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Case Report

Capecitabine associated acute pancreatitis: A case report

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ABSTRACT

Capecitabine, an oral pro-drug of Fluorouracil, has been used in treatment of many malignancies, including colorectal. Many adverse events have been associated with capecitabine including, hand foot syndrome, mucositis, diarrhea and nausea, but association of pancreatitis with capecitabine has been reported rarely. We report here, a case of capecitabine induced pancreatitis.

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1. Introduction

Capecitabine,[1] is an oral prodrug of 5 fluorouracil, commonly used in the treatment of various malignancies, including colorectal cancers, breast cancer, pancreatic cancer, hepato-biliary malignancy, among others. It is usually combined with other drugs as a part of multi-drug regimen but can also be used as a single agent therapeutic cytotoxic drug. Many adverse effects are associated with capecitabine like, diarrhea, palmer-planter erythrodysesthesia, mucositis, nausea and vomiting. Here, we report a case of capecitabine induced acute pancreatitis.

2. Case Report

A 70 years old male, without any other comorbidities presented with irregular bowel movements and persistent anemia. On evaluation, he was diagnosed with moderately differentiated adenocarcinoma of ascending colon with multiple lung metastasis. Mutational analysis for RAS, BRAF and Her 2 neu was done and diagnosed as wild type. In view of advanced disease (stage IV) and his performance status (ECOG PS 2), he was started on palliative chemotherapy with single agent capecitabine,[2] in a dose of 1250 mg/m2 twice a day for 14 days (total dose 2500 mg/m2 daily), followed by 7 days rest period. Cetuximab/ Panitumumab were not added for financial constraints. Patient tolerated the first cycle well without any major issues. During the second cycle, on day 9 patient presented to the emergency with abdominal pain, nausea and vomiting. He was admitted and evaluated for possible causes including infections. His laboratory parameters were normal except serum amylase and lipase levels, which were high (amylase 806 U/L and Lipase 1750 U/L). A provisional diagnosis of acute pancreatitis was made. Abdominal ultrasound was done, which did not show any abnormality in pancreas or any evidence of cholelithiasis. For confirmation, CT scan of the abdomen was performed as well, which also did not reveal any pancreatic abnormality or gall stones. Patient did not give any history of any other not prescribes drug consumption, or alcohol intake. Blood parameters for calcium and triglycerides were checked, which were normal. No evidence of any infection was found. A possible diagnosis of capecitabine associated acute pancreatitis was made, treated with intravenous hydration and bowel rest along with pain management with morphine. During the hospital stay of 6 days, on 5^{th} day, his amylase levels

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came down to 313 U/L and Lipase levels 617 U/L with symptomatic relief (Table 1). He did not have complaints of abdominal pain or vomiting and was started on oral diet along with hydration. A follow up abdominal ultrasound was performed which still did not show any pancreatic abnormality. Patient was discharged and followed up over the next two weeks.

After 2 weeks, laboratory levels of amylase and lipase were normalized and patient was asymptomatic for pancreatitis, restarted with 3^{rd} cycle of capecitabine with reduced dose 1000 mg/m2 twice a day for 14 days, followed by 7 days' rest. Patient again presented with similar symptoms of abdominal pain, nausea and vomiting on day 5 of the cycle. On evaluation again, amylase and lipase levels were found to be raised with normal abdominal ultrasound for pancreas. He was treated with intravenous hydration and bowel rest along with pain management with symptoms resolving on day 6 and lab parameters returning to normalcy by day 14. All other probable causes of pancreatitis were ruled out the second time as well including cholelithiasis, infections, hypertriglyceridemia, hypercalcemia, and alcoholism. After this second episode, capecitabine was stopped and patient was shifted to other regimen for treatment.

Table 1: Change in biochemical parameters during the pancreatitis episode

Date	S. Amylase (U/L)	S. Lipase (U/L)
First episode		
2/1/23	806	1750
6/1/23	313	617
Second episode		
30/1/23	510	1330
4/2/23	207	405
Normal Range S. Amylase : 30 – 110 U/L Normal Range S. Lipase : 23 – 300 U/L		

3. Discussion

At first presentation, a possible relation between capecitabine and pancreatitis was made, considering his signs, symptoms and laboratory findings. This relation became clearer after the second episode on rechallenge. Since the capecitabine has been stopped, no further episode of pancreatitis was reported in the next 5 months, after which the patient expired.

Capecitabine has been known to cause hyperbilirubinemia in approximately 25% of the patients but the exact mechanism is unknown. Any relation between the hyperbilirubinemia and pancreatitis has also not been documented. There are several other chemotherapeutic agents which has been associated with pancreatitis including asparaginase, ifosfamide, cytarabine, paclitaxel, vinorelbine and others.[3–6] However, as per our knowledge, capecitabine induced pancreatitis has been reported rarely before. One patient was 47 years old women with metastatic breast cancer who developed pancreatitis only once but not with rechallenge,[7] and another in 40 years old women in colorectal cancer, where rechallenge again induced the episode.[8] Another case reported patient developing hypertriglyceridemia induced acute pancreatitis with possible contributory effect of capecitabine.[9]

4. Conclusion

We advise to evaluate the patient prior who are to be started on capecitabine and have with possible risk factors for pancreatitis and closely monitored during therapy. Rechallenge with capecitabine should be avoided after an event of pancreatitis and other treatment options to be considered.

5. Abbreviations

1. RAS – Rat Sarcoma gene
2. BRAF – v-Raf murine sarcoma viral oncogene homolog B1
3. Her2neu – Human Epidermal Growth factor receptor 2
4. ECOG PS – Eastern cooperative oncology group Performance status
5. CT scan – Computed tomography scan

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7. Conflict of Interest Statement

The author declares no conflict of interest in preparing this article.

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