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**TITLE:** Tumor lysis syndrome in metastatic colon cancer after single FOLFOX cycle

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**Short Running Title:** Tumor lysis syndrome in metastatic colon cancer after single FOLFOX cycle.

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ABSTRACT

Introduction
Tumor lysis syndrome (TLS) is a life threatening oncological complication, often described in patients with a large tumor burden, more commonly among hematological malignancies.

Case Report
We present a case report of a 55-year-old male who presented to the emergency department with worsening abdominal pain, oliguria, nausea, vomiting and diarrhea of 1-day duration. One-month prior, the patient was diagnosed with metastatic colon cancer. He was started on FOLFOX regimen the day prior. Patient was found to be in acute kidney injury with hyperkalemia, hyperuricemia and hyperphosphatemia. Patient was admitted with a diagnosis of TLS (Cairo-Bishop grade II) and managed with aggressive intravenous hydration, furosemide and single dose of rasburicase. In two days, symptoms resolved with improvement in laboratory parameters and patient was discharged after 4 days.

Conclusion
There have been so far six published cases, reporting TLS in metastatic colon adenocarcinoma. Our case is the only one demonstrating that TLS can occur in metastatic colon cancer patient after a single cycle of FOLFOX therapy even in the absence of any pretreatment. Our patient had all known risk factors for developing TLS like large tumor burden, liver metastases, elevated pretreatment LDH, use of combination chemotherapy drugs and dehydration. Unlike previously reported 6 cases where TLS resulted in death, our patient survived. Therefore, a clinician should maintain high index of suspicion for TLS among metastatic colon cancer patients and should do prompt intervention to prevent potentially life threatening complications like cardiac arrhythmias, acute renal failure, seizures, or death.
Keywords: Tumor lysis syndrome, metastatic colon cancer, FOLFOX
INTRODUCTION
Tumor Lysis Syndrome is a life threatening oncologic emergency characterized by hyperuricemia, hyperkalemia, hyperphosphatemia and secondary hypocalcemia leading to complications like cardiac arrhythmias, acute renal failure, seizures, or death. It is the end result of high cell turnover, commonly seen among hematological malignancies with high proliferative rate or those with high sensitivity to treatment [1]. It is rarely observed in patients with solid tumors as a result of therapy or even spontaneously [2]. There have been so far six published cases reporting TLS in metastatic colon adenocarcinoma, four after FOLFIRI (5-flourouracil, Leucovorin, and Irinotecan) or Irinotecan chemotherapy, one after Cetuximab therapy and one after FOLFOX (5-Flourouracil, Leucovorin and Oxaliplatin) therapy in a patient who had received pretreatment with FOLFIRI [3-8]. We report a case of TLS after first dose of FOLFOX chemotherapy in a patient with metastatic colon carcinoma, managed successfully with intravenous hydration and Rasburicase.

CASE REPORT
A 55-year old African American man with past medical history of hypertension, emphysema, pneumothorax, prostate cancer status post prostatectomy presented to the emergency department (ED) with epigastric and right upper quadrant stabbing pain, anorexia and weight loss for 2 weeks. On arrival, patient had a blood pressure of 138/82 mm Hg, pulse rate of 85 beats per minute, afibrile at 36.4 C and respiratory rate of 20/min. Physical examination was significant for right upper quadrant tenderness and hepatomegaly. Blood work was significant for acute kidney injury, hyperkalemia, leukocytosis and abnormal liver function tests and negative for HIV, hepatitis B and hepatitis C. Ultrasound abdomen was significant for multiple hypo-densities in liver. Further imaging with CT scan showed multiple hypo-enhancing liver masses, 1.3 cm nodule in right adrenal gland, multiple cysts in kidney and a 2 cm round soft tissue mass in...
posterior caecum with adjacent posterior mesentery and mesenteric lymphadenopathy. Colonoscopy was positive for edematous ileocaecal valve but biopsy was negative for any malignant features. No other mass lesions were identifiable on colonoscopy. The liver biopsy was positive for malignant cells, adenocarcinoma type compatible with colonic primary. Further staining was negative for K-ras mutation and CK7 but positive for CD20. Patient also had an elevated CEA and CA 19-9 but normal AFP. Other labs were significant for CEA-9918.7 mcg/L, CA 19-9- 520 U/ml, AFP-1.9 mcg/L, Uric Acid- 9.7 mg/dL and LDH- 1196 U/L. Patient was given a diagnosis of stage IV colon cancer. Patient improved with supportive treatment and was discharged with oncology follow up. After about 20 days, patient was started on FOLFOX regimen, which consisted of Leucovorin (772 mg IV), 5-Fluorouracil (4632 mg IV) and Oxaliplatin (164 mg IV). Next day, patient presented to the ED with abdominal pain, nausea, vomiting and diarrhea. Patient was found to have acute kidney injury with creatinine of 1.9 mg/dl. In addition, patient was hyperkalemic (6.4 meq/L), hyperuricemic (20.3 mg/dl) and hyperphosphatemic (5.5 mg/dl) with normal calcium level (Table 1). There was no seizure activity or cardiac arrhythmia on telemetry monitor (Cairo-Bishop grade II TLS). Patient was admitted to the Step down unit with a diagnosis of Tumor Lysis Syndrome and managed with aggressive intravenous hydration, furosemide and single dose of rasburicase (6 mg). In two days’ symptoms resolved with improvement in potassium (4.6 meq/L) and uric acid (5.6 mg/dl) creatinine (1.4 mg/dl) (Table 1). Patient was transferred to the general oncology floor and was discharged four days later with oncology follow up.

