HYDROXYUREA AND TUMOR LYSIS SYNDROME – A RARE BUT CRITICAL COMPLICATION IN CML

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Introduction

- Tumor lysis syndrome (TLS) is an oncologic emergency characterized by the rapid release of intracellular contents, leading to electrolyte disturbances and acute renal failure.
- While TLS is more common in acute leukemias and aggressive lymphomas, it is rare in chronic myeloid leukemia (CML), especially when managed with hydroxyurea.
- We present a case of TLS following hydroxyurea use in a patient with CML.

Case Presentation

- A 75-year-old female with heart failure with preserved ejection fraction and CML in chronic phase was treated with bosutinib but discontinued therapy due to hepatotoxicity. Hydroxyurea was then initiated at 1,000 mg twice daily for cytoreduction prior to the onset of TLS
- She reported a feeling of malaise and shortness of breath.
- Vitals showed BP of 137/78 mmHg, HR 107 bpm, RR 22 c/pm, SpO2 99% on 2L of O2 and T 97.5 F.
- On exam, she was lethargic and in mild respiratory distress. Air entry was markedly reduced bilaterally with diffuse crackles.
- Laboratory tests revealed uric acid of 21 mg/dL, potassium 5.1 mmol/L, phosphorus 6.2 mg/dL, and low-normal calcium, consistent with TLS. Her white blood cell count had dropped from 165,000 to 17,000 and her serum creatinine rose from 2.3 to 2.8 mg/dL .

Table 1: Progression of patient's lab results

Lab variables	At hydroxyurea initiation (one week prior to presentation)	Day 1 of admission	Day 3 of admission	On discharge (day 6)	Reference range
WBC	165,000	17,000	6,500	6,000	6-11 x 10*3uL
Uric acid	N/A	21	8.1	3.3	2.6-8.0 mg/dl
Creatinine	2.3	2.8	2.7	2.5	0.4-1.0 mg/dl
Potassium	3.5	5.1	4.0	4.6	3.3-5.1 mmol/L
Phosphorus	2.6	6.2	5.6	4.6	2.6-4.5 mg/dl
Calcium	9.8	8.4	8.8	8.7	8.4-10.2 mg/dl

Hospital Course

- Given her lab results (Table 1), she was managed for TLS in the setting of recent hydroxyurea use. Hydroxyurea was promptly discontinued, and IV fluids were cautiously administered due to underlying heart failure. She received a single dose of rasburicase for severe hyperuricemia and febuxostat for maintenance.
- Electrolytes were closely monitored and gradually normalized. Renal function stabilized without the need for dialysis, and her cardiac status remained compensated with careful fluid balance.

Discussion and Conclusion

- TLS is rare in CML, particularly in the chronic phase and with hydroxyurea therapy given that it induces cell death particularly in the S-phase of the cell cycle. Most reported cases of TLS in CML occur during initiation of tyrosine kinase inhibitors or in accelerated/blast phases, where tumor burden is higher. In our patient, TLS developed after a rapid leukoreduction with hydroxyurea, highlighting that even "low-risk" agents can precipitate TLS in the right clinical context.
- Our patient met Cairo–Bishop criteria with hyperuricemia, hyperphosphatemia, hyperkalemia, low-normal calcium and renal dysfunction occurring within seven days.
- TLS should be considered in patients with CML and hyperleukocytosis undergoing cytoreductive therapy. TLS prophylaxis, including allopurinol or rasburicase and careful fluid management, is essential in preventing complications, particularly in patients with comorbidities.

References