Pediatric oncology Emergency

Learning Objective:

1-To know the most important pediatric oncology emergency

2-How you deal with this condition

3-As this lifethreating condition you should take action immediately

Disease – Related

- Tumor lysis syndrome.
- Anterior mediastinal mass.
- Spinal cord compression.
- Leukocytosis and leukostasis
- Uncal herniation
- Disseminated intravascular coagulation
- Hypercalcemia

Treatment – Related

- Fever and netropenia, sepsis.
- Cerebrovascular accident, stroke .
- Typhlitis.
- Pancreatites.
- Vesicant infiltration.
- Methotrexate toxicity.
- All trans – retinoic acid (ATRA) syndrome

- Veno- occlusive disease.

Tumor lysis syndrome(TLS)

- Severe metabolic abnormalities associated with the onset of therapy particularly in the setting of lymphoma and leukemic can have high morbidity and mortality.
- Occur as a result of spontaneous or treatment related breakdown of tumor cells release of intracellular contents from the tumor cells into the blood stream hyperuricemia hyperkalemia and hyperphosphatemia

Risk factor (TLS)

- Presence of bulky disease.
- Adenopathy, hepatosplenomegaly and high leukocyte count.
- ↑ lactate dehydrogenease, uric acid creatinine, and decreased urine output.
- TLS is highest at 12-72 hr after initiating chemotherapy.
- Symptom can also precede the therapy or occur as long as 7 days later.
- The main principle of TLS prevention and treatment.

Path physiology

- It can occur spontaneously prior to the administration of chemotherapy or follows the initiation of therapy.
- In tumors with a high proliferative rate, large tumor burden and high chemo sensitivity.
- Massive cell lysis, with the release of intracellular anions- cat ions and breakdown produced of nucleic acid and proteins into the bloodstream.

- Hyperuricemia is the most common finding due to release of intracellular nucleic acids and subsequent catablison of the purine nucleotides, adenosine and guanosine .
- Uric acid the final product of both endogenous and dietary purine nucleotide catabolism generate in the liver by oxidation of xanthine to uric acid by xanthine oxidant.
- Hyperkalemia - kidney inability to excrete the massive quantities of intracellular potassium .
- Hyperphosphatemia result from rapid release of intracellular phosphorus from tumor cells nephrocalcinosis - renal failure.
- Normal calcium and phosphorus ranger between 30 and 55 mg^2/dL^2 where this exceeds 70mg $^2/dL^2$ calcium phosphate dispositive in the kidney.

Incidence

- The higher incidence of TLS occur.
- Acute lymphoblastic leukemia (5.2%)
- High grade non –Hodgkin's lymph (6.1%).
- B-cell acute lymphoblastic.
- Acute myeloid leukemia .
- Chronic lymphoblastic leukemia
- Multiple myeloma
- Chronic myeloid leukemia in blast crisis.
- Hodgkin's disease
- Solid tumors that are highly chemo sensitive or that have high tumor burden, bulky metastatic disease or tumors that have present with renal compromise.
- Tumors with higher response to cytotoxic therapy such

Diagnosis

Tow classification systems for TLS have been developed

1- Hande – Garrow Definition of laboratory tumor lysis syndrome (L TLS)

L TLS: 25% increase over pretreatment values in serum phosphate, potassium, uric acid or urea nitrogen.

Or -25% decline in serum calcium.

(Any two of the above metabolic changes must occur within 4 days of treatment).

2- Hande –Garrow definition of clinical tumor lysis syndrome (C TLS).

- Rise in serum creatinine > 2-5mg /dL.

- Serum K level > 6.0mmol /L.

- Decline is serum calcium to < 6mg/dL.

- Development of life threatening arrhythmia or renal insufficient, cardiac arrhythmias, sudden death and seizures.

(TLS is defined as the presence of laboratory tumor lysis syndrome and any one of the above criteria) .

