ONCOLOGIC EMERGENCIES

LEUKOSTASIS

(Last updated: 01/16/2020; Reviewer: Bibek Karki, M.B.B.S)

PRESENTING COMPLAINTS: Fever, Shortness of breath, headache, tinnitus

FINDINGS

- **A** Check airway
- **B** ↑ RR, increased work of breathing
- **C** ↑ HR
- **D** Dizziness, variable altered (V,P,U,D), focal deficits
- **E** Fever
- **Lpc** ↓PaO_2 (maybe falsely lower), ↓SpO_2, ↑WBC count, ↑blast cells (may be mistaken as ↑platelets), ↑lactate
- **U_{PC}** B-lines

***V** (verbal), **P (**pain), **U** (unconsciousness), **D** (delirious)

U_{PC} (point of care ultrasound) **L_{PC}** (point of care labs)

DEFINITION

Hyperleukocytosis is asymptomatic ↑ in total WBC > 50,000/microL. Leukostasis is symptomatic hyperleukocytosis (a medical emergency) usually with WBC count >100,000/microL with respiratory or neurological symptoms due to tissue hypoxia.

PATHOPHYSIOLOGY:

The mechanism of leukostasis formation remains unclear. There are two acceptable theories:

- The interaction of "overcrowded" leukemic blast cells and vascular endothelium causes release of cytokines and specific adhesion molecules. This results in accumulation of large and less deformable blast cells causing blood hyperviscosity and formation of plugs of blast cells in the microcirculation leading to leukostasis.
- Blast cells are immature and constantly dividing cells, leading to the increased metabolic activity. Such increased metabolic activity cause local hypoxemia, resulting in the production of various cytokines. Those cytokines cause endothelial damage and subsequent hemorrhage, which precipitates further hypoxic injury and attract more leukemic cells.
- This affects all organs. But, central nervous system and the lungs are the most sensitive to those changes.

OTHER HISTORY

Most commonly seen in patients with acute myeloid leukemia (AML) or chronic myeloid leukemia (CML)

Predisposing conditions: Blood transfusion, dehydration, diuretics

Signs and Symptoms: Chest pain, distress; CNS symptoms: Blurry vision, confusion, imbalance (gait instability), somnolence, coma; other less common symptoms: Priapism, acute limb ischemia, bowel infarction

DIFFERENTIAL DIAGNOSIS

Acute and chronic leukemia of myeloid and lymphoid type

OTHER INVESTIGATIONS

- **Monitor**: Vital signs, urine output, Electrolytes, Uric acid, Tele monitoring if there is significant electrolyte abnormalities.
- **Labs:** ↑WBC, Pseudo hyperkalemia, pseudo thrombocytosis, Tumor lysis syndrome (↑K^+, ↑PO_4^{3-}, ↑Uric acid , ↓ Ca, ↓ HCO_3^-), DIC (↓ fibrinogen , ↑fibrin degradation products,↑ D-dimer, ↓ platelets, ↑ PT, ↑ PTT, ↑LDH with schistocytes on peripheral blood smear)
- **Biopsy of the involved tissue:** White cell plugs in the microvasculature (Pathological diagnosis, but a risky procedure to obtain biopsy from the affected tissues)

