*Case Report*

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# Acute Pancreatitis: It's not always "On the Rocks"

**Himanshu Gupta**

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**Abstract**

Acute pancreatitis is one among the common causes of pain abdomen presenting to emergency department. Some of the most common causes of acute pancreatitis include gallstones, alcohol use, hypertriglyceridemia and Drugs. Over 500 drugs are implicated as a causative agents and account for less than 2% of cases.

Sodium valproate, one of the commonly prescribed anti-epileptic drug is known to cause acute pancreatitis.

Here, we are presenting a case of a 26-years-old male who is a known case of juvenile myoclonic epilepsy on sodium valproate who presented with acute pancreatitis.

**Our reasons for highlighting this case are:**

To illustrate a patient with juvenile myoclonic epilepsy on sodium valproate developing acute pancreatitis with other adverse effects like gum hypertrophy, vitamin B12 and folate deficiency.

**Keywords:** Acute pancreatitis; Valproic acid; Valproate; Drug induced; Juvenile myoclonic epilepsy; Anticonvulsants; Interstitial pancreatitis.

## INTRODUCTION

Acute pancreatitis is an inflammation involving just the pancreas, may affect surrounding tissues or may cause organ dysfunction. Most cases (~80%) involve only mild inflammation with mortality rate of <1%.

Alcohol abuse, Gallstone Disease and Severe Hypertriglyceridemia are the most common triggers of acute pancreatitis.[1,2]

**Author's Affiliation:** Assistant Professor, Department of Emergency Medicine, Jaipur National University Institute for Medical Sciences and Research Centre, Jaipur 302017, Rajasthan, India.

**Corresponding Author: Himanshu Gupta**, Assistant Professor, Department of Emergency Medicine, Jaipur National University Institute for Medical Sciences and Research Centre, Jaipur 302017, Rajasthan, India.

**E-mail:** dr.himanshu1182@gmail.com

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Common causes include:

**Table 1:** Causes of acute pancreatitis

| | |
|---|---|
| Common | Gallstones (35%-75%) |
| | Alcohol (25%-35%) |
| | Idiopathic (10%-20%); increases with age |
| Uncommon | Hypertriglyceridemia (1%-4%) |
| | ERCP |
| | Drugs (1.4%- 2%) usually mild disease |
| More uncommon (total <8% of cases) | Abdominal trauma |
| | Post-operative complication, especially post- cardiopulmonary bypass |
| | Hyperparathyroidism |
| | Infection( bacterial, viral or parasitic) |
| | Autoimmune diseasetumor (pancreatic, ampullary) |
| | Hypercalcemia |
| | Cystic fibrosis |
| Rare | Ischaemia |
| | Posterior penetrating ulcer |
| | Toxin exposure |
| Unknown | Congenital abnormalities |

**Table 2:** Drugs associated with acute pancreatitis

- Acetaminophen
- Amiodarone
- Angiotensin converting enzyme inhibitors and angiotensin receptor blockers (enalapril and losartan)
- Antibiotics ( erythromycin, metronidazole, tetracycline, trimethoprim-sulfamethoxazole)
- Antiepileptics ( carbamazepine, valproic acid)
- Azathioprine
- Cannabis
- Chemotherapy agents (6- mercaptopurine, cisplatin, L-asparaginase, ifosfamide, tamoxifen, cytarabine, pegaspargase)
- Codeine ( and other opiates)
- Dexamethasone ( and other steroids)
- Didanosine
- Diuretics (chlorothiazide, hydrochlorothiazide and furosemide)
- Estrogens
- Mesalamine
- Methimazole
- Pravastatin and simvastatin
- Anti-tuiberculars (dapsone, isoniazid, rifampin)

Juvenile myoclonic epilepsy (JME) also known as Janz syndrome or impulsive petit-mal epilepsy. It falls into idiopathic as well as hereditary forms of epilepsy. JME is one of the most common childhood/juvenile epilepsy syndromes accounting 5%-10% of all cases. JME has equal sex incidence, usually manifesting between 12-18 years of age. Valproic acid is the drug of choice with alternatives including levetiracetam, lamotrigine, topiramate and zonisamide.

