INTRODUCTION
Cardiotoxicity is a recognized chemotherapy induced adverse event. Cardiac events associated with chemotherapy vary from mild transient blood pressure and/or electrocardiographic (ECG) changes to more serious arrhythmias, myocarditis, pericarditis, myocardial infarction and cardiomyopathy, which may end in left ventricular dysfunction or congestive heart failure.

Various chemotherapy agents are known to be cardiotoxic. The drugs that predominantly cause irreversible cell destruction due to their cumulative effects, have been designated as type I agents (Table 1), and those without cell destruction as a dominant characteristic are classified as type II agents. Type II agents do not exhibit toxicity that is related to cumulative dose, and their effects are reversible.

Though cardiotoxicity due to 5-FU is known, it is not very common. Experience of this toxicity is not reported much in this part of world. The purpose of this case report is to make clinicians familiar about this rare toxicity and to discuss about the ways to try and prevent it.

CASE REPORT
55 years old male patient presented with history of pain abdomen for 1 year duration. He was evaluated and USG abdomen revealed gall bladder stone. He underwent laparoscopic cholecystectomy however his pain persisted. He was again evaluated and contrast enhanced CT scan of abdomen was done. CT scan revealed mass lesion in the caecum. Patient was evaluated in detail, including cardiac evaluation before surgery. Clinical examination and ECG were normal. However echocardiography was not done. He was taken up for surgery and right hemicolectomy was done. Final biopsy was Ca Colon-Adenocarcinoma, TNM-pT4bN2bM0., AJCC stage IIIc, Duke stage 3.

In view of advanced stage, he was planned for adjuvant chemotherapy with FOLFOX-4 regimen (Table 2). He received 1st cycle of chemotherapy without any complications. After 2 days of chemotherapy, patient complained of vague discomfort along with multiple episodes of vomiting. He was managed conservatively with oral medication and recovered well. Second cycle of chemotherapy was started after 14 days according to schedule. Day 1 of chemotherapy, which included oxaliplatin followed by rapid infusion of Leucovorin & 5-FU, followed by 22 hours of 5-FU infusion, was uneventful. However on day 2, 1 hour after starting planned for 22 hours infusion of 5-FU, patient complained of dull aching persisting pain over left shoulder. Injection Tramadol was given IV and infusion was stopped. However pain persisted and he complained of vague discomfort over left precordium also. ECG was done which showed ST-T changes consistent with acute myocardial injury (Figure 1). Cardiac enzymes (CK-NAC and CK-MB) as well as Troponin I were negative. Cardiologist consultation was sought. Echocardiography was done which revealed global hypokinesia, mild MR, absent a wave in mitral inflow, LV systolic dysfunction...
Patient was admitted in ICU and managed conservatively. Serial cardiac enzymes were normal. Follow up ECG showed gradual normalization (Figure 2-5). Patient was kept on regular follow up. ECG (Figure 6) and ECHO done after 6 weeks were normal. He is now on 3 weekly CAPOX regimen (Capecitabine + Oxaliplatin). He has completed 2 cycles and is on continued followup.

**DISCUSSION AND REVIEW OF LITERATURE**

As early as 1967, there were reports of heart failure in children treated with doxorubicin\(^4\). Since then the cytostatic antibiotics of the anthracycline class remain the most common cardiotoxic chemotherapeutic agents.

5-FU is administered widely for varied types of malignancies like gastrointestinal, breast, and head & neck cancer. Common adverse clinical reactions such as myelosuppression, diarrhea, and mucositis have been shown to be related to the modalities of 5-FU administration like dose, schedule, or route\(^5\). For instance, in similar doses of 5-FU given by continuous intravenous infusion instead of bolus injection, the continuous intravenous infusion provoked less hematotoxicity but caused more mucositis and palmo-plantar dysesthesia\(^6\).

Although the clinical features of 5-FU cardiotoxicity are recognized widely now, the underlying physiopathology of this syndrome has not been demonstrated clearly. Various hypotheses have been proposed, which include ischemia secondary to coronary artery spasm, a direct toxicity on the myocardium, 5-FU interactions with the coagulation system, and an immune-allergic phenomena\(^12\). The study done by de Forni suggested that 5-FU cardiotoxicity closely resembles the stunned myocardium syndrome and might be related to a diffuse ischemia or a direct toxicity\(^8\).

**CONCLUSION**

Prophylaxis against 5-FU cardiotoxicity starts with identifying patients with underlying coronary artery disease and avoiding regimens that contain continuous 5-FU infusion in this group. Using IV bolus administration rather than continuous administration may be advisable but benefit of continuous 5-FU infusion cannot be over emphasized.

**REFERENCES**


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* Does not include all potential cardiotoxic chemotherapeutic agents.

**Table 1: Cardiotoxic chemotherapeutic agents**

<table>
<thead>
<tr>
<th>Type I agents</th>
<th>Type II agents</th>
</tr>
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<tbody>
<tr>
<td>Doxorubicin</td>
<td>Transtuzumab</td>
</tr>
<tr>
<td>Daunorubicin</td>
<td>Sunitinib</td>
</tr>
<tr>
<td>Epirubicin</td>
<td>Lapatinib</td>
</tr>
<tr>
<td>Idarubicin</td>
<td></td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td></td>
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<tr>
<td>Cyclophosphamide</td>
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</tbody>
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**Table 2: FOLFOX-4 Regimen**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Days</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxaliplatin</td>
<td>85 mg / m(^2)</td>
<td>D 1</td>
<td>Over 2 hrs</td>
</tr>
<tr>
<td>Leucovorin</td>
<td>200 mg / m(^2)</td>
<td>D 1 + D 2</td>
<td>Over 30 mins</td>
</tr>
<tr>
<td>5-FU</td>
<td>400 mg / m(^2)</td>
<td>D 1 + D 2</td>
<td>Over 30 mins</td>
</tr>
<tr>
<td>5-FU</td>
<td>600 mg / m(^2)</td>
<td>D 1 + D 2</td>
<td>22 hrs infusion</td>
</tr>
</tbody>
</table>
Figure 1: At the time of onset

Figure 2: After 15 minutes

Figure 3: After 1 hour 30 mins

Figure 4: After 10 hrs

Figure 5: After 15 hours

Figure 6: After 6 weeks


6. Lokich JJ, Ahlgren JD, Gullo JJ. A prospective randomized comparison of continuous infusion fluorouracil with a conventional bolus schedule in metastatic colorectal carcinoma: A Mid-Atlantic Oncology Program study. J ClinOn-


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