CASE REPORT

Sodium valproate induced necrotising pancreatitis: A case report

Ali MF, Loh KY

Ali MF, Loh KY. Sodium valproate induced necrotising pancreatitis: A case report. Malays Fam Physician 2013;8(3);28-30

Keywords:
pancreatitis, valproic acid, drug induced, anticonvulsants, intellectual disability/ mental retardation, complications

Authors:

Mohd Fairuz Ali
MBBS, MMed (Fam Med)
(Corresponding author)
Department of Family Medicine, UKM Medical Centre, JlnYaacob Latiff, Bandar TunRazak, 56000 Cheras, Kuala Lumpur, Malaysia.
Tel: +60127003024
Fax: +60391456680
Email: phere1@gmail.com

Loh Keng Yin
MMed (FamMed)
Department of Clinical Sciences, Universiti Tungku Abd.Rahman, Bdr Sg Long, Kajang 43000
Selangor, Malaysia.
Email: manjusri_loh@yahoo.com

Abstract

Sodium valproate is one of the most common first-line antiepileptics prescribed for primary and secondary generalised seizures. However, serious complications associated with sodium valproate, such as acute pancreatitis, need to be considered when choosing this medication for treating epilepsy in certain populations such as children and persons with intellectual disability. We report a case of a 21-year-old man with intellectual disability who presented to the emergency department with an acute abdomen, vomiting and diarrhoea. He had to undergo an emergency exploratory laparotomy during which acute necrotising pancreatitis was diagnosed intra-operatively. We believe that the recent increase in sodium valproate dosage for his epilepsy was the cause of the pancreatitis. Carers of such persons should be adequately informed regarding possible life-threatening complications of medications prescribed to avoid delay in diagnosis and unwanted incidents.

Introduction

Acute pancreatitis is an acute inflammatory process involving the pancreas. One of the subtypes of acute pancreatitis is acute necrotising pancreatitis, which is a severe form of acute pancreatitis characterised by the presence of one or more diffuse or focal areas of non-viable pancreatic parenchyma due to inflammatory changes.[1] This condition is commonly caused by choledocholithiasis, ethanol abuse, trauma and drugs, including statins, diuretics, antiretroviral agents and anticonvulsants.[1,2] Although sodium valproate-associated pancreatitis cases are rare, it has been reported since 1979 with some fatal cases reported through the years.[2,3] The incidence of sodium valproate-induced pancreatitis has been estimated to be 1:40,000.[4] It is more commonly reported in young people.[2,4,5] The objective of this case report is to illustrate a patient with intellectual disability who developed necrotising pancreatitis after the dosage of sodium valproate for the treatment of his epilepsy was increased.

Case Summary

The patient was a 21-year-old man with intellectual disability diagnosed with generalised tonic-clonic epilepsy on regular sodium valproate treatment since childhood. Despite being compliant to treatment, he developed frequent attacks of breakthrough seizures. In a recent visit, his therapeutic dosage of sodium valproate was increased from initial 600 mg BD to 800 mg BD.

Two weeks after taking 800 mg BD of sodium valproate, he developed an acute abdomen with vomiting and diarrhoea. He was brought to the emergency department by his father for treatment. His total white cell count (WCC) was 20.7×10^9 /L with a neutrophilic picture (77%) (15.9×10^9 /L) and the serum amylase level was 1283 U/L, which was more than 10 times the normal value.

He underwent an emergency exploratory laparotomy during which necrotic body and tail of the pancreas with multiple saponification spots were observed. The diagnosis of acute necrotising pancreatitis was made intra-operatively. Necrosectomy of the affected areas was done and two large bore drainages were left temporarily in the lesser sac and sub-hepatic recess to prevent the development of pseudocysts. He recovered well from the surgery. However, he developed diabetes mellitus post surgery and had to be started on insulin treatment. The sodium valproate was replaced by phenytoin. He remained well with no recurrence of his pancreatitis and no surgical complications were reported on subsequent follow-up. Currently, his epilepsy is well controlled.