THERAPEUTIC INTERVENTIONS

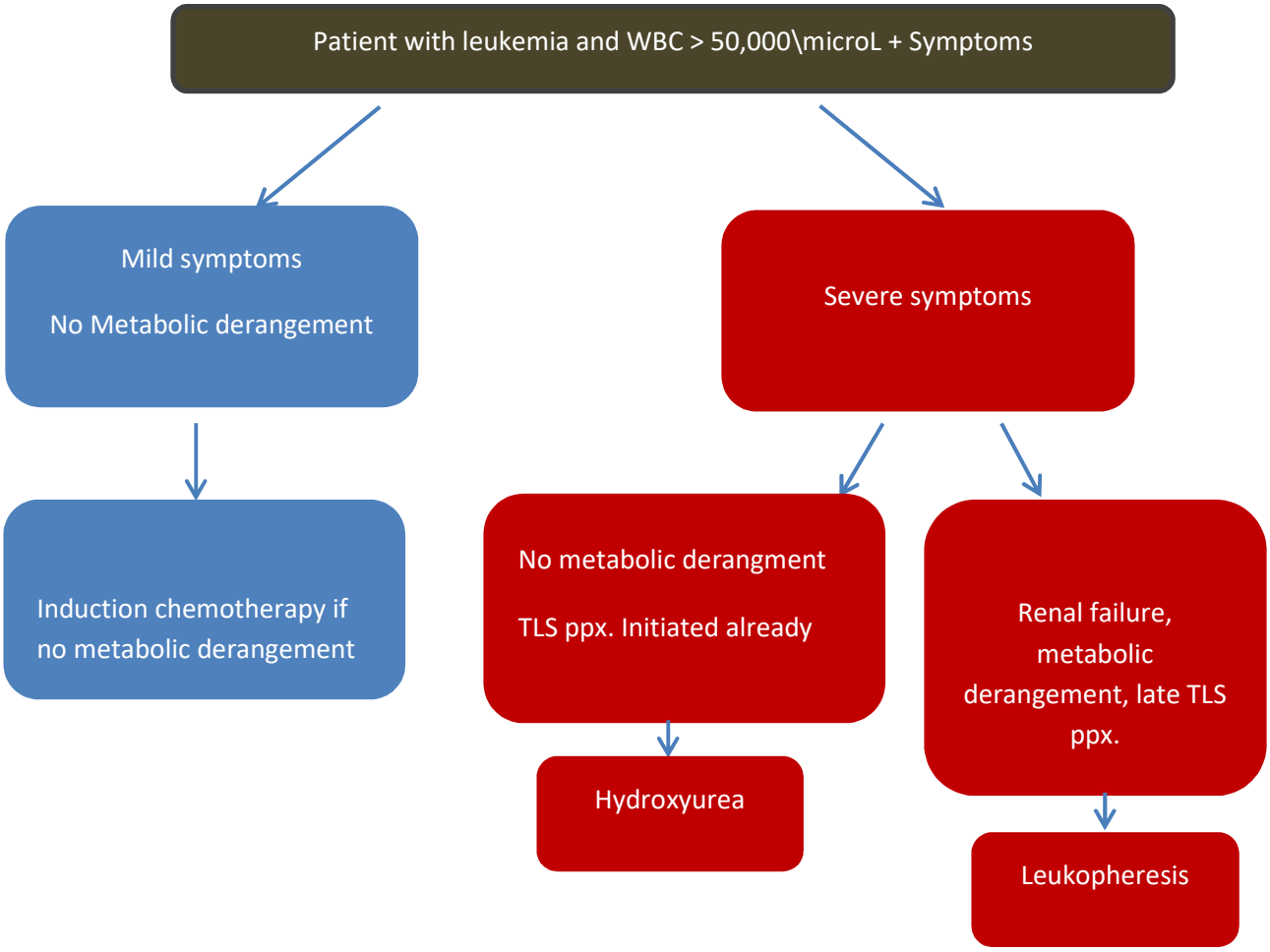
- For patients with symptomatic or asymptomatic hyperleukocytosis: Induction chemotherapy (to achieve rapid cytoreduction)
- For patients with asymptomatic hyperleukocytosis (whom induction chemotherapy needs to be delayed): Initial hydroxyurea is an alternative cytoreductive therapy of choice.
- For patients with symptomatic hyperleukocytosis (whom induction chemotherapy needs to be delayed): Initial leukopheresis with hydroxyurea is an alternative cytoreductive therapy of choice.
- Leukopheresis: Indicated for rapid control of symptoms in severely symptomatic patients and/or those with renal insufficiency and significant metabolic derangement.
- Supportive care: Fluid hydration, RBC transfusion: Hold until the blast count is reduced, but transfusion can be given slowly if it is required, Platelet transfusions and coagulation factors: Indicated for those with coagulation abnormalities.
- Co-infection/sepsis is common, start empiric antimicrobial therapy and deescalate according to culture sensitivities

ONGOING TREATMENT

Prophylaxis:

- Serial electrolyte testing and cardiac monitoring if tumor lysis is suspected.

