depleting endogenous antioxidants, which triggers direct acinar cell injury (2, 4). These alterations compromise membrane integrity, facilitating premature zymogen activation within the acinar space (2, 5). VPA-induced damage may also involve microvascular impairment mediated by toxic metabolites, causing pancreatic ischemia and necrosis (4, 5).

Unlike dose-dependent drug toxicities, VPA-associated AP is an idiosyncratic hypersensitivity reaction, occurring entirely independent of daily dosages or serum

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concentrations (4, 6). Consequently, this adverse reaction can develop unpredictably during short-term use or mai maintenance therapy, carrying a substantial risk of systemic complications if not promptly recognized (4, 7). We report a patient who developed VPA-induced NP following short-term use of valproic acid, emphasizing that a high index of clinical suspicion, early diagnostic confirmation, and immediate supportive intervention are crucial for optimizing patient prognosis.

CASE PRESENTATION

A 5-year-old male patient was admitted to the emergency department with an abrupt onset of irritability, confusion, somnolence, vomiting, and high fever. His medical history was notable for seizures since age 6 months, a low-grade cerebellar cyst excision at age 2, and secondary hydrocephalus managed with a ventriculoperitoneal shunt. He had neurodevelopmental delay and secondary epilepsy, with increased seizure frequency. Two months prior to admission, levetiracetam was replaced with VPA. His medications included clobazam (11 mg/kg/day) and VPA at an uncommonly low maintenance dose of 0.5 mg/kg/day.

Physical examination revealed a body weight of 12.2 kg (-3.5 Standard Deviation Score (SDS)) and height of 96 cm (-3.2 SDS), reflecting severe malnutrition. The patient was lethargic and somnolent, with a Glasgow Coma Scale score of 10. Abdominal examination demonstrated severe epigastric tenderness associated with generalized rebound tenderness. Pancreatic enzyme levels were markedly elevated: amylase 884 U/L and lipase 742 U/L. Urgent cranial MRI demonstrated no acute pathology or shunt malfunction. Alternative etiological factors were systematically excluded. Normal serum calcium and triglyceride levels ruled out metabolic and hyperlipidemic pancreatitis, while viral serologies for hepatotropic viruses, Epstein–Barr virus, and cytomegalovirus were negative. There was no history of abdominal trauma, biliary obstruction, systemic disease, or exposure to other pancreatitis-associated medications.

Due to excessive bowel gas on ultrasound, a contrast-enhanced abdominal computed tomography (CT) scan was performed. It established acute necrotizing pancreatitis, showing focal expansion of the distal half of the pancreatic body and tail with a central area of non-enhancement and diffuse peripancreatic fluid collections (Figure 1). VPA was immediately discontinued and replaced with levetiracetam. Management included bowel rest, aggressive intravenous fluid resuscitation, analgesics, and empirical antimicrobial therapy with meropenem (60 mg/kg/day). After 48 hours, the patient's neurological status improved, and he was transferred to the pediatric gastroenterology unit. Fever resolved by the 96th hour. Enteral nutrition was gradually reintroduced. Serial tests showed normalization of pancreatic enzymes, and follow-up imaging confirmed resolution of necrotic changes. He

was successfully discharged on hospital day 12 and remained asymptomatic at a 1-month follow-up (Table 1).

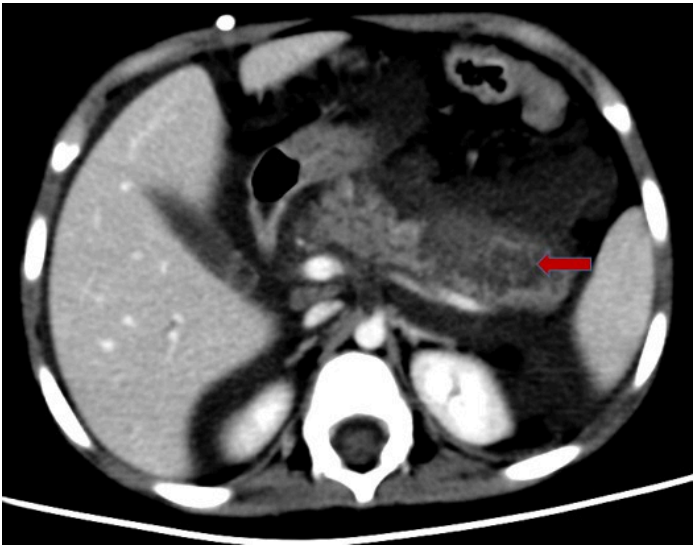


Figure 1. Axial contrast-enhanced abdominal computed tomography (CT) scan of the 5-year-old patient. The arrow indicates a significant focal enlargement and a distinct area of central hypodensity with a total lack of contrast enhancement involving the distal half of the pancreatic body and the pancreatic tail, findings highly characteristic of acute necrotizing pancreatitis. Diffuse free fluid collections are also visible in the adjacent peripancreatic and tissue planes.

Table 1. Timeline of laboratory parameters during inpatient management (Days 1–10) and outpatient follow-up (Day 30).

