Case Report

# A Rare Case Report on Nilotinib Induced Acute Pancreatitis in CML Patient

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**ABSTRACT**

Nilotinib is a novel, potent and selective Bcr Abl kinase inhibitor which is used to treat certain types of CML. Chronic Myeloid Leukemia is a progressive and often fatal haematopoetic neoplasm. Nilotinib works by slowing or stopping the growth of cancer cells. We present the case report of an elderly men who developed life-threatening acute pancreatitis as an adverse event after having started the drug Nilotinib (Tasigna) 150 mg BD. The purpose of this case report is to educate pharmacists and physicians who prescribe this medication to be aware of potential life-threatening adverse events. Since no other treatment options are available and he was also resistant to imatinib, the patient was continued with Nilotinib along with management of pancreatitis.

**Keywords:** Nilotinib, acute pancreatitis, chronic myeloid leukemia, ADR.

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## INTRODUCTION

Nilotinib is an aminophenylpyrimidine-derived tyrosine kinase inhibitor (TKI) with a selective effect against Abl tyrosine kinase, and it now constitutes one of the key drugs of molecular targeting therapy for Bcr-Abl-positive leukemia. It is a drug that has been utilized by oncologists since 2007[1]. CML is a type of myeloproliferative disorder, thus belonging to a group of disorders that affect the myeloid cell lineage and include polycythemia vera, essential thrombocythemia, and primary myelofibrosis.

These are typically caused by an acquired genetic defect of the myeloid stem cells. CML is usually diagnosed incidentally through a complete blood count obtained for other reasons or through recognition of constitutional symptoms like fever, chills, and weight loss combined with splenomegaly. Traditionally, tyrosine kinase inhibitors have been associated with pancreatitis, yet incidence of acute pancreatitis has been reported to be less than one percent. Pancreatitis is inflammation of the pancreas. Pancreatitis can occur as acute pancreatitis — meaning it appears suddenly and lasts for days. Mild cases of pancreatitis improve with treatment, but severe cases can cause life-threatening complications[2]. Here we present a case on Nilotinib induced acute pancreatitis in a CML patient.

## CASE REPORT

A 85 year old geriatric Patient came to hospital complaining of fever fatigue, loss of appetite and anorexia. He had a medical history of CML and was on Imatinib. He was admitted in the hospital for further evaluation. On admission his lab investigations were done and showed severe electrolyte imbalance. A Reverse transcriptase PCR (RTPCR) sequencing analysis was done to detect mutations in the kinase domain of the BCR-ABL fusion gene and showed Imatinib resistance. As per oncologist advice he was started on Nilotinib 150mg BD. Two days after initiation of therapy patient developed severe upper abdominal pain, loose stools, vomiting etc. On evaluation he had tenderness to palpitation in the epigastric region without guarding or rebound tenderness. Pancreatic lipase wase tested to rule out pancreatitis and levels were found to be increased.

A review of current medications with potential to cause acute pancreatitis was performed**.** The possible drugs implicated was nilotinib since he developed abdominal pain after administration of nilotinib**.** A Naranjo causality assessment was done which showed a probable cause of nilotinib induced acute pancreatits[4]. A re-challenge and de challenge could not be performed since the drug cannot be stopped. So, the treatment for pancreatitis was given along with nilotinib. Tab pancreolipase was added, antiemetic agent ondansetron as well as anti-diarrheal agent racecadrotril was given to the patient. The patient condition improved symptomatically.

On clinical examination patient was found to be conscious, oriented heart rate was 88b/m, respiratory rate 24/min, BP 118/70mmHg. Oxygen saturation of 92% on room air was found. Lab investigations were as follows.

| Parameter | Observed value |
|---|---|
| Sodium | 124mEq/l |
| Potassium | 2.69mEq/l |
| Calcium | 6.6mg/dl |
| Magnesium | 1.2mg/dl |
| Crp | 140 |
| Pancreatic lipase | 175u/l |
| Amylase | 158u/l |

## DISCUSSION

Nilotinib was first approved by the FDA in October 2007. It is usually reserved for patients that are imatinib resistant. Patients receiving imatinib have been reported to have an up to 90% hematologic response. However, this patient was previously treated with imatinib and reported severe electrolytic disturbances like hypokalemia, hypomagnesemia, hypocalcemia, hypophosphatemia and hyponatremia. Later he was found to have point mutation in *BCR-ABL* gene who do not respond to imatinib. Nilotinib has been shown to respond to 32 of the 33 point mutations in the*BCR-ABL*gene[3.]The patient was started on nilotinib and after 3days he was presented with acute abdominal pain, vomiting and loose stools and was found to have acute pancreatitis from nilotinib. All tyrosine kinase inhibitors are known to cause elevation in serum lipase. Although the exact mechanism for pancreatitis is unclear there are a few proposed hypotheses regarding the increase in serum pancreatic lipase levels.

## CONCLUSION

More patients on nilotinib might potentially experience pancreatitis. As newer agents are being utilized more frequently, it is vital for clinicians to monitor patients closely after starting new drugs. This is especially true about medications that have the potential to cause life threatening adverse reactions. The case study indicates the importance of monitoring ADR and creating awareness among health professionals.

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