- Initiation of tumor lysis prophylaxis: - Allopurinol and rasburicase (indicated before starting cytodestructive therapy), adequate hydration



CAUTIONS

- Acute promyelocytic leukemia: Leukopheresis can worsen coagulation profile in patients with acute promyelocytic leukemia.
- Pregnancy: Hydroxyurea should not be used in pregnant patients.
- Risk of developing tumor lysis syndrome: - Risk of tumor lysis syndrome increases substantially with delivery of chemotherapy or hydroxyurea.

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SUPERIOR VENACAVA (SVC) OBSTRUCTION

(Last updated: 01/16/2020; Reviewer: Bibek Karki, M.B.B.S)

PRESENTING COMPLAINTS: Swelling of the face and upper extremities, SOB, chest pain

FINDINGS

- **A** Check airway
- **B** ↑/N RR, stridor
- **C** N BP
- **D** Variable altered (V,P,U,D)*
- **E** Swelling over the extremities, cyanosis, facial plethora
- **Lpc** PT, aPTT
- **U_{PC}** Venous congestion and thrombus in the subclavian, axillary, and brachiocephalic veins

***V** (verbal), **P** (pain), **U** (unconsciousness), **D** (delirious)

U_{PC} (point of care ultrasound) **L_{PC}** (point of care labs)

DEFINITION

Superior venacava (SVC) syndrome is a constellation of signs and symptoms due to partial or complete obstruction of blood flow through the SVC.

PATHOPHYSIOLOGY

Obstruction occurs either by a thrombus inside the SVC or more commonly compression or direct invasion from outside. The obstruction leads to increase venous pressure proximal to the vessel and edema in areas drained by the SVC. There is an initial transient decrease in cardiac output due reduced venous return from the upper body; however, this is usually dampened by development of collateral flow. Thus, persistent drop in cardiac output is likely related to direct compression of the heart by the mass causing the SVC obstruction.

OTHER HISTORY

Signs and Symptoms: Distended neck veins, difficulty swallowing, hoarseness, cough, facial swelling or fullness often exacerbated by leaning forward; If cerebral edema is present: headache, confusion, coma

ETIOLOGY AND DIFFERENTIAL DIAGNOSIS

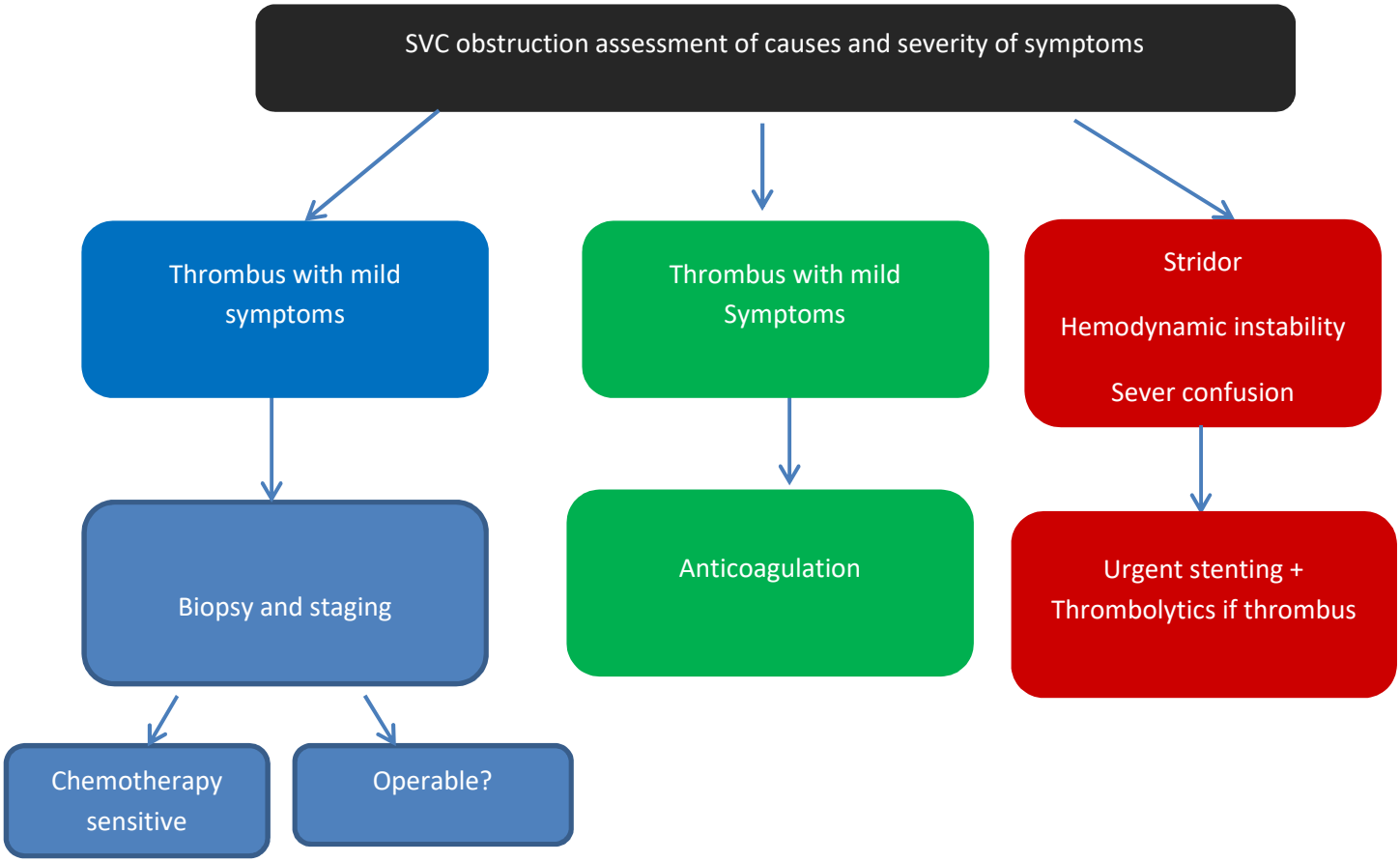
Lung cancer (high incidence in SCLC), Non-Hodgkin's lymphoma, thymoma, primary mediastinal germ cell tumors, thrombosis, fibrosing mediastinitis, radiation induced fibrosis

