***Case report***

SINUSOIDAL OBSTRUCTION SYNDROME FOLLOWING CAPEOX IN COLORECTAL CANCER: A DIAGNOSTIC CHALLENGE

**ABSTRACT**

**Background:** Oxaliplatin, especially when used in combination with capecitabine (CapeOX), is associated with hepatotoxicity, including hepatic sinusoidal injury. Sinusoidal Obstruction Syndrome (SOS) is a rare but potentially serious adverse effect that can complicate chemotherapy regimens for colorectal cancer.

**Case Summary:** We report the case of a 54-year-old woman who developed hepatic dysfunction with jaundice, ascites, and coagulopathy following two cycles of CapeOX as adjuvant chemotherapy for rectal adenocarcinoma. Extensive workup ruled out viral, autoimmune, and other common etiologies. Transjugular liver biopsy revealed hallmark histopathological features of SOS, including sinusoidal congestion, perisinusoidal fibrosis, and perivenular hepatocyte dropout. Causality assessments using RUCAM (score: 8) and the Naranjo scale (score: 6) indicated a probable chemotherapy-induced liver injury. Prompt discontinuation of the CapeOX regimen and initiation of supportive therapy resulted in clinical and biochemical improvement within one week.

**Conclusion:** This case underscores the need for vigilance regarding hepatic complications in patients undergoing CapeOX chemotherapy. SOS should be considered in patients presenting with unexplained liver enzyme abnormalities, jaundice, or ascites. Early recognition and discontinuation of the offending agents are critical for reversing liver injury and improving outcomes.

**Keywords:** Sinusoidal Obstruction Syndrome, CapeOX, Oxaliplatin, Capecitabine, Drug-induced liver injury, Colorectal cancer, Transjugular liver biopsy

**INTRODUCTION**

Colorectal cancer continues to be a major global health concern due to its high incidence and mortality rates [2]. In cases of locally advanced rectal cancer, preoperative treatment strategies are primarily aimed at improving local tumor control, reducing tumor size, and increasing the chance of a complete pathological response [5]. Commonly used regimens such as FOLFOX, CAPOX, and FOLFOXIRI—comprising oxaliplatin in combination with other agents—are standard in treating metastatic colorectal cancer. These regimens are frequently administered before procedures like conversion hepatectomy. However, prolonged use of oxaliplatin-based therapies may lead to unintended liver toxicity, particularly affecting healthy liver tissue [11]. One of the key mechanisms of this hepatotoxicity involves damage to sinusoidal endothelial cells, resulting in the breakdown of the sinusoidal lining, dilation of sinusoids, development of perisinusoidal fibrosis, and eventual blockage of hepatic venules, culminating in a condition known as sinusoidal obstruction syndrome (SOS) [10].

**CASE DESCRIPTION**

A 54-year-old female with a known diagnosis of locally advanced rectal adenocarcinoma (pT3N2b) presented to the gastroenterology department with complaints of abdominal distension, intermittent fever, decreased appetite, and yellowish discoloration of the eyes and urine for the past two weeks.She had previously undergone chemoradiation therapy comprising 25 fractions to the rectal lesion from November to December 2024 and had completed two cycles of chemotherapy with the CAPEOX regimen (Capecitabine and Oxaliplatin) prior to presentation. Her past medical history was significant for bronchial asthma, spinal tuberculosis 16 years ago, and a hysterectomy performed two years ago.

On admission, the patient was conscious, oriented, afebrile, and hemodynamically stable. However, physical examination revealed pallor, icterus, hepatomegaly, and ascites. There were no signs of hepatic encephalopathy or systemic infection.

Laboratory findings revealed markedly elevated serum transaminases and total bilirubin levels. Coagulation studies showed a prolonged prothrombin time and an increased INR, indicating impaired hepatic synthetic function (Table 1). Hematological investigations revealed anemia with a hemoglobin level of 7.4 g/dL, a total leukocyte count of 9,410/mm³, an ESR of 31 mm/hr, and thrombocytopenia with a platelet count of 65,000/mm³. Renal function tests and serum electrolytes were within normal limits. Additional laboratory testing for IgM dengue, ANA, ASMA, and IgG were negative. Viral hepatitis was ruled out based on negative serologies for hepatitis A, B, C, and E, as well as for Epstein-Barr virus, CMV, and herpes simplex virus. Common infectious and autoimmune causes of jaundice were excluded.

A diagnostic paracentesis was performed, revealing a high serum-ascites albumin gradient (SAAG) and low-protein ascitic fluid, with no features suggestive of spontaneous bacterial peritonitis (SBP). Ultrasound of the abdomen showed grade 2 fatty liver and mild ascites. MRI of the abdomen revealed diffuse heterogeneous liver enhancement, hepatomegaly, ascites, and pleural effusion. Portal vein Doppler showed absence of colour flow in the main portal vein. FibroScan findings were consistent with F0–F1 fibrosis and sluggish portal venous flow. In light of these findings and the clinical suspicion of drug-induced liver injury, the CAPEOX regimen was discontinued as it was considered the likely cause of acute hepatic insult.