**DISCUSSION**

There have been reports of about 100 cases of TLS in patients with solid tumors [9]. Irrespective of the cancer type, there is a 20-50% increase in mortality for undiagnosed or late-diagnosed cases of TLS in solid tumors [9]. The fatality rate for these 100 reported cases was 41% [10]. TLS is characterized by constellation of electrolyte abnormalities. Cellular material rich in potassium, phosphorous and uric acid is released as a consequence to
cellular death, either mediated by cancer therapy or spontaneously in rapidly dividing
tumors. This leads to hyperkalemia, hyperuricaemia and hyperphosphatemia. Due to
binding of calcium with phosphorous, hypocalcemia is observed. This in turn may
lead to acute impairment of renal function, cardiac arrhythmogenicity, central
Large tumor burden, liver metastases, elevated pretreatment LDH, use of
combination chemotherapy drugs and dehydration are major risk factors, which
place a patient at higher risk of developing TLS [2]. And hence a watchful monitoring
is essential to prevent, diagnose and manage the metabolic complications
associated with TLS.
There have been so far six published cases, reporting TLS in metastatic colon
adenocarcinoma. Four of these were after FOLFIRI (5-flourouracil, Leucovorin, and
Irinotecan) or Irinotecan chemotherapy, one after cetuximab therapy and one after
FOLFOX therapy in the setting of pretreatment with FOLFIRI therapy. Our case is
the first of its type to demonstrate that TLS can occur in a metastatic colon cancer
patient after a single cycle of FOLFOX therapy even in the absence of any
pretreatment. Our patient had all known risk factors for developing TLS like large
tumor burden, liver metastases, elevated pretreatment LDH, use of combination
chemotherapy drugs and dehydration. Unlike previously reported 6 cases where TLS
resulted in death, our patient survived. Therefore, a clinician should maintain high
index of suspicion for TLS among metastatic colon cancer patients and should do
prompt intervention to prevent potentially life threatening complications like cardiac
arrhythmias, acute renal failure, seizures, or death.

CONCLUSION
Tumor Lysis Syndrome has been rarely described in metastatic colon cancer. This is
the first case describing TLS in a patient with metastatic colon cancer after single
cycle of FOLFOX chemotherapy. Henceforth, it is important to maintain high
suspicion for TLS while treating metastatic colon cancer with chemotherapy like
FOLFOX to prevent potentially life threatening complications like cardiac arrhythmia,
acute renal failure, seizure or death.
CONFLICT OF INTEREST

None of the authors has any conflicts of interest or financial relationship with the company that produces or distributes the drugs described in the case report.

AUTHOR’S CONTRIBUTIONS

Akanksha Agrawal, M.D.
Group 1-Contributed to conception and design, analysis and interpretation of data
Group 2-Drafting the article, revising it critically for important intellectual content
Group 3-Final approval of the version to be published

Deepanshu Jain, M. D.
Group 1-Contributed to conception and design, analysis and interpretation of data
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Group 3-Final approval of the version to be published

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Group 1-Contributed to conception and design, analysis and interpretation of data
Group 2-Drafting the article, revising it critically for important intellectual content
Group 3-Final approval of the version to be published

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REFERENCES


Table 1: Comparison of Laboratory Parameters at Initial Visit, after single FOFOX cycle and after TLS treatment

<table>
<thead>
<tr>
<th>Laboratory Parameters</th>
<th>Initial Visit (Before FOLFOX chemotherapy)</th>
<th>Second Visit After FOLFOX chemotherapy</th>
<th>After Rasburicase and intravenous hydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bilirubin (mg/dL)</td>
<td>2.3</td>
<td>10.1</td>
<td>6.0</td>
</tr>
<tr>
<td>Direct Bilirubin (mg/dL)</td>
<td>1.7</td>
<td>7.7</td>
<td>4.8</td>
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<tr>
<td>Alkaline Phosphatase (U/L)</td>
<td>646</td>
<td>732</td>
<td>415</td>
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<tr>
<td>AST (U/L)</td>
<td>205</td>
<td>344</td>
<td>136</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>119</td>
<td>95</td>
<td>56</td>
</tr>
<tr>
<td>Uric Acid (mg/dL)</td>
<td>9.7</td>
<td>20.3</td>
<td>5.6</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>5.1</td>
<td>6.4</td>
<td>4.6</td>
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<tr>
<td>Blood Urea Nitrogen (mg/dL)</td>
<td>36</td>
<td>61</td>
<td>30</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.3</td>
<td>1.9</td>
<td>1.4</td>
</tr>
</tbody>
</table>