OTHER INVESTIGATIONS

- Labs: Tumor markers (eg, HCG, AFP for patients with germ cell tumors), ↓Hb, ↓WBC, ↓Platelets, ↑ Ca, ↑Uric acid ↑ serum LDH
- Coagulation study: Prothrombin time (PT), activated partial thromboplastin time (aPTT)
- Imaging:
  - Chest x-ray can show the underlying cause and widened mediastinum.
  - CT scan with contrast: more sensitive and specific than chest x-ray.
  - Duplex ultrasonography of upper extremity indirectly shows findings suggestive of SVC obstruction.
  - MRI venography in patients allergic to contrast.
  - Superior vena cavogram (Gold standard)

THERAPEUTIC INTERVENTIONS

- Depends on the underlying symptoms, etiology, extent of disease and prognosis.
- Emergent therapy is required in patients who presents with respiratory failure due to airway obstruction, laryngeal edema and cerebral edema. This usually involves stenting of the vessel.
- Immediate radiation therapy used to be the modality of choice because SVC obstruction was dealt with as a medical emergency. However, the obstruction most of the time develops over weeks; moreover, the radiation will negatively impact any biopsy results and affect diagnosis. For this reason, it is not recommended as an emergent therapy.
- Endovenous stenting has replaced radiation therapy for the most part in patient who are severely symptomatic and require immediate treatment.
- Anticoagulation is indicated in patients who have a thrombus as the etiology of the obstruction.
- Thrombolytic therapy is used in certain occasions but comes with a high risk of bleeding.
- Chemotherapy is the treatment of choice in symptomatic patients with small cell lung cancer, Non-Hopkins lymphoma and thymoma.
- Steroids can be used to reduce swelling and to treat steroid responsive malignancies like lymphoma and thymoma.



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TUMOUR LYSIS SYNDROME (TLS)

(Last updated 01/16/2020; Reviewer: Bibek Karki, M.B.B.S.)