Discussion

The exact mechanism of how sodium valproate causes pancreatitis remains unknown as it appears that there is no association between the dosage or serum level with its development.[2] 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.[6] In pharmacological studies, the maximum tolerated dosage of sodium valproate is 400 mg to 2500 mg per day and the dosage of this patient was 1600 mg per day, which was still within the tolerated range.[7] His serum sodium valproate level on admission was 609 μmol/L, which was within the normal level (347–693 μmol/L). In the majority of cases reported, the serum sodium valproate level was within the normal range.[6] For this patient, no other likely cause of necrotising pancreatitis was identified as he did not have a history of trauma or consuming any other drugs or alcohol except the sodium valproate for his epilepsy. Subsequent post-operative CT scan and blood test results were also unremarkable. The only suspected factor was the recent increase in the sodium valproate dosage to control his epilepsy. Similar incidents have been reported where acute pancreatitis develops after a recent increase in the sodium valproate dosage.[2] Therefore; we concluded that the higher dosage of sodium valproate might have led to the necrotising pancreatitis.

The incidence of drug-induced pancreatitis, due to sodium valproate in particular, is higher among children and young adults, as it is the most common antiepileptic agent used in these age groups.[3,8] A study on antiepileptic utilisation in paediatric patients, conducted in a Malaysian public hospital reported that sodium valproate was the main antiepileptic used (36.8%), followed by carbamazepine (30.2%) and lamotrigine (10.4%), as monotherapy or in combination with other antiepileptics for various types of seizures.[9] Moreover, other causes of pancreatitis are rare for this age group.[10]

There are also many reported cases of sodium valproate-induced pancreatitis among those with neurological deficits, including mental retardation, cerebral palsy and developmental delay.[4-6,8] However, there is still no definite evidence showing the association between neurological deficits and incidence of sodium valproate-induced pancreatitis in the literature.[5] Nonetheless, due to the limitation in providing accurate history, there is a risk of a delay in diagnosis and misdiagnosis in these groups.[8,11]

Conclusion

Acute pancreatitis is a potentially fatal complication observed in people taking sodium valproate. Therefore, physicians prescribing sodium valproate for epilepsy should be of this complication and counsel patients who are on it to be alert of symptoms such as sudden abdominal pain, fever, diarrhoea and vomiting. Patients who are on sodium valporate must seek immediate medical attention if these symptoms develop. Physicians also need to consider the background of patients in terms of their ability to report such symptoms before prescribing this medication and maintain a high index of suspicion for pancreatitis, especially in high-risk groups. Prompt investigations for acute pancreatitis using as blood tests such as serum amylase and lipase as well as radiology imaging must be done in patients on sodium valproate presenting with acute abdomen.

Conflict of interest

None

Acknowledgement

Mr. Hairol Azrin Othman, Consultant in General, Hepatobiliary & Pancreatic Surgery, Surgical Department, Universiti Kebangsaan Malaysia Medical Centre.

References

1 Baron TH, Morgan DE. Acute necrotizing pancreatitis.N Engl J Med. 1999;340(18):1412-7.

2. Yazdani K, Lippmann M, Gala I.Fatal pancreatitis associated with valproic acid, review of the literature.Medicine. 2002;81(4):305-10.

3. Batalden PB, Van Dyne BJ, Cloyd J.Pancreatitis associated with valproic acid therapy.Pediatrics. 1979;64(4):520-2.

4. Gerstner T, Büsing D, Bell N et al. Valproic acid-induced pancreatitis:16 new cases and a review of the literature. J Gastroenterol. 2007;42(1):39-48.

5. Yaman A, Kendirli T, Odek Cet al. Valproic acid-induced acute pancreatitis and multiorgan failure in a child. Pediatr Emerg Care. 2013;29(5):659-61.

6. Hamad AE, Fawzi ME. Valproate associated acute pancreatitis. Neurosciences. 2000;5(3):156-8.

7. Perrott J, Murphy NG, Zed PJ. L-carnitine for acute valproic acid overdose: a systematic review of published cases. Ann Pharmacother. 2010;44(7-8):1287-93.

8. Grauso-EbyNL, Goldfarb O, Feldman-Winter LB, et al. Acute pancreatitis in children from valproic acid: case series and review. Pediatr Neurol. 2003;28(2):145-8.

9. Hasan SS, Bahari MB, Babar ZU, et al. Antiepileptic drug utilisation and seizure outcome among paediatric patients in a Malaysian public hospital. Singapore Med J. 2010;51(1):21-7.

10. Nitsche CJ, Jamieson N, Lerch MM, et al. Drug induced pancreatitis.Best Pract Res Clin Gastroenterol. 2010;24(2):143-55.

11. Yoshikawa H. Letter to editor on:The difficulties of diagnosing VPA-induced pancreatitis in children with severe motor and intellectual disabilities. Eur J Paediatr Neurol. 2004;8(2):109-10.