Valproic acid (sodium valproate) is a branched chain aliphatic carboxylic acid with a broad spectrum of anti-convulsant activity. It acts by multiple mechanisms:

i ) A phenytoin like frequency dependent prolongation of $Na^+$ channel inactivation.

ii ) Weak attenuation of $Ca^{2+}$ mediated 'T' current (ethosuximide-like).

iii ) Augmentation of release of inhibitory neurotransmitter GABA by inhibiting its degradation (by GABA-Transaminase) as well as probably by increasing its synthesis from glutamic acid.

**Table 3:** Adverse Effects of Valproic Acid

- Anorexia, vomiting, heart burn
- Drowsiness, ataxia, tremor
- Alopecia
- Rashes, thrombocytopenia
- Asymptomatic rise in serum transaminase levels
- Pancreatitis PCOD
- Teratogenic ( spina bifida and other neural tube defects)
- B12, Folate deficiency ( rare)
- Gingival hyperplasia (rare)

## *Case Presentation*

A 26-year-old male came to our emergency medicine department with complaints of pain in abdomen for 7 days and vomiting for the past one day. Cardiac monitor was connected and IV line was secured with samples taken for lab investigations.

On rapid assessment, airway was patent and protected. Breathing was self with respiratory rate of 16 per minute and monitor showing $SPO_2$ 99% on room air. Bilateral air entry was equal with no added sounds.

Circulation assessment showed pulse rate of 92 per minute, regular rate, Afebrile, BP- 132/82 mmHg. Cardiac Auscultation suggested normal S1, S2 heart sounds. Abdomen was soft with tenderness noted in epigastric region on deep palpation; no guarding or rigidity noted. There was no distension, hepato-splenomegaly or free fluid and bowel sounds were normal.

Disability assessment revealed GCS of 15/15, random blood glucose was 76 mg/dl, with no focal neurological deficit and pupils were bilaterally equal and reacting to light. There were no significant contributory findings on exposure.

AMPLE history revealed patient to be a follow-up case of juvenile myoclonic epilepsy on regular treatment with tablet sodium valproate 500 mg per oral twice daily for last 8 years with last active seizure around 3 months ago. Patient had this epigastric pain since last 7 days dull ache to start with, which progressed to moderate to severe pain with 5 out of 10 on pain scale on presentation to ED. He also had vomiting around 4 times since last one day.

A provisional diagnosis of acute pancreatitis was made and samples were sent for amylase and lipase along with other tests. ECG and chest X-ray PA view were normal.

| Investigations | Result (units) |
|---|---|
| Hemoglobin | 13.1 g/dl |
| TLC | 10.6 th/cmm |
| Neutrophil/Lymphocyte | 80.6/9.7 % |
| Platelet count | 183 th/cmm |
| MCV | 112.4 FL |
| MCH | 34.8 pg |
| Billirubin Total | 0.38 mg/dl |
| Billirubin Direct | 0.26 mg/dl |
| Billirubin Indirect | 0.12 mg/dl |
| AST | 36 U/L |
| ALT | 33 U/L |
| Alkaline Phosphatase | 60 U/L |
| Total Protein | 6.7 g/dl |
| Albumin | 3.8 g/dl |
| Globulin | 2.9 g/dl |
| Serum Urea | 10.98 mg/dl |
| Serum Creatinine | 0.96 mg/dl |
| Sodium | 134 mmol/L |
| Potassium | 4.08 mmol/L |
| Chloride | 94.0 mmol/L |
| Amylase | 298 U/L |
| Lipase | 417.94 U/L |
| HIV/HBsAg/ HCV | Non-reactive |
| Folate | 2.05 ng/ml |
| Vitamin B12 | <159 pg/ml |
| Peripheral blood smear | RBC's macrocytic normochromic. |
| Total Cholesterol | 100.4 mg/dl |
| Triglycerides | 131.99 mg/dl |
| LDL | 65.74 mg/dl |
| HDL | 13.12 mg/dl |
| VLDL | 26.40 mg/dl |
| Valproate level | |