PRESENTING COMPLAINTS: Fatigue, Nausea, vomiting, muscle cramps, seizure

FINDINGS

- **A** Check airway
- **B** ↑/N RR, stridor
- **C** ↓/N BP
- **D** Chest pain, distress
- **E** Cyanosis, swelling over the extremities
- **Lpc** ↑K^+, ↓ Ca, ↑ PO_4^{3-}, ↑ Uric acid
- **U_{PC}** Not pertinent

***V** (verbal), **P (**pain), **U** (unconsciousness), **D** (delirious)

U_{PC} (point of care ultrasound) **L_{PC}** (point of care labs)

DEFINITION

Cairo-Bishop definition:

- Laboratory TLS:
  ≥2 abnormal serum values (K^+ ≥6 mEq/L, Ca ≤7 mg/dL, PO_4^{3-} ≥6.5 mg/dL for children or ≥4.5 mg/dL for adults, Uric acid ≥8 mg/dL or increase in 25% from baseline value) within 3 days before or 7 days after chemotherapy in a setting of adequate hydration (± alkalization) and a hypouricemic agent(s)
- Clinical TLS: Laboratory TLS + one of the following features: Serum Creatinine: ≥ 1.5 x upper limit of normal (not attributable to the rise in Cr after drugs administration like, Amphotericin), cardiac arrhythmia/sudden death, seizure

OTHER HISTORY

Diarrhea, anorexia, arrhythmia, heart failure, tetany, hematuria

Predisposing Conditions: Hematologic malignancies and solid tumors (high rates of proliferation) and/or following initiation of chemotherapy, renal insufficiency, dehydration or use of nephrotoxic drugs: Increases the risk of development of tumor lysis syndrome

DIFFERENTIAL DIAGNOSIS

Rhabdomyolysis (hyperphosphatemia and hyperkalemia). However, etiology and underlying disease can differentiate it from tumor lysis syndrome.

OTHER INVESTIGATIONS

- **Monitor:** Urine output, electrolytes, uric acid, tele monitoring if electrolyte abnormalities
- **Labs:** Elevated serum potassium, uric acid, phosphorus and low calcium.

The Cairo-Bishop scoring system can be used to define the exact level of abnormalities needed for diagnosis and also grade the severity of disease which aids in guiding therapy.

THERAPEUTIC INTERVENTIONS

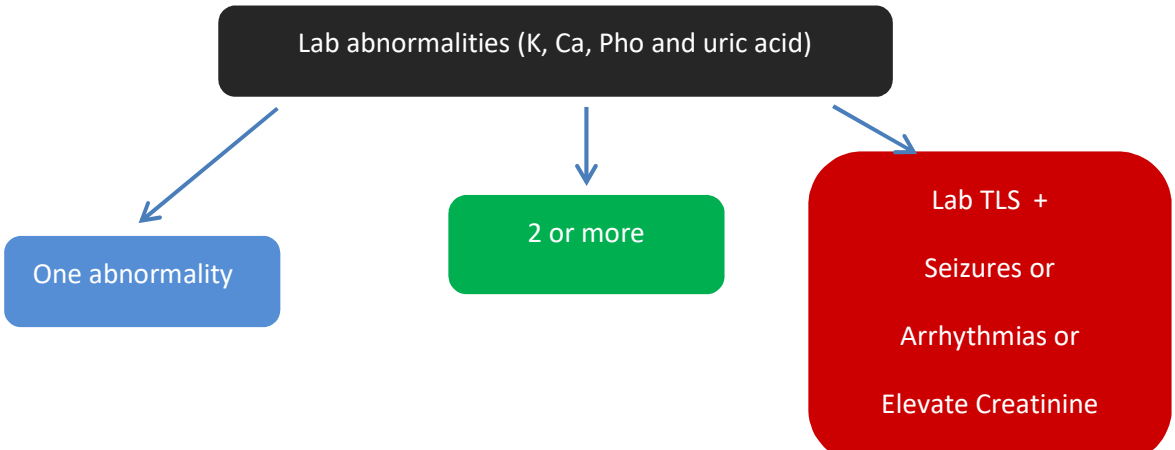
- Cardiac monitoring preferably in the ICU
- Serial electrolytes check every 4-6 hours.
- Fluid hydration, diuretics to flush the uric acid from kidney tubules.
- Repeated doses of rasburicase as necessary.
- Potassium and phosphate lowering therapy.
- Replacement of calcium if the patient is symptomatic from hypocalcemia (ex. Tetany).
- Nephrology consultation and renal replacement therapy if there is anuria, persistent hyperkalemia and/or fluid overload.

