24 HOURS OF ACUTE PROMYELOCYTIC LEUKEMIA

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INTRODUCTION:

Once an almost universally fatal diagnosis, Acute Promyelocytic Leukemia (APL) now has a cure rate of 80-90%. This is largely due to the introduction of all-trans retinoic acid (ATRA). Unfortunately, early death from hemorrhagic complications are seen in 10-25% of newly diagnosed patients, especially in those presenting with leukocytosis greater than 10,000/mL. Risk for disseminated intravascular coagulation (DIC), leukostasis, and differentiation syndrome complicate the treatment algorithm for these patients. This case highlights the difficult clinical considerations for supportive and therapeutic care in a young patient with hyperleukocytosis at presentation.

CASE SUMMARY:

13:00 — 18 year old pregnant female presented to the emergency department with acute vaginal bleeding and abdominal pain. Initial workup was consistent with a completed first trimester abortion. On exam, she was ill-appearing, tachycardic, and had a petechial chest rash. Labs and sample pathology pictures are listed in Table 1.

Table 1: Pertinent Admission Labs

<table>
<thead>
<tr>
<th>Complete Blood Count</th>
<th>Peripheral Blood Smear</th>
<th>DIC Labs</th>
<th>Tumor Lysis Labs</th>
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</thead>
<tbody>
<tr>
<td>WBC: 260,000 /μl</td>
<td>- Marked Leukocytosis</td>
<td>- INR: 1.95</td>
<td>- Uric Acid: 5.8 mg/dL</td>
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<tr>
<td>- Atypical Cells: 8.2%</td>
<td>- Anemia</td>
<td>- D-dimer: &gt;4.0 mg/L</td>
<td>- Potassium: 2.6 mmol/L</td>
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<tr>
<td>- Hemoglobin: 8.1 g/dL</td>
<td>- Thrombocytopenia</td>
<td>- Phosphorous: 1.5 mg/dL</td>
<td>- Calcium: 8.9 mg/dL</td>
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<tr>
<td>- Hematocrit: 24.5%</td>
<td>- 90% blasts</td>
<td>- Corrected Calcium: 8.9 mg/dL</td>
<td>- Creatinine: 0.03 mg/dL</td>
</tr>
<tr>
<td>- Platelets: 38 K/μl</td>
<td>- hypergranular promyelocytes</td>
<td>- Fibrinogen: 2.6 mg/dL</td>
<td>- DHE: 1277 K/μl</td>
</tr>
</tbody>
</table>

18:00 — Fluorescent In-Situ Hybridization (FISH) analysis identified t(15;17):PML/RARA, confirming APL. Leukapheresis and cytotoxic chemotherapy were deferred to worsening DIC. ATRA was immediately started for induction, along with prophylactic dexamethasone for differentiation.

03:00 — She developed altered mental status with worsening respiratory status requiring emergent intubation.

04:00 — CT head: multiple intracranial hemorrhages, severe brainstem herniation with associated brainstem infarct (Figure 3). Exam with dilated, fixed pupils. Given extent of hemorrhage, completed infarct and coagulopathy, no surgical intervention could be performed.

06:00 — Discussion with multiple care teams concluded these findings were incompatible with life.

12:00 — Family withdrew care. Patient was terminally extubated.

DISCUSSION:

Early ATRA administration is essential for improving survival outcomes in all patients with APL. ATRA differentiates myeloid blasts into mature cells, thereby lowering the cancer burden and risk for coagulopathic hemorrhage (Figure 4). Unfortunately, these newly matured cells also acquire the ability to infiltrate into and damage tissue, a consequence known as differentiation syndrome. This is seen in approximately 25% of patients undergoing induction therapy, especially in patients with leukocytosis.

Another complication following induction therapy is hyperleukocytosis that may result in leukostasis. This occurs in 50% of patients receiving ATRA.

Initial cytoreduction and early glucocorticoid treatment can minimize the extent of differentiation syndrome and hyperleukocytosis. However, aggressive cytoreduction with cell lytic therapy or leukapheresis also increases the risk for severe DIC.

Treatment decisions require careful consideration of these potential complications. Even so, risk for mortality during the first 24 hours of APL remains high.

CONCLUSIONS:

— APL is a medical emergency. Early mortality from hemorrhagic complications occur in 10-25% of patients.
— Early ATRA administration is essential for improving survival outcomes, however, it is not without complications.
— Aggressive cytoreduction with leukapheresis is contraindicated in APL.

REFERENCES:

