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Acute Pancreatitis: An Extremely Rare Complication of Etoricoxib

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Abstract: Acute pancreatitis is the acute inflammation of the pancreas. It can be resulted due to many causes. Acute pancreatitis due to non-steroidal anti-inflammatory drugs is not commonly observed in the clinical practice. Etoricoxib is a type of non-steroidal anti-inflammatory drugs which belongs to the group of selective cyclooxygenase two enzyme inhibitors. Etoricoxib induced severe acute pancreatitis is not reported in literature. Here we describe a patient with severe acute pancreatitis caused by etoricoxib. The improvement of symptomatology and the biochemical profile was remarkable after the omission of etoricoxib. This case highlights the importance of considering etoricoxib as a cause of acute pancreatitis which needs further exploration.
Keywords: acute pancreatitis, adverse drug reaction, analgesia, cyclooxygenase two enzyme inhibitor, etoricoxib.

INTRODUCTION

Drug induced acute pancreatitis is rare among the extended list of causes of pancreatitis and it is difficult to diagnose in the absence of any specific investigation. Diagnosis is usually established by excluding more common aetiology [1]. It is usually mild to moderate in severity and resolves with the omission of the causative agent. The prognosis is good in such circumstances. Acute pancreatitis due to non-steroidal anti-inflammatory drugs is rare. The mechanism could be due to pancreatic cell lysis due to the toxicity of the drug or its metabolites.

CASE REPORT

A 73 year female with reasonably controlled diabetes mellitus, on metformin 500mg twice daily had undergone an uncomplicated transpedicular fixation of the fourth and fifth Lumbar Vertebrae under general anaesthesia. She was given etoricoxib 90mg daily as post-operative analgesia from day one after the surgery. She was readmitted two weeks after the surgery with acute onset of tightening type of central chest pain and epigastric pain for 3 days. She did not report vomiting, breathlessness or fever. She had severe anorexia and denied any history of trauma to chest or abdomen. She was a teetotaler. On admission to the emergency unit she was looking ill, tachycardic with a pulse rate of 112bpm, blood pressure 130/79mmHg; her oxygen saturation on ambient air was 99%. Abdomen was tender without signs of peritonitis including guarding or rigidity. Serial electrocardiograms did not reveal any dynamic changes and troponin I titre was within normal limits. 2D Echocardiogram was normal. Initial haematological investigations revealed, white blood cells 16000/microl (4000-10000) with neutrophil 67% (40-80%), C reactive protein 85.6mg/dl (<0.6). Biochemical profile revealed aspartate aminotransferase (AST) 821U/L (15-37), alanine aminotransferase (ALT) 700U/L (16-63), serum amylase 3258U/L(25-115), total bilirubin 42.8micromol/l (0-17.1), direct bilirubin 25.7micromol/l (0-3), alkaline phosphatase 108U/L (46-116), lactate dehydrogenase 428U/l (313-618), imaging including abdominal radiograph and chest radiograph were normal. Contrast enhanced computer tomography scan of abdomen showed evidence of acute pancreatitis. Gastro duodenoscopy findings were also unremarkable.

A clinical diagnosis of acute pancreatitis was made based on the clinical findings and investigations. In the absence of any obvious aetiological factor, patient's medications were reviewed. Etoricoxib was the only newly added medication apart from metformin 500mg twice daily. Etoricoxib was withheld while metformin was continued throughout the hospital stay and after discharge. Three days after the omission of analgesic, improvement of clinical profile was remarkable. Serum amylase level had come down to 1288U/L on third day and after a week she was discharged home with a serum amylase level of 253U/L. AST and ALT levels were also started to decrease in parallel with amylase . AST and ALT were 358U/L and 678U/L respectively on day three and subsequently on discharge 51U/L and 287U/L. When

she was reviewed as an outpatient after couple of weeks, serum amylase level was within the normal limits (87U/L), AST 47U/L (15-37) and ALT 52U/L (16-63). She was doing well and followed up to date.

DISCUSSION

Etoricoxib is a relatively new member to the family of nonsteroidal anti-inflammatory drugs. It has a potent analgesic effect which acts as a selective cyclooxygenase (COX) 2 enzyme inhibitor by blocking the catalysis of the prostaglandin G2 synthesis. COX 2 enzymes is associated with inflammation in contrast to COX 1 enzyme which functions as a protector of the gastric mucosa.