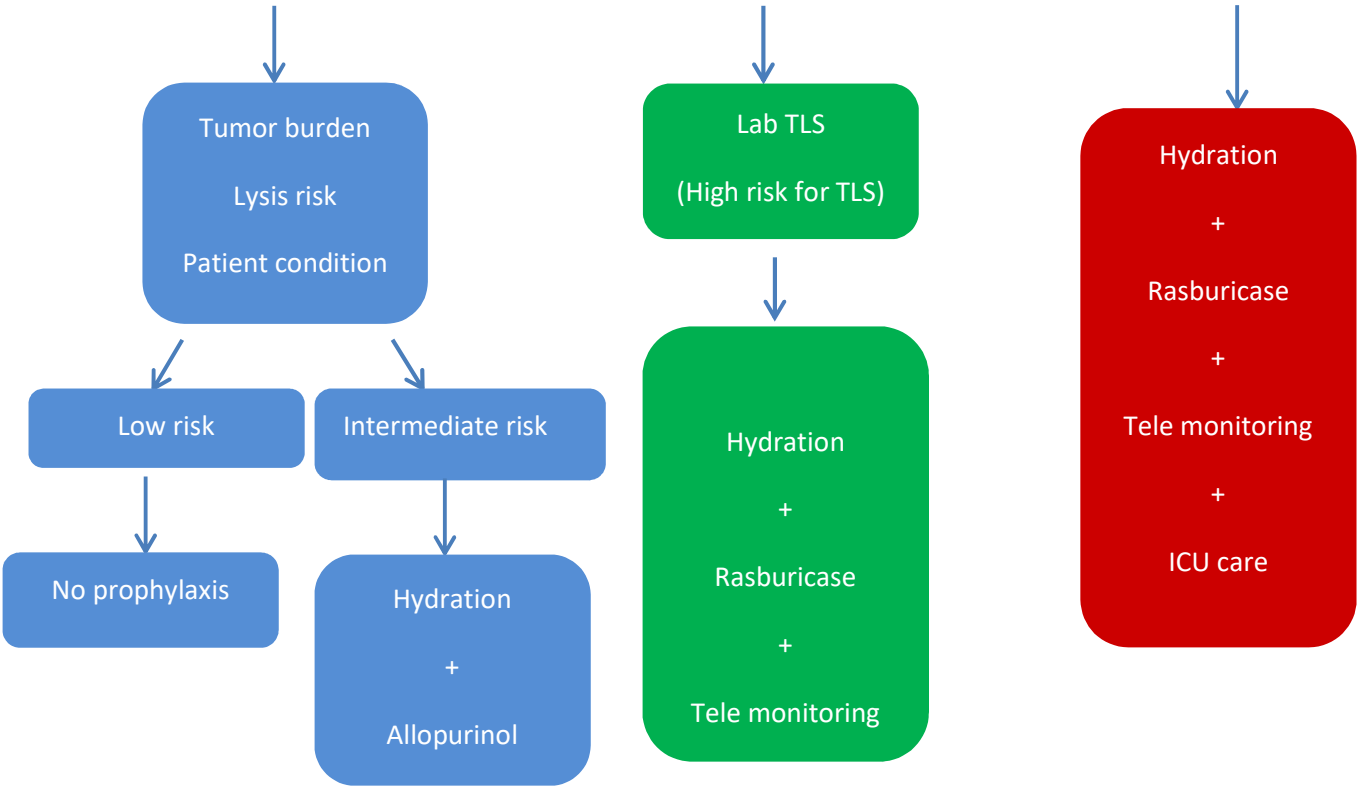
ONGOING TREATMENT

- Hydration
- Uricosuric agents: In asymptomatic disease; approach depends on the severity of laboratory abnormalities, tumor burden, lysis risk and patient condition (renal dysfunction, dehydration, hypotension, lactic acid level)

CAUTIONS

Rasburicase is contraindicated in patients with glucose 6 phosphate dehydrogenase deficiency and can also cause severe methemoglobulenemia and anaphylaxis.





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