Parameters	1	2	3	4	5	6	7	8	9	10	30
Amylase (U/L)	884	999	928	902	429	242	267	327	305	308	82
Lipase (U/L)	742	683	-	-	115	82.9	99.1	142	135	169	25
ALT (U/L)	13	9.5	7.1	5.3	8.2	6.9	9.1	11.5	13.6	19.6	17.6
AST (U/L)	21.6	21.5	9.2	26.6	24.9	16.6	18.1	23.5	17.4	23.9	26
BUN (mg/dL)	9.4	7	7.2	9.5	6.1	4.1	2.1	1.3	5.4	14.3	8.2
Urea (mg/dL)	20.1	14.9	15.4	20.3	13	8.7	4.5	2.7	11.5	30.6	17.5
Creatinine (mg/dL)	0.3	0.2	0.3	0.3	0.2	0.2	0.1	0.2	0.2	0.3	0.3
TB (mg/dL)	0.2	0.17	0.21	0.38	0.35	0.46	0.42	0.22	0.28	0.22	0.09
WBC (10 ³ /μL)	17.2	15.9	13.2	15.8	14.7	12.8	12.3	14.5	14.1	12.8	7.9
ANC (10 ³ /μL)	14.2	13	10.4	11.9	9.4	7.9	6.8	7.9	7.8	7.3	3
ALC (10 ³ /μL)	1.57	1.5	1.2	1.1	1.4	3.3	3.1	3.5	4.2	3.9	3.8
HGB (g/dL)	12.3	11.9	10	8.9	8.3	8.1	7.8	7.9	7.9	8.2	10.5
HCT (%)	37.1	35.4	29.4	26.7	24.8	23.9	22.9	23	23.3	24.9	33
PLT (10 ³ /μL)	314	314	267	206	178	278	306	388	442	561	488
CRP (mg/L)	4.1	43.9	147	162	179	141	86	63	45	41	4.5
PCT (ng/mL)	0.69	0.78	0.77	0.7	0.61	0.49	0.35	0.29	0.19	0.15	0.09

ALC: Absolute lymphocyte count, ALT: Alanine aminotransferase, ANC: Absolute neutrophil count, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen, CRP: C-reactive protein, HCT: Hematocrit, HGB: Hemoglobin, PCT: Procalcitonin; PLT: Platelet, TB: Total bilirubin, WBC: White blood cell count

DISCUSSION

We described a rare case of VPA-induced acute NP in a 5-year-old child. The clinical significance lies in the development of extensive pancreatic necrosis following a remarkably short duration of anticonvulsant exposure, compounded by the patient's underlying neurodevelopmental delay. While VPA-associated AP is a well-recognized adverse event in the pediatric population, progression to necrotizing forms remains exceptionally uncommon (1,6). A critical and highly unique feature of the case is the distinct temporal and quantitative relationship between VPA exposure and symptom onset. VPA-associated pancreatitis typically manifests weeks to years after starting therapy (4, 6). However, our patient developed severe NP within only two months of starting valproate. Because the severity of pancreatic inflammation does not correlate with dosage or serum concentration, this case underscores that VPA-induced NP is an idiosyncratic hypersensitivity reaction (4). Diagnosing drug-induced NP requires systematic exclusion of alternative etiological factors (8). In our patient, metabolic, infectious, traumatic, and biliary causes were ruled out. Clinically, the patient presented with a complex combination of gastrointestinal and neurological symptoms. Grauso-Eby et al. emphasized that clinicians must maintain a high index of suspicion for pancreatitis in any child taking VPA who presents with nonspecific abdominal symptoms or fatigue and apathy (6). In pediatric patients with neurodevelopmental delay, communication barriers frequently obscure early abdominal physical findings, causing severe pain to manifest primarily as altered mental status. Therefore, an early screening using serum pancreatic enzymes remains paramount. Contrast-enhanced CT remains the gold standard for NP diagnosis and staging by showing characteristic non-enhancing areas of parenchymal necrosis (1, 8).

The cornerstone of managing VPA-induced NP centers on immediate drug discontinuation and aggressive supportive care (4, 7). Upon diagnostic confirmation, VPA was withdrawn, and the patient's anticonvulsant regimen was safely transitioned to levetiracetam. Management focused on aggressive fluid resuscitation, analgesia, and bowel rest, with enteral nutrition were gradually reintroduced as clinical symptoms resolved (1). Although the routine use of empirical antibiotics in sterile necrosis is not universally mandated, empirical antimicrobial therapy was initiated in this case due to the persistent high fever and clinical suspicion of infected necrosis, resulting in complete defervescence within 96 hours and avoiding the need for invasive surgical intervention (1, 8). Rapid clinical and radiological improvement following VPA withdrawal supports a causal relationship. Given the risk of recurrence, sodium valproate must be permanently avoided in this patient.

CONCLUSION

This case highlights the unpredictable, idiosyncratic nature of sodium valproate-associated pancreatic toxicity in children. Short-

term exposure to VPA, even at a low maintenance dosage, can rapidly progress to NP. Clinicians must maintain a high index of suspicion and initiate prompt diagnostic screening in any pediatric patient receiving VPA who presents with nonspecific abdominal symptoms or acute neurological deterioration. Early clinical recognition, immediate drug discontinuation, and timely supportive management are vital to minimizing complications, avoiding invasive interventions, and optimizing patient outcomes.



Informed Consent	Written informed consent was obtained from patient who participated in this study.
Peer Review	Externally peer-reviewed.
Author Contributions	Conception/Design of Study- A.M., E.T.; Data Acquisition- A.M., E.T.; Data Analysis/ Interpretation- A.M., E.T.; Drafting Manuscript- A.M., E.T., L.A., Z.G.T., Z.Ö., Ö.D.; Critical Revision of Manuscript- A.M., E.T., L.A., Z.G.T., Z.Ö., Ö.D.; Final Approval and Accountability- A.M., E.T., L.A., Z.G.T., Z.Ö., Ö.D..
Conflict of Interest	The authors have no conflict of interest to declare.
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