Etoricoxib is used extensively in modern practice as an analgesic in particular to relief postoperative pain. It also provides a significant pain relief in rheumatoid arthritis, osteoarthritis and gouty arthritis [1]. Oedema, fluid retention, hypertension have been frequently observed in patients taking etoricoxib[2]. Light headedness, headache, palpitation, arrhythmia, and bronchospasms are some of the common adverse effects. Dermatological adverse reactions of the drug include pruritus, rash or urticaria. Fixed drug eruptions, Stevens Johnson Syndrome, toxic epidermal necrolysis were rarely witnessed in literature. Etoricoxib induced thrombocytopenia also has been reported, however the association between etoricoxib and thrombotic tendency is yet to be proven. Acute pancreatitis is an extremely rare adverse effect of etoricoxib. Etoricoxib induced acute pancreatitis is not found in medical literature to date from this part of the world.

Drug induced acute pancreatitis is less than 2% of all causes of pancreatitis and it is difficult to diagnose in the absence of any specific investigation [3]. The diagnosis of drug induced pancreatitis is established mainly by excluding more common causes. Class 1 drugs such as azathioprine, angiotensin converting enzyme inhibitors, frusemide, valproic acid, antiretroviral drugs are well known culprits of acute pancreatitis. But there are many other drugs can be associated in aetiology. Drug induced acute pancreatitis is usually mild to moderate in severity and responds well when the offending agent is withheld. Although the underlying mechanism is unclear in etoricoxib induced acute pancreatitis, it may be due to lysis of the pancreatic cells caused by toxic metabolites of the drug or even by the direct toxicitiy.

CONCLUSION

In this particular clinical scenario, patient had a dramatic improvement in both clinical and biochemical profiles, after the discontinuation of etoricoxib with supportive management of acute pancreatitis would strongly support the diagnosis. This is a case of a possible etoricoxib induced acute pancreatitis with a score of eight according to the Naranjo adverse drug reaction (ADR) probability scale [4]. Naranjo ADR probability scale is a globally accepted scoring system which has been recommended to use when reporting an adverse drug reaction. Furthermore rapid decline of serum amylase level is more in favour of drug induced acute pancreatitis rather than other causes. Half-life of serum amylase is 12 hours. It starts to eliminate from the body after 24 hours. Once the offending drug is discontinued, pancreatic cell irritation disappears soon and amylase levels would normalize abruptly. Etoricoxib which was the causative drug in this case, was not rechallenged because of the possibility of life threatening sequelae of acute pancreatitis.

Hepatotoxicity due to etoricoxib is not frequently described among the reported cases caused by non-steroidal anti-inflammatory drugs according to the limited data [5]. It is known to cause raised AST and ALT. But significant hepatic dysfunction is extremely rare in practice. Elevated transaminases more than 15 folds upper limit of normal as in this case can be attributed to hepatic toxicity caused by etoricoxib, which is further supported by gradual decline of transaminase levels following the withdrawal of the medication. Possible association between etoricoxib induced hepatic involvement and pancreatitits to be established by further observational studies.

REFERENCES

1. Brooks, P., & Kubler, P. (2006). Etoricoxib for arthritis and pain management. *Therapeutics and clinical risk management*, *2*(1), 45.
2. Kaurich, T. (2008, January). Drug-induced acute pancreatitis. In *Baylor University Medical Center Proceedings* (Vol. 21, No. 1, pp. 77-81). Taylor & Francis.
3. Badalov, N., Baradarian, R., Iswara, K., Li, J., Steinberg, W., & Tenner, S. (2007). Drug-induced acute pancreatitis: an evidence-based review. *Clinical gastroenterology and hepatology*, *5*(6), 648-661.
4. Naranjo, C. A., Busto, U., Sellers, E. M., Sandor, P., Ruiz, I., Roberts, E. A., & Greenblatt, D. J. (1981). A method for estimating the probability of adverse drug reactions. *Clinical Pharmacology & Therapeutics*, *30*(2), 239-245.
5. Nikose, S., Arora, M., Singh, P. K., Naik, S., Khan, S., & Nikose, D. (2015). Hepatotoxicity and Changes in Liver Enzymes Due to Use of Non-Steroidal Anti Inflammatory Drugs (NSAIDs) in Non-Traumatic Musculoskeletal Painful Disorders. *Molecular Enzymology and Drug Targets*, *1*(2).