**Fig. 1:** Gingival hyperplasia

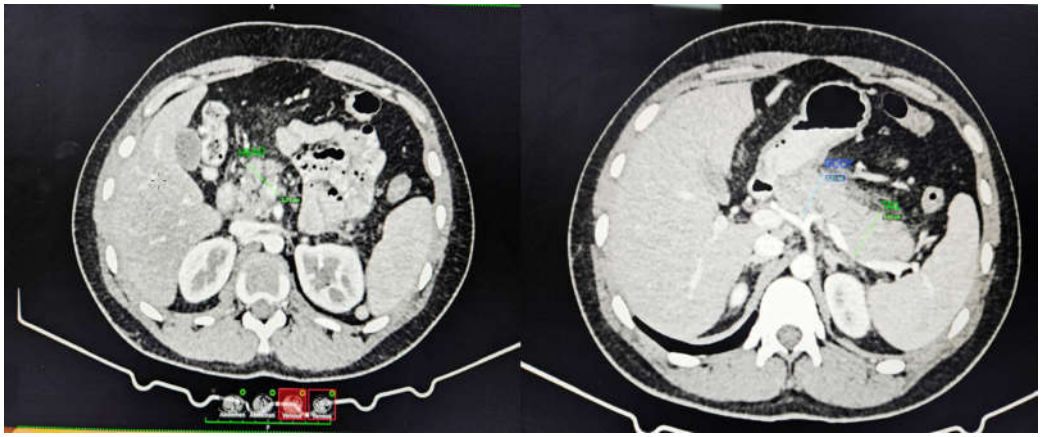

**Fig. 2:** Contrast enhanced CT scan of abdomen showing diffuse bulky pancreas. Head, body and tail measures 33 mm, 32 mm and 35 mm respectively. Homogenous contrast enhancement is noted.

## DISCUSSION

Drugs could also lead to acute pancreatitis. Since 1950's after the first cases of Drug-associated pancreatic injury reported, around 500 drugs have been shown to be associated with pancreatitis.[3]

Valproic acid (Sodium Valproate) is also listed as a cause of acute pancreatitis.[4,5] Pancreatitis is an unusual reaction to sodium valproate therapy, approximately seen in one out of forty thousand patients.[6] According to previous reports, such adverse effects can occur after prescribing this medicine for 1 week for 8 years.[7] The recommended maximum daily dose of sodium valproate is 2500mg[8] and our patient was receiving 1000mg sodium valproate per day.

In this study, our patient exhibited typical abdominal pain localizing to epigastrium, accompanied by vomiting.

Laboratory findings indicated that the levels of amylase and Lipase elevated, computed tomography was used to confirm the abnormality of his pancreas.

Other laboratory indices were within the normal range, except for raise MCV, decreased levels of Folate and Vitamin B12. Peripheral smear suggested macrocytosis which is not uncommon hematological side effect of valproate therapy and is not dose dependent.[9]

Patient also exhibited gingival hyperplasia (fig. 1). though rare but it is a known adverse effect of valproate therapy.[10]

Other causes of acute pancreatitis were taken into consideration, as the patient had no history of trauma, no history of alcohol abuse and no gall stone disease on ultrasonography or CT studies of abdomen. His serum triglycerides were within normal range. He was not taking any other drug apart from valproic acid.

Taken together, we assumed that the cause of acute pancreatitis in this patient was sodium valproate treatment. The exact mechanism of how sodium valproate causes pancreatitis remains unclear as it appears that there is no association between the dosage or serum level with its development.[11] In the majority of cases reported, the serum sodium valproate level was within the normal range.[12] The association of sodium valproate and pancreatitis is sometimes referred to as idiosyncratic as pancreatitis can develop after 1 week to 8 years of exposure to sodium valproate. In our case the patient was on treatment with Valproate for around last 8 years that is consistent with published data. Serum Valproate level for our patient were within normal range.

The reason why sodium valproate induces acute pancreatitis may be related to the damage caused by free radicals on pancreatic tissue, including superoxide dismutase, catalase and glutathione peroxidase depletion.[13]

## CONCLUSION

Acute pancreatitis can be fatal. Although drug-induced pancreatitis is rare, physicians should bear in mind its possibility. To prevent drug-induced pancreatitis, the latest knowledge of medicines connecting their use to the occurrence of pancreatitis is required. Physicians should be aware of drug allergy history and patients' comorbid conditions, while maintaining vigilance against the signs of severe toxic reactions.

Acute pancreatitis is considered as one of the idiosyncratic adverse reactions to antiepileptic drugs. As rare as drug-induced acute pancreatitis can be, it should not be overlooked. Therefore, physicians need to consider the medical history of patients before prescribing this medication.

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