A RUCAM score of 8 was calculated, suggesting a probable drug-induced liver injury. Additionally, the Naranjo Adverse Drug Reaction Probability Scale yielded a score of 6, further indicating a probable adverse drug reaction due to chemotherapy. A transjugular liver biopsy was performed, which revealed hepatocellular and canalicular cholestasis with rosette formation, sinusoidal congestion with perisinusoidal fibrosis, and perivenular hepatocyte dropout—possibility of chemotherapy induced sinusoidal obstruction syndrome may be considered.

Supportive management was initiated, which included IV antibiotic, injectable vitamin K for three days, oral ursodeoxycholic acid (Ursocol) twice daily, and IV N-acetylcysteine (NAC) 600 mg twice daily. The patient also received cirrhosis-specific therapy with Cirrosam 400 mg twice daily, diuretics including torsemide (Dytor) 10 mg once daily and spironolactone (Aldactone) 25 mg once daily, hepatoprotective agents (Heptagon twice daily), and syrup lactulose (Looz) 20 mL at bedtime for bowel regulation.

She received a total of one unit of packed red blood cells (PRBC), eight units of platelets, eight units of fresh frozen plasma (FFP), and 100 mL of 20% human albumin on alternate days during admission. Urine output remained adequate throughout the hospitalization. After one week of inpatient care, her liver function tests showed a trend toward improvement, and the patient became symptomatically better. She was subsequently discharged with advice to follow up in the gastroenterology department after two weeks. Further chemotherapy was advised only after consultation with her oncologist.

**Table.1**-Lab investigations on admission and after 1 week

|  |  |  |
| --- | --- | --- |
| Lab investigation | On admission | After 1 week |
| ALT | 651 U/L | 124 U/L |
| AST | 1335 U/L | 97 U/L |
| SAP | 128 U/L | 149 U/L |
| TOT BILIRUBIN | 7.7 mg/dl | 7.3 mg/dl |
| DIR BILIRUBIN | 5.6 mg/dl | 5.4 mg/dl |
| S.ALBUMIN | 3.1 mg/dl | 3.4 |
| S.GLOBULIN | 2.8 gm/dl | 3.6 gm/dl |
| INR | 2.49 | 1.34 |
| PT | 32.4 | 18.1 |
| Hb | 7.4g/dl | 9.8 |
| Total Count | 9410/mm3 | 3470 |
| ESR | 31mm/hr |  |
| CRP | 124 |  |
| GGT | 60 |  |

**DISCUSSION**

Sinusoidal obstruction syndrome (SOS), previously termed veno-occlusive disease, is a form of hepatic injury caused by toxic insult to sinusoidal endothelial cells. Oxaliplatin is a well-recognized culprit, particularly when combined with fluoropyrimidines such as 5-FU or capecitabine, as seen in regimens like FOLFOX and CapeOX. In this case, we report a 54-year-old woman who developed acute liver injury after two cycles of adjuvant CapeOX chemotherapy for rectal adenocarcinoma. The diagnosis of SOS was confirmed via transjugular liver biopsy, which demonstrated hallmark histopathological features including sinusoidal congestion, perisinusoidal fibrosis, and perivenular hepatocyte dropout.

Multiple studies have documented capecitabine-associated hepatotoxicity, though SOS remains a rare manifestation. Habib et al. and Jiang et al. have both reported reversible but severe liver injury due to capecitabine, underscoring the importance of monitoring liver function even in oral fluoropyrimidine-based regimens [1, 2]. While oxaliplatin is more strongly associated with sinusoidal injury, synergistic toxicity from its combination with capecitabine may amplify endothelial damage, as evidenced by this case and supported by Kim et al., who demonstrated a higher incidence of SOS in gastric cancer patients treated with CapeOX compared to S-1/oxaliplatin.[8]

Our patient’s clinical course aligns with observations from Toda et al. and Kai et al., who elucidated the pathogenesis of oxaliplatin-induced SOS, noting the critical role of endothelial disruption, impaired sinusoidal flow, and hepatocellular injury [9, 10]. The absence of alternative causes, elevated RUCAM and Naranjo scores, and prompt improvement upon drug withdrawal support a diagnosis of chemotherapy-induced SOS. Notably, imaging findings of hepatomegaly and portal flow abnormalities, though non-specific, further corroborate the diagnosis.The reversal of liver function abnormalities within one week of discontinuation and supportive care suggests that early recognition and withdrawal of the offending agents can lead to favorable outcomes.

**CONCLUSION**

This case highlights an uncommon but significant complication of adjuvant CapeOX chemotherapy—sinusoidal obstruction syndrome. Given the increasing use of this regimen in colorectal and other gastrointestinal malignancies, clinicians should maintain a high index of suspicion for SOS in patients presenting with jaundice, hepatomegaly, and ascites during or after chemotherapy. Liver biopsy remains the gold standard for diagnosis, while causality assessment tools like RUCAM and Naranjo scores aid in identifying drug-induced liver injury. Early diagnosis, prompt discontinuation of the offending agents, and supportive therapy are essential to reversing hepatic injury and preventing long-term complications

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