Clinical manifestations and treatment

- Nausea, anorexia.
- Cardiac arrhythmia .
- Seizures .
- Muscle cramps, tetany.
- Oliguria or anuria.
- Alterations in consciousness

Management of patients at risk for TLS

1) Fluids and Alkalinization :-

- Aggressive hydration 3000ml/m2/day (1/2 G.S).
- Urine output should be maintained more than 100ml/m2/hr – urine s.q ≤ 1.010.
- Diuretics may be used (mannitol 0.5g/a) furosemide 0.5-1 mg//g.
- Urine alkalinization (urine PH ≥ 6.5-7.5 / sod. Bica.40 mg/m2.

Hyperkalemia (serum K≥ 6.0mm/L

Neuromuscular sign and symptoms muscle weakness, cramps, and paresthesias.

Cardiac manifestations may include peak T-wares, malignant arrhythmias and conduction disturbances

Hyperuricemia

- Serum uric acid ≥ 8.0mg/ or 25% ↑from baseline 3 day before or 7 day.
- Intraluminal renal tubular ,acute renal dysfunction.
- Management of hyperuricemia are allopurinol and rasburicase.
- Allopurinol oral or iv…. 100mg/m2 every 8hr, 200-400 mg/m2/day.
- Recombinant form of urate oxidase (rasburicase 0.15-0.20mg/kg IV for 5-7 days. ↓ uric acid level by 4 hours after treatment.

Adverse reactions of Rasburicase

- Contraindicated : patients with G6PD (Hemolytic anemia).
- Rash, increased liver enzyme.

- headache, vomiting and nausea.
- Antibody formation to rasburicase
- Patients with asthma and those with a high risk of hypersensitivity should be monitored.

Uremia and Acute Renal failure

- Uric acid crystal obst. uropathy.
- Renal precipitation of calcium phosphate.
- Xanthinuria.
- Nephrotoxic drugs.
- Intravscular volume depletion.

Treatment

- Hemodialysis.
- Continuous hemofiltration

Hyper leukocytosis and leukostasis

Is life threatening pediatric oncologic emergency that requires immediate initiate of appropriate therapy.

Definition

Hyperleukocytosis is generally accepted as a (WBC) count higher than 100x10`/L or higher than 50x10`/L most frequent is:

Infant acute lymphoblastic leukemia.

- T- cell ALL.

- Subtypes of ALL.
- AML&CML.

Leukostasis

Stasis of leukemia cells within blood vessels and migration of blast cells into tissues can lead to the clinical entity of leukostasis

1. Most frequently in AML. (M4-M5) subtypes.
2. Clinical symptoms from leukocytosis occur at (WBC) higher than 200-300 x10`/L ALL.
3. Leukostasis have been observed in patients with WBC 100x10`/L

Clinical symptoms of leukostasis

- Depend on the system affected
- Any small vessels, any organs (pulmonary and neurologic symptoms).

Hyperleukocytosis → leukostasis → renal failure, papilledeme, dactylitis, - priapism and clitorism, acute myocardial infarction and cardiac failure .

- Asymptomatic
- Clinical leukostasis can present subtly and evolve rapidly.
- Pulmonary symptoms: tachypnea, oxygen desaturation, dyspnea and progress rapidly to acute respiratory disease syndrome (ARDS) and Resp. failure.
- Neurologic symptoms: headache, tinnitus, ataxia, behavioral changes, seizures and stroke.
- Hemorrhagic stroke in a highly morbid complication of hyperleukocytosis → Microgranular variant of M3 AML (M3v).

- Symptoms may be caused by release of intracellular components of blast cells after lysis including enzymes > injury in surrounding tissue → aleveolar damage and interstitial .

Treatment

1. Hydration, urinary alkalinization and Allopurinol
2. Urate oxalate decrease the risk for TLS
3. Cranial radiation to decrease the chance of intracerebral hg. (400 to 600 rad)
4. The use of low dose prednisone.
5. Exchange transfusion.
6. Leukapheresis (Pt wt < 12kg unable to undergo leukapheresis) → 50-60% is WBC) (ALL-AML but no APML → ↑ hg)
7. Hydroxyurea.

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